

Composites Science and Technology

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Fiber and Ceramic Filler-Based Polymer Composites for Biomedical Engineering

 Springer

Composites Science and Technology

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Editors

Fiber and Ceramic Filler-Based Polymer Composites for Biomedical Engineering

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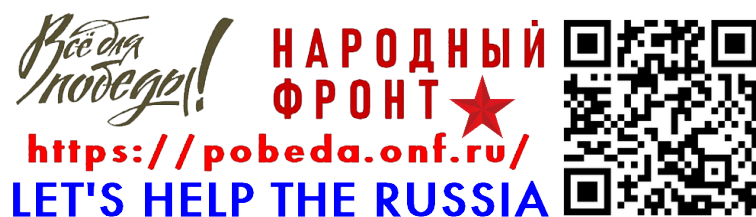
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ISSN 2662-1819

ISSN 2662-1827 (electronic)

Composites Science and Technology

ISBN 978-981-97-3908-0

ISBN 978-981-97-3909-7 (eBook)

<https://doi.org/10.1007/978-981-97-3909-7>

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Preface

Step right into the world of cutting-edge materials science! *Fiber and Ceramic Filler-Based Polymer Composites for Biomedical Engineering* takes readers on an enthralling adventure into the fascinating realm of cutting-edge materials destined to transform biomedical systems.

Because of their exceptional combination of characteristics—including their light weight, flexibility, and adaptability—polymer composites have become major players in many different industries. From tissue engineering to medical device fabrication, these materials have enormous promise in the field of biomedical applications, which aim to solve urgent healthcare problems. Polymer composites based on fibers and ceramic fillers are the subject of this book, which explores their design, production, characterization, and biomedical uses in great detail. We hope that by delving deeply into the physics and engineering behind these cutting-edge materials, readers will have a better grasp of what makes them tick. We start by taking a high-level look at polymer composites, which will set the stage for learning about their makeup, structure, and processing methods. We continue by discussing how the fibers and ceramic fillers contribute to the composites' improved mechanical, thermal, and biological characteristics. We go deep into the pros and cons of several filler types, including carbon fibers and bioactive ceramics. Polymer composites based on fibers and ceramic fillers have great promise in a wide range of biomedical applications, and this book showcases state-of-the-art research and development initiatives to that end. These materials provide novel answers to some of the most critical problems in modern medicine, such as scaffolds for regenerating damaged tissues and implants for mending broken bones.

It is with great pleasure that we, the editors and contributors to this volume, bring you this varied and insightful compilation of work by some of the most eminent minds in the subject. Our sincere desire is that this book will prove to be an invaluable tool for scholars, practitioners, and students in the field of biological materials engineering, encouraging fresh perspectives and partnerships to propel the field ahead.

Our heartfelt appreciation goes out to every author who has shared their wisdom and experience with this project, and to all the readers who believe in the power of science and technology to improve people's lives.

Now we can start exploring!

Bengaluru, India
Ramat Gan, Israel
Hamilton, Canada
Bengaluru, India

Jyotishkumar Parameswaranpillai
Sayan Ganguly
Poushali Das
Jineesh Ayippadath Gopi

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Introduction, History of Fiber and Ceramic Filler-Based Polymer Composites for Biomedical Applications



Partha Sarathi Satapathy, Eswaribeeram, Saurabh Thakur, Rishabh Rana, Anand Kumar, Romita Sharma, Selvan Ravindran, and Sunaina Sharma

Abstract Intriguing polymer composites with fiber and ceramic fillers for use in medicine are explored in this chapter. It begins with a thoughtful introduction before moving on to an exploration of the development of these extraordinary materials throughout history, beginning in the 1960s. This chapter focuses on the earliest efforts to develop bioactive bone substitutes by adding ceramic fillers, particularly hydroxyapatite, into polymers. As a result, these composites have found widespread use in fields as disparate as orthopedic implants and prosthetics since their introduction of carbon fibers in the 1980s. Dental and orthopedic implants, wound dressings, and biodegradable stents are just some of the many cutting-edge medical technologies discussed as the story progresses. The chapter concludes with a look into the future, illuminating trends such as the incorporation of nanotechnology, the development of personalized medicine via 3D printing, the use of bioresorbable electronics, the use of advanced imaging, and the necessity of moving from research to regulatory approvals and commercialization.

Keywords Polymer composites · Fiber · Ceramic · Fillers · Electronics

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1 Introduction

Industrial sectors across the board are tapping into nature's vast biomass, forestry, and agriculture-based wastes as a possible source of materials for renewable energy [1]. Natural fillers raw materials for the polymer composite industry are increasing being sourced from agricultural plants, crops, and pods. In many poor and underdeveloped countries, the agriculture, farming, and isolated or rural areas might all benefit economically from the research, development, and improvement of these bio-based materials. For a very long time now, composites have been widely developed and prepared using natural or lignocellulosic fibers. Natural fibers have been increasingly used as bio-filler/reinforcement materials in composites due to the rise of the notion of ecological safety and the use of renewable materials towards a greener society [2]. Researchers, material scientists, and businesses are all interested in natural fibers because of their distinct advantages over traditional or synthetic fibers [3]. Natural fibers are suitable for use as filler in polymer composites due to their attractive and possible advantages, such as reduced tool wear, low cost, low density per unit volume, and acceptable specific strength, as well as their sustainable renewable and degradable features. It's common knowledge that many different kinds of natural fibers are being used as additives or reinforcements. When compared to composites made from natural fibers, those made from synthetic fibers like carbon fibers and glass fibers pose significant ecological and health hazard difficulties for the employees engaged in their respective manufacturing processes.

Reinforcement fibers of high strength are incorporated into polymeric matrices to form composites known as fiber reinforced polymer (FRP) materials. FRPs are composite materials made from a polymer matrix reinforced with high-strength fibers like glass, aramid, carbon, natural fiber, etc. The FRPCs can be made with or without fillers, and they can be manufactured using either synthetic or natural fibers. When compared to solid polymers, the benefits of synthetic FRPCs stand out. These composites are not only strong and stiff, but also have a long fatigue life and may be tailored to the required application. Corrosion resistance, wear resistance, aesthetics, temperature-dependent behavior, environmental stability, thermal insulation, and conductivity are just few of the areas where synthetic FRPCs can be further enhanced. The use of natural fiber in reinforcing composites has a number of technical and environmental advantages. Natural fibers such as jute, straw, Flax, hemp, wood, sugarcane, bamboo, grass, kenaf, sisal, coir, rice husks, wheat, barley, oats, kapok, mulberry, banana fiber, raphia, pineapple leaf fiber, papyrus, etc. have all been studied for their potential usage in plastics.

Increasing the mechanical and physical properties of polymer composites, nanoparticles are currently seen as a promising filler material [4–13]. Since nanoscale fillers are often defect-free, their use in polymer composite area setup is an exciting new direction with the potential to overcome the limitations of the conventional micrometer scale [13–24]. Changes in relaxation behavior, as well as mechanical, molecular mobility, and thermal characteristics, are attributed to the high matrix-filler interfacial area that comes from uniform and homogenous dispersion of nanoparticles

[25]. Typically, nano-sized filler is found in the minor zone, while only a small fraction of micro-sized particles are involved in the plastic zone's deformation. This allows the brittle matrix to benefit from the nanofillers' ability to strengthen fracture and mechanical characteristics. The creation of nanocomposites benefits greatly from the use of nanofillers with a high aspect ratio (the ratio of the biggest to the smallest dimension) [26]. For nanocomposite creation, nanofillers are typically introduced on a weight basis nano fillers' particular surface area has an intense, continuous effect on composite characteristics.

In most cases, a composite material will have multiple discontinuous phases that are interspersed throughout a continuous one. Hybridization occurs when a composite contains multiple discontinuous stages of various types [27]. The matrix is the continuous phase, whereas the reinforcement is the discontinuous phase. Composites are made by combining different materials with each other that have complementary physical and mechanical qualities [28]. Mechanical and thermal properties can be enhanced by including high-modulus reinforcements with high tensile strength into a polymer matrix [29]. Composites made with a polymer matrix have several advantages over metals, including a lower density that results in lower fuel consumption (in aviation and automobiles), higher speeds (in competitive sports or for missiles), and a greater payload (in transportation) [30]. Organic, mineral, and metallic matrices are used to divide composites into their respective groups. Reinforced plastics (resins and short fibers), laminated tires (rubber, steel, organic resins, glass fibers, carbon, and boron), and cardboard (resins and cellulose fibers) are all examples of organic composites [31]. Concrete (cement, sand, and additives), carbon-carbon composites (carbon and carbon fibers), and ceramic composites (ceramics and ceramic fibers) are all examples of mineral composites [32]. Finally, metallic composites (aluminum/boron fibers and aluminum/carbon fibers) have been used in several industries [33], including packaging, automobiles, light buildings, civil engineering, aviation, sports, biomedicine, thermomechanical components, and aerospace, are impacted by the use of composite materials.

2 Types of Composites

The nature of the matrix, the nature of the reinforcement, and the nature of the matrix-reinforcement interface are the three aspects of the composite that must be specified in order to gain access to the material description. Figure 1 shows the different types of fillers and their composites. Therefore, the composite material is a system comprised of several different elements.

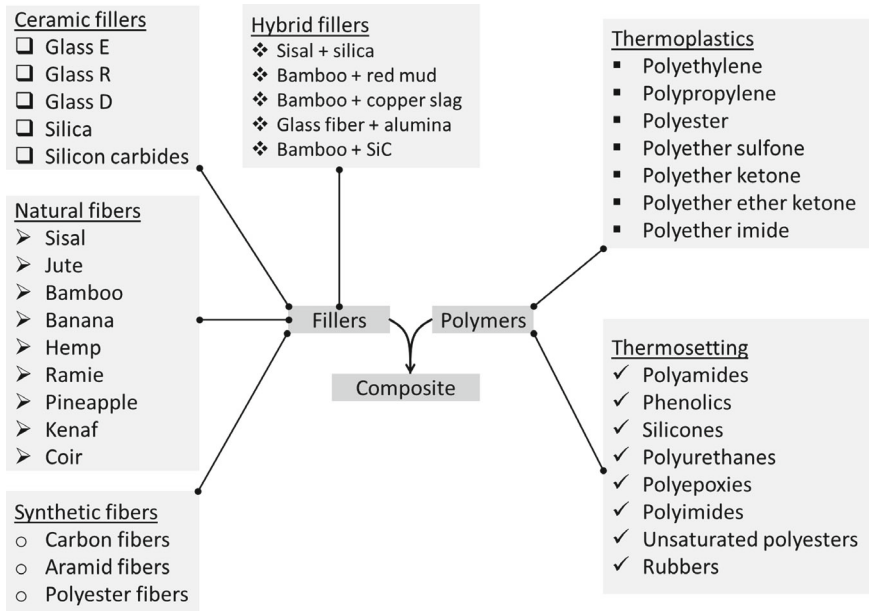


Fig. 1 Different types of fillers and their polymer composites

3 Large Diffusion Composites

LDCs, or large diffusion composites, are typically engineered materials with a high degree of diffusion for a variety of uses. In this sense, diffusion refers to the dispersal of a chemical or particle population throughout a material. These composites are engineered to allow for the quick and easy transport of specific elements or molecules. It's possible that the “large” in “large diffusion composites” refers to the materials’ impressive diffusion capacity or the fact that they were developed specifically for uses that call for a lot of diffusion.

Many different industries can benefit from using large diffusion composites which are summed up here;

- These composites can be used into gas separation membranes as a means of regulating gas flow and excluding unwanted gases. One possible application is in hydrogen purification procedures, where they would be used to isolate hydrogen from impurities.
- Large diffusion composites can improve the overall reaction rate in catalytic processes by facilitating the movement of reactants and products to and from the active catalytic sites.
- Pharmaceutical companies can use these substances as drug delivery systems to regulate the body’s uptake and elimination of medicinal medicines.

- **Energy Storage:** Large diffusion composites can be utilized to boost the performance and durability of energy storage devices by facilitating the transport of ions (such as lithium ions in lithium-ion batteries).
- In sensors and detectors, where the quick diffusion of target molecules is essential for precise and fast measurements, these composites can also be used.

Large diffusion composites can range in design and performance depending on the materials employed and the task at hand. In addition to other desirable properties like mechanical strength, stability, and selectivity, they are designed to maximize the diffusion of targeted chemicals.

4 High Performance Composites

High-performance composites are a category of man-made materials that are designed to outperform more common substances like metals, plastics, and ceramics in terms of mechanical, thermal, chemical, and/or electrical qualities. These composites are often made by mixing two or more constituent elements to attain specific desired qualities, and they are meant to provide greater performance in a variety of demanding applications. High-performance composites share a number of defining qualities and characteristics. High-performance composites are lauded for their superior strength and stiffness despite their light weight. They have the potential to offer high load bearing capacities while still being relatively lightweight.

Wear, corrosion, and fatigue are no match for the resilience of many composites. This ensures their dependability throughout time, making them ideal for uses like aircraft components. Many high-performance composites can resist both high and low temperatures without suffering a substantial loss of mechanical characteristics. Because of this, they can be implemented in the aviation, automotive, and manufacturing sectors. While most materials would corrode or disintegrate in a chemical environment, many composites are built specifically to withstand such exposure. High-performance composites can be used in electronics, heat exchangers, and other areas due to their high electrical and thermal conductivity, depending on their exact composition.

Composites provide designers a lot of leeway in terms of how they can shape the material to best suit their needs. Because of this adaptability, material qualities can be tailored to a specific use case. High-performance composites often have small thermal expansion rates, meaning they don't swell or shrink a lot when the temperature changes. This quality is highly sought after for use in precise engineering. In situations where there are cyclic loads, such as aircraft constructions, the fatigue resistance of these materials is crucial.

The following are some examples of high-performance composites:

- Reinforced with carbon fibers and a resin matrix, these composites are exceptionally strong for their low weight. The aircraft, vehicle, and sports goods industries all make use of them

- Composites made of glass, aramid, or carbon fibers and a polymer matrix are called fiber-reinforced polymers (FRPs). Their applications include the building, shipping, auto, and aerospace sectors
- High-temperature and wear-resistant Ceramic Matrix Composites (CMCs) are made by fusing ceramics and fibers. They have numerous high-temperature industrial uses, including in gas turbines and in the aerospace industry
- Improved strength and stiffness coupled with superior thermal conductivity are provided by Metal Matrix Composites (MMCs), which combine metallic matrix with ceramic or other reinforcements. They are used in aviation, automobiles, and electronics, among other fields.

When it comes to solving complex engineering problems, high-performance composites are often the only option, making them indispensable in many fields. Their popularity keeps rising as innovators perfect their application and production methods.

5 Ceramic and Glass Particle Based Polymer Composites

Bone tissue engineers frequently use synthetic bone graft materials including bioactive glass and bioactive calcium phosphate-based ceramics [34]. Among the first synthetic materials discovered to interact with bone [35], Bioglass[®] was developed by Hench and colleagues. Composed of Na_2O , CaO , SiO_2 , and P_2O_5 , this glass breaks down over time. It was discovered that bioactive glass-based implants used in animal models for bone regeneration could not be withdrawn without fracturing bone. Other types of bioactive glass and calcium phosphate ceramics were developed thanks to this finding, which sparked a new wave of research into bioactive inorganic materials. Bone is a natural composite material made up of a polymer matrix called collagen and inorganic ceramics including hydroxyapatite, calcium sulfate (CaSO_4), and calcium carbonate (CaCO_3) [36]. Mechanical strength and support for bone regeneration are provided by inorganic components, while the collagen matrix allows cellular connections and tissue development. Bone cell proliferation and differentiation are aided by the calcium ions released by the inorganic phase.

Substrates and scaffolds for bone regeneration have been fabricated using CaP, CaSO_4 , and CaCO_3 either singly or in composite form as fillers in a polymer matrix [37]. Hydroxyapatite, a type of CaP, is a major structural component of native bone and is resorbed by bone cells in living organisms. It is possible to classify CaP as amorphous calcium phosphate (ACP), biphasic calcium phosphate (BCP), or hydroxyapatite (HA). Physical and chemical properties, as well as surface textures, determine the bone forming activity (osteoconductivity or osteoinductivity) of CaP ceramics [38]. CaP's bone-forming activity has primarily been demonstrated in non-load-bearing clinical circumstances, such as those encountered in orthopedic, dental, ear, nose, and throat procedures. CaP particles cannot resist load bearing situations due to their fragility and processing difficulty. While it is simple to synthesize synthetic

polymers into structures with adaptable mechanical properties, these materials do not exhibit adequate bone-forming capacity. Bone grafts with desirable mechanical properties and bone forming activity can be made by mixing polymers with CaP particles to create polymer-based ceramic composites.

Tetragonal ZrO_2 material is one of the inorganic fillers that has potential as a modulator of UHMWPE characteristics. In fact, despite being biocompatible and bioactive, its remarkable mechanical and tribological qualities make it one of the most promising functional and structural materials for biomedical applications [39]. Yttria (Y_2O_3) is typically used as a stabilizer in biomedical grade Zirconia (3Y-TZP or $\text{ZrO}_2\text{-YO1.5}$) [40], which is used for manufacturing femoral heads and is well recognized as an excellent option for preparing dental implants. Phase transition towards the monoclinic phase (ageing process) remains a major worry for the long-term durability of the material, which can restrict its use in the biomedical area. $\text{ZrO}_2\text{-Al}_2\text{O}_3$ composites have been used to tackle the issue recently, because they exhibit a weak or nonexistent phase transition. Combining Alumina's (high) hardness and (high) stiffness with Zirconia's (mentioned) qualities are crucial to the success of these composites. To achieve a material that is cheap, can be mass-produced, has strong mechanical properties, and is good at interacting with cells, Alumina Toughened Zirconia (80–20 wt%) (ATZ) was disseminated in a UHMWPE matrix. To get the UHMWPE/ATZ composites ready, we first used a homogenizer and then molded them under pressure [41]. The field of orthopedic surgery is currently experiencing a boom in tissue engineering development. Because of the necessity for their surfaces to interact with living organisms, biomedical polymers and composites must be biocompatible. As proteins are thought to be the primary and most essential substrate in mediating polymer-organism interactions, it is considered that the presence or absence of proteins on a material surface determines the biocompatibility of the material as a whole. Polymer surfaces are decorated with bioceramic particles (aragonite and calcite) to produce appropriate protein adsorption and cell responses, in accordance with the principles for creating biocompatible materials. In another article, the adhesion characteristics of a polyurethane/calcium carbonate composite has been reported [42]. In order to gain insight into the phenomena of cell adhesion and, more specifically, the proteins involved in osteoblast adhesion on contact with the materials, we used atomic force microscopy (AFM) to study the adhesion between fibronectin (FN) and composites PUR/ CaCO_3 surfaces. The detachment force is also shown to be correlated with the surface free energy (SFE). In the end, human bone derived cells (HBDC) were cultivated on PUR/ CaCO_3 composites to evaluate the material's cellular biocompatibility. Biodegradable polymers such as polyhydroxyalkanoates are gaining popularity for use in tissue engineering. Materials ranging from hard and brittle to soft and elastomeric are all included in the polyhydroxyalkanoates family. The category of polyhydroxyalkanoates has been expanded over the years as researchers look into their potential as sutures, cardiovascular patches, wound dressings, guided tissue repair/regeneration devices, and tissue engineering scaffolds, among many other biomedical uses. Researchers have explored the idea of developing composites combining polyhydroxyalkanoates with inorganic phases in an effort to enhance the materials' mechanical properties,

decrease their rate of degradation, and impart bioactivity. Some polymers that have been researched extensively to construct composites with hydroxyapatite, bioactive glass, and glass ceramic fillers or coatings include poly(3-hydroxybutyrate), poly(3-hydroxybutyrate-co-3-hydroxyvalerate), and poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) [43]. Recent years have seen a surge in research and development efforts focused on three-dimensional (3D) printing technologies due to their widespread industrial and academic applications. One of the biggest problems with 3D printing, especially in the medical field, is the scarcity of high-performance materials that may be used in the process. In the context of contemporary biotechnology, the physicochemical qualities of individual constituent materials may fall short of expectations. This work produced and tested a range of titanate nanofiller (nanowire and nanotube) augmented polycaprolactone (PCL) composites, all of which were 3D-printable and provided improved mechanical properties, with the goal of improving the materials' performance and expanding their applications [44]. To produce PCL and PCL/nanofiller microfiber composites, melt electrowriting additive manufacturing was employed (Fig. 2). Nanofiller aggregation considerably varies the viscosity during the printing process, which can lead to poorly printed structures, yet improved nanofiller dispersion enabled intact and uniform sample morphology. The modified ceramic/PCL composite provided improved and stable mechanical properties, with a Young's modulus of 1.67 GPa, which is over 7 times greater than that of pure PCL (0.22 GPa). The concept of improving biocompatible polymers with modified nanofillers has significant promise in the field of individualized 3D printing for biomedicine, as the cell safety features are preserved (similar to PCL).

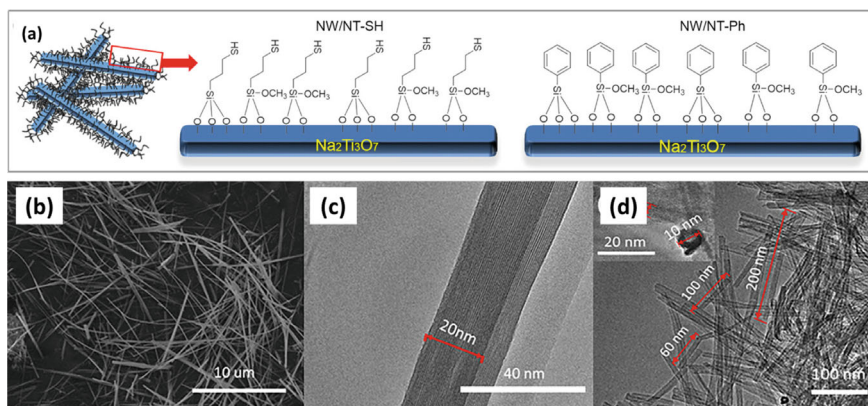


Fig. 2 a Synthesis of Titanate based polymer composite with functionalization b–d SEM images of titanate nanowires used in polymer composite fabrication. Reproduced with the permission from Ref. [44] © 2020 American chemical society

6 Magnetic Particle Based Polymer Nanocomposites

Since hybrid nanomaterials include the best of both organic and inorganic components, they have attracted a lot of attention. Magnetic polymer nanocomposites stand out in this group because they possess desirable magnetic characteristics, are highly stable, and are also biocompatible. *In situ*, *ex situ*, microwave reflux, co-precipitation, melt blending, ceramic-glass processing, and plasma polymerization are all viable options for creating organic–inorganic magnetic nanocomposites. As well as being used as *in vivo* imaging contrast agents, drug transporters, heavy metal adsorbents, and magnetically recoverable photocatalysts for the breakdown of organic pollutants, these nanocomposites have also been used as superparamagnetic or negative contrast agents. The magnetic properties of transition metals like iron (Fe), nickel (Ni), and cobalt (Co) are being investigated for their potential in a variety of disciplines [45]. At low and room temperatures, these magnetic metals are ferromagnetic, but at high temperatures they switch to a paramagnetic state. There have been reports in the literature of studies on the synthesis and magnetic characteristics of Fe, Ni, and Co nanoparticles. The magnetic properties of these metals' oxides are well-documented as well. Iron oxide nanoparticles stand out among these because of their utility in both medicine and industry [46]. Oxides of iron contain the elements iron (Fe), oxygen (O), and hydroxide (OH). Iron oxides come in 16 different forms: oxides, hydroxides, and oxide-hydroxides. The saturation magnetization of magnetite is the greatest of the three primary forms of iron oxides (hematite, magnetite, and maghemite) [14].

A polymer magnet, sometimes known as a plastic magnet, is a magnet that is not constructed of metal, but rather an organic polymer. This is a recently discovered category of magnetic materials that has scientists excited. Poly(1,3,5-triaminobenzene) was synthesized by Torrance et al. [47], and it was reported to exhibit a ferromagnetic phase when oxidized with iodine up to 400 °C. This was followed by the report of the synthesis of an organic pi-conjugated polymer with a very large magnetic moment and magnetic order at temperatures below 10 K by Rajca et al. [48].

Since therapeutic materials (such as medications and genes) and imaging agents (such as magnetic nanocrystals) may be easily introduced into nanocomposites, they are frequently employed to acquire precise diagnoses and provide effective therapy for a range of ailments. Cancer diagnosis and treatment, as well as medication behavior monitoring, can all be accomplished using a single nanocomposites-based system. In another study, the authors detailed the synthesis of four pyrenyl-based polymers (Py-PEG, Py-DEX, Py-HA, and Py-PEG-conjugated heterofunctional PEG) and their use in the development of multifunctional nanocomposites for applications such as multimodal imaging, targeted cancer detection, and pH-sensitive drug delivery [49]. As an example, these nanocomposites can be utilized to distribute magnetic particles for MRI-based early cancer detection, to efficiently categorize patient groups for targeted treatment, and to monitor disease progression in real time, all at the same time. Due to their potential use as magnetic carriers in the biomedical field, magnetic nanoparticles have received a lot of attention in recent years. The potential for these compounds to be used as MRI agents, mediators of

hyperthermia cancer treatment, and in targeted therapeutics has increased as they have been utilized as effective delivery channels. The development of “smart” polymers that can adjust their properties in response to changes in their surroundings, such as temperature and pH, has also received considerable research attention. With this background, this paper examines the current state of stimuli-responsive magnetic systems in biomedical domains. Poly(lactic acid) (PLA) bone scaffolds with Fe_3O_4 nanostructures and self-fit potential were created in an intriguing study using an external magnetic field [50]. The idea behind this method is that the friction created when the ferromagnetic nanostructures meet while under magnetic stimulation causes local heat, which in turn stimulates bone development. As a result, the polymer chains were triggered into regaining their previous shape by these concentrated areas of energy. One benefit of this strategy is that it allows for the safe implantation of a compacted intelligent scaffold, which can then be converted to a more desired shape at a later time (for example, by expanding to increase pressure on the fractured bone to encourage bone development or release medications). To investigate the impact of magnetite nanoparticles on cell proliferation and cellular responses, Shahrousvand et al. produced organic–inorganic polyurethane (PU) nanocomposites with included magnetite. Fourier transform infrared spectroscopy, scanning electron microscopy, atomic force microscopy, differential scanning calorimetry, X-ray diffraction, and electrochemical impedance spectroscopy were all used to assess the properties of PU-IONs [51]. The bulk morphological, mechanical, electrochemical, and biological properties of polyurethane nanocomposites are all altered by the incorporation of iron oxide nanoparticles (IONs). The addition of more magnetite nanoparticles enhanced the electrical conductivity and hydrophilicity of PU-IONs, which in turn altered their water uptake, biodegradation, and cytotoxicity. Cell adhesion, cell staining, and the MTT assay were used to determine whether or not PU-IONs were biocompatible. Based on the findings, magnetite polyurethane nanocomposites may be useful in cell therapy, tissue engineering, and even nerve restoration.

7 Magnetic Hydrogels in Biomedical Applications

Hydrogels’ adjustable qualities (e.g., mechanical, chemical, biocompatible) make them useful in many biomedical engineering applications since they mimic the native extracellular matrix (ECM) in many ways. However, the lack of controllability, actuation, and quick-response qualities of hydrogels makes it difficult to use them in applications such as creating 3D tissue structures and active targeting in drug delivery. Due to their unique active response qualities and wide range of potential uses, magnetic hydrogels have recently gained attention as a promising new biocomposite. Therapeutic drug delivery, bioimaging, and regenerative engineering are just some of the many biomedical applications that are inspiring the development of thermoresponsive magnetic hydrogels for on-demand release of biomolecules [52]. A research group reported about various magnetic nanoparticles and thermoresponsive polymers that go into the making of these clever nanoengineered hydrogels.

They also focused on some of the promising new uses for these stimuli-responsive hydrogels in the field of biomedicine.

Hydrogels, because of their mechanical and physical qualities, have garnered a lot of attention. Because of their exceptional biocompatibility, hydrogels hold great promise as a biomaterial. Biomedical applications have been proposed for magnetic hydrogels, which are based on hydrogels including magnetic nanoparticles. Magnetic hydrogels are advantageous because they can quickly react to externally applied magnetic fields and stop magnetic nanoparticles from escaping into the environment. Here, we describe the development, characterization, and preliminary testing of a hybrid stent made of magnetic hydrogel for the therapeutic application of magnetic hyperthermia [53]. In order to achieve external gelation and improve the heating rate, magnetic hydrogel was first created by dissolving alginate with magnetic nanoparticles in a bath of calcium chloride ($5\text{--}15\text{ mg mL}^{-1}$). After 15 days, there was essentially no leakage of iron oxide nanoparticles from the hydrogel, even at a concentration as high as $1\text{--}8\text{ mg mL}^{-1}$, ensuring their safe usage in biological applications (Fig. 3). As a result, magnetic hybrid stents were constructed in a straightforward fashion; with the magnetic hydrogels providing the basis for the heating efficiency to be tested in both an agarose phantom model and an ex vivo tissue sample subjected to 30 mT and 765 kHz magnetic hyperthermia settings. Excellent heat generation from the hybrid stent and simple temperature control by tweaking magnetic nanoparticle concentration ($2\text{--}8\text{ mg mL}^{-1}$) were seen in both cases of hyperthermia.

Gelatin hydrogels and Fe_3O_4 nanoparticles (about 40–60 nm) were chemically cross-linked with genipin (GP) as the cross-linking agent to make the magnetic

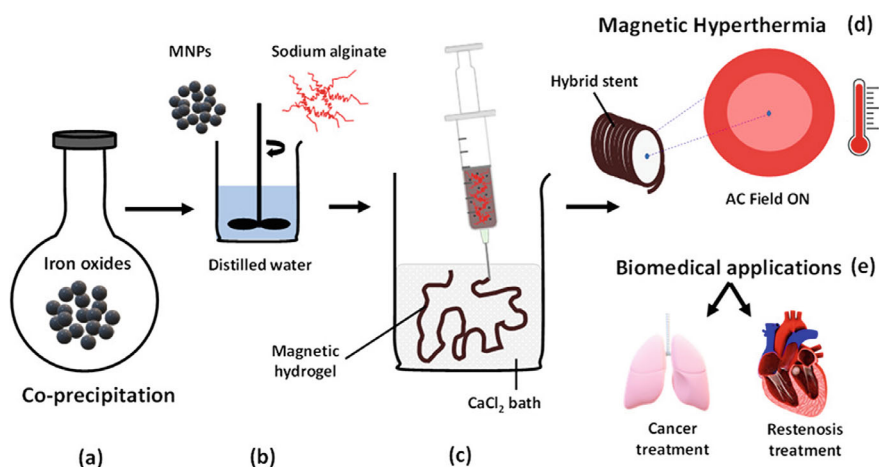


Fig. 3 Diagram of how the magnetic hybrid stent works. **a** The coprecipitation method can be used to make MNPs that are 15 nm in size. **b** A mix of MNPs, water, and sodium alginate powder. **c** A needle is used to make the magnetic hydrogel. **d** Plan of the hybrid stent and spread of heat during the hyperthermia test. **e** How the hybrid stent can be used in medicine to treat cancer in hollow organs like the stomach or to keep arteries from narrowing again. Reproduced with the permission from Ref. [53] © 2022 American Chemical Society

hydrogels. The cross-sectional SEM image shows that the Fe_3O_4 nanoparticles were pretty evenly spread throughout the gelatin matrix [54]. Also, *in vitro* release results show that the drug release profile of the resulting hydrogels can be controlled by turning the mode of a given magnetic field on or off. When magnetic fields were put on magnetic hydrogels, the rate at which they released vitamin B_{12} was much slower than when the fields were turned off. This suggests that the hydrogels are in a close configuration because Fe_3O_4 nanoparticles are sticking together. Based on this on-and-off process, gelatin-ferrite hybrid composites could be used to make smart magnetic hydrogels that could be used in new drug delivery systems. In the range of 6–18 wt% gelatin content, thermoreversible gelatin-based ferrogels can be prepared in water with a consistent structure specified by the crosslinking degree [55]. It is also reported that the concentration of magnetite nanoparticles can be adjusted between 20 and 70 wt%. Collagen's potential to bind iron and hydroxide ions has been shown by modeling studies, and this, in turn, has led researchers to hypothesize that collagen serves as a nucleation seed for iron hydroxide aggregation, leading to the intergrowth of collagen and magnetite nanoparticles in their formative stages. Small-angle neutron scattering (SANS) with contrast-matching is used to characterize the intricate structure of the individual ferrogel components. Small-angle X-ray scattering and microscopy are supplementary tools for characterizing the magnetite structure. While the size of the magnetite nanoparticles, which is roughly 10 nm, appears to be limited by the gel mesh size, SANS reveals an unaltered gelatin structure with an average mesh size bigger than the nanoparticles with regard to gel concentration. Inflation tests confirm that magnetite modulates the ferrogels' magnetic and mechanical properties by acting as a crosslinker. Flexible electronics, medicinal devices, and soft robotics are just a few of the potential fields of application for magnetic hydrogels. But the majority of currently available magnetic hydrogels are brittle and have a subpar magnetic response. Nontoxic polyacrylamide (PAAm) hydrogel is used as the matrix in this research, while functional additive [3-(trimethoxysilyl)propyl methacrylate coated Fe_3O_4] is used as the inclusions to create a robust, resistant, and sticky magnetic hydrogel. Because it contains so many magnetic particles (up to 60% by weight of the polymers and water combined), this magnetic hydrogel not only has a higher modulus and durability than pure hydrogel (Fig. 4), but it also reacts quickly to a magnetic field. Hydrogels adhere to both hard and soft surfaces that are abundant in hydroxyl groups [56]. Polydimethylsiloxane (PDMS)-coated magnetic hydrogel shows promising underwater performance. Even when subjected to cyclic loading, the link between magnetic hydrogel and PDMS remains strong. This hydrogel is used to show how well magnetomechanical coupling can work in an artificial muscle. Many fields will benefit from the adhesive tough magnetic hydrogel, including microfluidics, controlled drug delivery systems, and the coating of soft objects. This method can be used with a wide variety of practical soft materials.

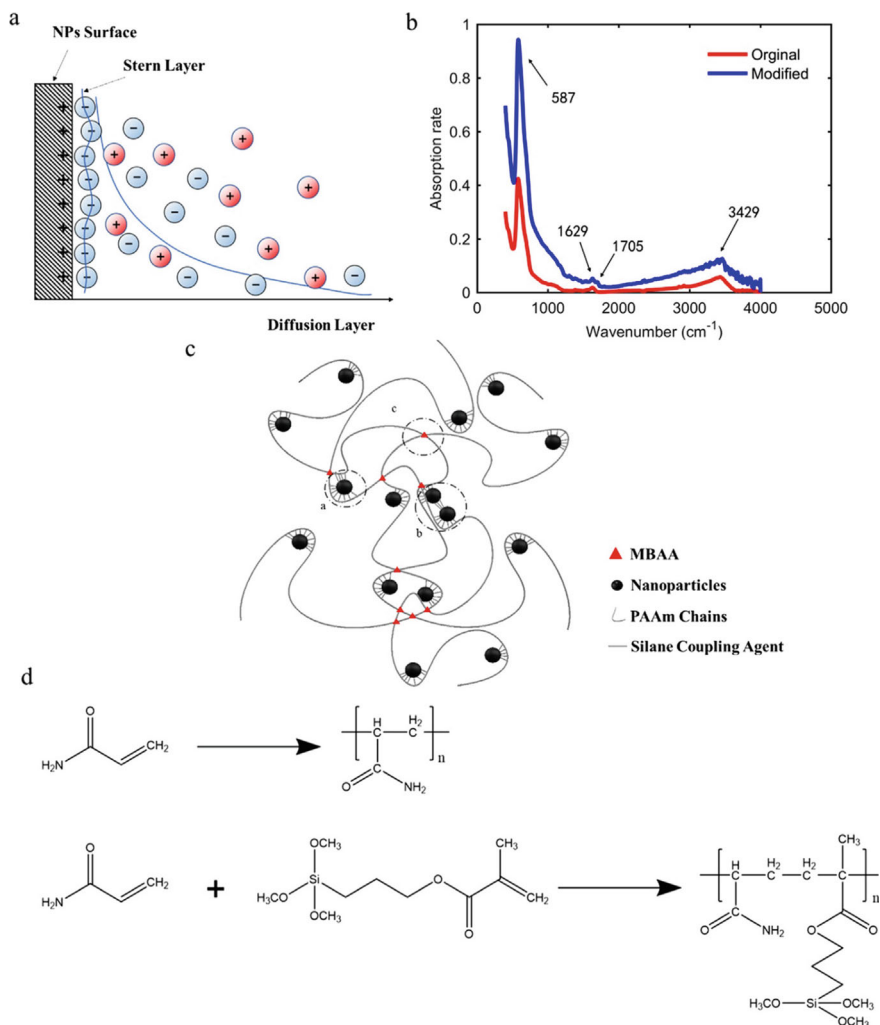


Fig. 4 This picture shows the magnetic hydrogel. **a** Structure with two layers for the particle dispersion device. **b** FT-IR bands of Fe_3O_4 before and after it was changed. **c** System for spreading out magnetic hydrogel. **d** The idea behind how hydrogels are made. Reproduced with the permission from Ref. [56] © 2019 American Chemical Society

8 Summary and Future Outlook

Polymer composites including fibers and ceramic fillers have made a fascinating journey through the history of biomedical uses. Their development since the 1960s shows an unchanging dedication to using polymers and fillers in tandem to simulate or improve the mechanical and biological qualities of native tissues. Beginning with

an emphasis on integrating ceramic fillers, most notably hydroxyapatite (HA), into polymers, this overview summarizes the development of these composites. This first research has already revealed their immense potential for use in bone healing and reconstruction. The later introduction of carbon fibers in the 1980s was a turning point because of the amazing mechanical qualities they endowed upon orthopedic implants and prosthetics.

Over the course of the development, scientists have cast a larger net, exploring a plethora of polymers and fillers to develop composites specifically suited to meet a variety of biomedical requirements. Tissue engineering scaffolds, drug delivery systems, dental and orthopedic implants, wound dressings, and biodegradable stents are just a few of the many uses for these adaptable materials. The composites have proven their worth as tough competitors in the search for improved healthcare solutions in these cutting-edge endeavors, demonstrating their ability to increase healing and well-being.

Numerous game-changing innovations are likely to characterize the future of polymer composites with fiber and ceramic filler for use in healthcare. Their bright future is predicted to be shaped by several important trends and fields of research:

- There is hope that incorporating nanoparticles like graphene into these composites may improve their electrical conductivity and mechanical qualities. Pioneering uses in neural interfaces, bioelectronic devices, and cutting-edge sensors could all benefit from this development.
- A new age in personalized medicine will begin with the widespread availability of 3D printing and additive manufacturing techniques. These methods will enable the manufacturing of implants and medical devices that are uniquely suited to each patient, accommodating for their unique anatomy and medical history.
- Composite materials designed for absorption by the body hold great promise for advancing the field of implanted electronics and sensors. Improving patient care and well-being, these materials will facilitate real-time monitoring, diagnostics, and therapeutic actions.
- In order to keep up with the rapid growth of imaging technologies like MRI and CT scans, it is important to create new materials that are compatible with these diagnostic methods. To further improve the efficacy of medical therapies, polymer composites can be engineered to be MRI-friendly and radiolucent.
- Obtaining necessary governmental approvals and successfully navigating the path to commercialization lie ahead as this field's research advances and bears fruit. To ensure that these ground-breaking technologies are translated into accessible healthcare treatments for the general population, researchers, industry stakeholders, and regulatory bodies must work together.

In conclusion, the history of polymer composites containing fibers and ceramic fillers for use in biomedical applications is one of dramatic development and boundless opportunity. Their decades-long journey exemplifies human creativity and the unrelenting need to improve healthcare. These composites, which combine the best features of polymers and fillers, will undoubtedly leave a lasting impression on the

field of medicine in the future. As the boundaries of materials science and engineering are pushed further, these composites have the potential to shine in a variety of applications, such as neural interfaces, diagnostics, implanted electronics, and tailored medicine. The future of these composites in biomedicine is brighter than ever, promising to transform the landscape of healthcare as we know it, thanks to innovation, collaboration, and an unyielding commitment to improve human health.

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Ceramics and Glass Ceramics for Biomedical Applications



Niranjan Patra, Prathipati Ramesh, Salvatore Grasso,
and Aldo R. Boccacini

Abstract This chapter explores the diverse landscape of ceramic materials utilized in biomedical applications. Ceramics have garnered significant attention due to their exceptional mechanical properties, biocompatibility, and potential to enhance the performance of medical devices and tissue engineering scaffolds. This chapter delves into the various types of ceramic fillers, including calcium phosphates, hydroxyapatite, bioglass, glass ceramic, alumina, and zirconia, detailing their distinctive properties and roles in different biomedical applications. The ceramic fillers, in the form of particles or fibres and their properties are discussed in the context of biomedical applications along with strategies to optimize filler-matrix interactions. By providing a comprehensive overview of different ceramic fillers, this chapter serves as a valuable resource for the scientific community in the field of biomaterials seeking to harness the potential of ceramic fillers for innovative biomedical applications.

Keywords Ceramic fillers · Biomedical applications · Calcium phosphates · Hydroxyapatite · Alumina · Zirconia

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1 Introduction

In the ever-evolving landscape of biomedical engineering, the search for innovative materials to enhance the performance and efficacy of medical devices and therapies remains a constant endeavor. Bioceramic fillers have garnered substantial attention, owing to their exceptional biocompatibility, mechanical properties, and diverse functionalities. The integration of ceramic fillers within biomedical applications has opened avenues for advancements in areas ranging from bone regeneration and tissue engineering to drug delivery and diagnostic tools [1–15]. Over the past decades, the landscape of biomedical materials has been redefined by a quest for materials that not only mimic natural tissues but also offer unprecedented functionalities [16–20]. The need for materials that can interact seamlessly with the biological environment, promoting healing and regeneration, has driven researchers to explore a well diversified options. Ceramic materials have emerged as prominent candidates, demonstrating an impressive combination of properties that align with the demands of biomedical applications.

Ceramics, with their exceptional hardness, durability, and resistance to chemical degradation, have long been used in orthopedic and dental applications such as implants and prosthetics [1, 10, 21, 22]. However, their brittle nature and limited flexibility have spurred investigations into enhancing their mechanical performance and extending their potential applications. One approach that has gained traction is the incorporation of ceramic fillers into polymer matrices, creating composite materials that synergize the advantages of both components [4, 6, 9, 23–25]. The biocompatibility of any material intended for biomedical applications is of paramount importance. Ceramic fillers, often derived from biocompatible materials like hydroxyapatite (HA), tricalcium phosphate (TCP), and bioactive glasses, exhibit a high degree of compatibility with living tissues. This compatibility is not limited to mechanical aspects; it extends to the interaction between the materials surface and the surrounding biological environment. This interaction can be manipulated to induce desired cellular responses, making ceramics versatile tools in tissue engineering and regenerative medicine. One of the intriguing aspects of ceramic fillers lies in their potential for multi-functionality [10, 26]. Apart from bolstering mechanical properties, these fillers can be engineered to carry and release therapeutic agents, enabling targeted drug delivery systems. Additionally, their electrical and thermal conductivities can be harnessed for applications such as neural interfacing and hyperthermia-based cancer therapies.

This chapter provides a comprehensive understanding of the role and impact of ceramic fillers in the realm of biomedical applications. The subsequent sections delve into the various types of ceramic fillers, their synthesis methods, and the techniques used to incorporate them into polymer matrices. Furthermore, the chapter discusses the biocompatibility and bioactivity aspects of ceramic fillers, shedding light on the interactions between these materials and biological systems. The exploration of multi-functionality through ceramic fillers highlights the potential to revolutionize therapeutic strategies. In summary, the integration of ceramic fillers into

biomedical applications presents a promising avenue for advancements in health-care. With their unique combination of biocompatibility, mechanical properties, and multi-functionality, ceramic fillers hold the potential to transform a wide range of therapeutic and diagnostic strategies. This chapter sets the stage for a detailed exploration of the various facets of ceramic fillers, offering insights into their synthesis, properties, and applications, and envisioning a future where these materials play a pivotal role in shaping the landscape of biomedical engineering.

2 Ceramic Fillers for Biomedical

Calcium phosphates, Calcium sulphates, Bioactive glasses, glass ceramics, alumina, and zirconia, all ceramic based materials, have been explored for medical applications including implant devices [27, 28]. Ceramics are a promising class of biomaterials because they are biocompatible and have a structure that is analogous to that of natural bone.

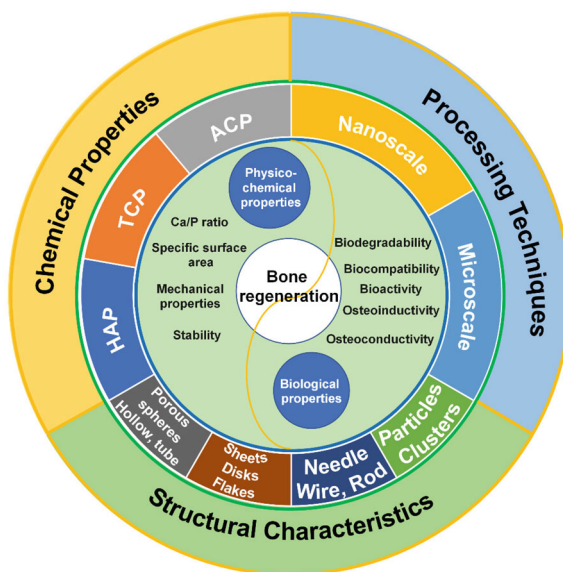
Ceramic materials, particularly calcium phosphate-based materials like β -tricalcium phosphate (β -TCP) and hydroxyapatite (HAp) have been widely researched for a wide variety of orthopaedic and dental applications [15, 29–33]. The breakdown and bioactivity of calcium phosphates, which play a significant role in human biology, are both affected by the Ca/P ratio. Nanoparticles, cement, and coating forms of these biomaterials are all useful in the medical field [34, 35]. Calcium phosphate-based materials are being used in a variety of biological contexts, including bone repair, coating of orthopaedic implants, dental applications, and drug delivery [26, 34–41]. Bioceramics based on calcium orthophosphates are depicted in Fig. 1. Calcium phosphates, as a family of ceramics, have gained great attention for various biomedical applications due to their biological functions and the possibility to modify their mechanical properties. Recent years have seen intensive research and development of calcium phosphate polymer composites (especially HAp and TCP).

2.1 *Physical and Chemical Properties of Ceramic Fillers*

Ceramics are inorganic materials that often include both metallic and non-metallic components chemically linked together via ionic bonds with a varying degree of covalent character. The nature of these linkages and the plexus that forms the microstructure of each material determines largely its characteristics [43]. They come in both crystalline and non-crystalline forms, and the latter often feature a crystalline phase scattered in an otherwise amorphous structure. Ceramic fillers meant for biomedical applications are not reactive within the live body [44].

Ceramic biomaterials can be catagorised based on their chemical properties (their molecular bioactivity when interacting with human organisms) such as inert, low or medium surface activity, and bioresorbable (adsorbable). There is a significant delay

Fig. 1 Chemical properties, processing methods, and structural features of biomaterials based on calcium phosphate for bone regeneration. Adapted from Ref. [42]



before stable connections are established between implants and tissues when using inert bioceramics like alumina (Al_2O_3) because these materials do not promote the connection with living tissues, can withstand low-pH environments for thousands of hours, and possess high chemical inertia. After implantation, a network of fibrous connective tissue of different thickness forms around the implant, providing both structural support and mechanical isolation. This makes them ideal for permanent implants due to their great biocompatibility and mechanical strength [45]. In addition to binding to specific proteins, low and medium activity materials can also release ions, which aids in implant integration with living tissues [12].

2.2 Mechanical Properties of Ceramic Filler Composites

Ceramic materials primary mechanical characteristics includes poor tensile strength, high hardness due to an internal microstructure comprised of strong ionic or covalent bonds, and a low fracture toughness and resistance to shock loads due to a lack of plasticity. Ceramic materials suffer from brittle fracture even at low energy levels, which is a major drawback compared to metal alloys which exhibit ductile behavior [46]. Ceramics, although being brittle, outperform metals in terms of hardness and flexibility. When subjected to tensile strains at normal temperature, both crystalline and non-crystalline ceramics shatter before any plastic deformation occurs; this behavior also contributes to the materials low fatigue strength. Cracks occur and spread in a direction orthogonal to the applied force, characterising the brittleness. Transgranular and elongated cracking occur in crystalline ceramic materials. Internal holes,

microcracks, grain misalignments, impurities, microscopic notches, and so on all contribute to these weak responses because they exist at micro-scales [47]. These flaws occur during manufacturing due to thermal gradients created by repeated heating and cooling. Mechanical characteristics in ceramics tend to improve with increasing microstructure fineness.

Understanding maximum stress a ceramic component can withstand is crucial due to the materials inherent flaws. Fracture toughness refers to a materials ability to withstand the destructive propagation of a crack, and the K_{IC} coefficient is the related metric for this property. The K_{IC} coefficient is defined as the value of the stress for a pre-existing crack in a standard specimen for fast propagating it by tugging the specimen. When compared to metals, ceramics have a much lower value (often less than $10 \text{ MPa m}^{1/2}$, typically in the range of $2\text{--}4 \text{ MPa m}^{1/2}$) [48]. Ceramics shows worst behavior under tensile loads than they do under compressive test. While the maximum stress measured in tension or compression is the same for metals, it is roughly 15 times greater for brittle materials. Ceramics have a fracture toughness that is dependent on both the magnitude and duration of the tensile stress applied [43]. In general, the kinetics of the chemical decomposition of ceramics is characterized by very slow rates; although strength attenuation and final failure of ceramics can occur without cyclic loading since the mechanism driving material failure is chemical rather than mechanical. Ceramic fibers are utilized as reinforcement for composite materials due to their high specific elasticity value (E/ρ).

2.2.1 Calcium Phosphates

Calcium phosphates are the primary inorganic components of hard tissues of biological origin like cellular and animal skeletons. Carbonated hydroxyapatite (HA) provides structural integrity, hardness, and mechanical performance in bone, teeth, and tendons. Large crystals of calcium phosphate, formed over long periods of time and subjected to high pressure and temperature, can be found as mineral deposits in dead things. Calcium phosphates generated biologically, on the other hand, are typically nanocrystals that precipitate under mild circumstances (atmospheric pressure and ambient temperature).

In comparison to calcium carbonate (CaCO_3) and silicon dioxide (as silicic acid $\text{SiO}_2 \cdot n\text{H}_2\text{O}$), which are found in massive quantities in marine unicellular organisms, calcium phosphates are rather few. Iron oxides, found in snail teeth and magnetotactic bacteria, are another major type of biomineral [49, 50]. Because many diseases develop from skeletal system (bone) or dental system (teeth) anomalies, calcium phosphates are of particular importance in biomedicine because they are present in vertebrates (such as humans). Although calcium phosphate is essential to life, it is important to note that on rare occasions, calcium phosphate minerals crystallise in an irregular manner, in places where this is not desired. Atherosclerosis, stone formation, and dental calculus are all examples of abnormal crystallization, also known as ectopic mineralization.

Both calcium and phosphorus can be found in abundance on Earth. About 3.4 wt% calcium and 0.10 wt% phosphorus can be found in the Earth's crust [51]. Calcium phosphates can vary depending on whether or not water is incorporated into the oxides of these two elements. All calcium phosphates are colourless crystalline solids unless they have been artificially or naturally doped with a transition-metal ion. There are a few calcium phosphates that are completely insoluble in water, yet they all dissolve in acids. There are structural differences between ortho- (PO_4^{3-}) , pyro- $(\text{P}_2\text{O}_7^{4-})$, and poly- $(\text{PO}_3)^{n-}$ phosphates. However, only calcium orthophosphates will be discussed in this chapter.

Normal (bones, teeth, fish enameloid, and some kinds of shells) and pathological (dental and urinary calculus and stones, atherosclerotic lesions) calcifications in biological systems have calcium orthophosphates as their primary inorganic constituent [52, 53]. Most HA (also known as “biological apatite or dahllite”) is a weakly crystalline, nonstoichiometric sodium-, magnesium-, and carbonate-containing HA. Human bones are mostly water (10 wt%), collagen (30 wt%), and calcium orthophosphates (50 wt%). Microscopical analyses of the junction between implanted calcium phosphate biomaterials and the host bone revealed the presence of weakly crystallised nonstoichiometric carbonated apatite, analogous to bone apatite [44, 54]. Since numerous calcium phosphates with varying stoichiometries exist, short notations have historically been used to distinguish between them. The solubility and molar ratio of calcium to phosphorus are critical factors. The Ca/P ratio for these pristine materials can range from 0.5 to 2.0. In general, a lower ratio indicates that the calcium phosphate is more acidic and soluble in water for apparent solubility as a function of pH and concentration of calcium [31].

2.2.2 Monocalcium Phosphate Monohydrate (MCPM)

The most acidic and water-soluble calcium phosphate compound is monocalcium phosphate monohydrate ($\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O}$). It forms in the industrial manufacturing of phosphorus-containing fertiliser (Triple superphosphateTM) from highly acidic fluids [51]. It changes into monocalcium phosphate anhydrate ($\text{Ca}(\text{H}_2\text{PO}_4)_2$) when heated over 100 °C. MCPM is never detected in biological calcifications due to its high acidity and solubility, respectively. However, some medical calcium phosphate cements utilise MCPM [11, 55–57]. Additional uses include addition to baking powders, foods, and drinks as antacids, acidulents, and mineral supplements.

2.2.3 Dicalcium Phosphate Dihydrate (DCPD)

The mineral brushite (dicalcium phosphate dihydrate, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) is very simple to crystallise from water. When heated over 80 °C, DCPD changes into dicalcium phosphate anhydrate. DCPD is significant biologically because it is present in many types of pathological calcifications, including dental calculi, crystalluria, chondrocalcinosis, and urinary stones [52]. Bone mineralization and enamel dissolving in

acids (dental caries) have both been linked to the intermediate DCPD. DCPD is used in calcium phosphate cements or surgical procedures and in toothpaste alongside fluoride-containing chemicals (such as NaF) for cavity prevention [15, 30, 58–61]. Fertilizers, glass, calcium supplements, and mineral supplements in cereals are some of the other uses.

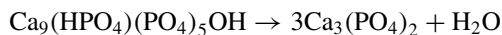
The mineral monetite, also known as DCPA (dicalcium phosphate anhydrate, CaHPO_4), is the anhydrous version of DCPD. DCPA, like DCPD, crystallizes from aqueous solutions, but at a lower temperature of 100 °C. DCPA is not seen in either normal or pathological calcifications, in contrast to DCPD. In addition to its employment in calcium phosphate cements, this material is put to use as a polishing agent, a source of calcium and phosphate in dietary supplements, a tableting aid, and a component of toothpaste [33, 62–66].

2.2.4 Octacalcium Phosphate

During the precipitation of thermodynamically more stable calcium phosphates (such as Hydroxyapatite, calcium-deficient hydroxyapatite (CDHA), octacalcium phosphate (OCP, $\text{Ca}_8(\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$) is frequently discovered as an intermediary phase. The atomic configurations of the calcium and phosphate ions in OCP apatitic layers are very similar to those in HA, and these apatitic layers are separated from the hydrated layers by water molecules. As one of the stable components in human dental and urinary calculi, OCP has significant biological relevance [67, 68]. The development of apatitic biominerals in the body depends on it. Transmission electron microscopy (TEM) reveals a central OCP inclusion (also called central dark line) in several biological apatites and in certain synthetically precipitated HA. OCP has not been directly observed in vascular calcifications but is thought to represent the precursor phase to biological apatites in both natural and artificial heart valves [69, 70].

2.2.5 β -tricalcium Phosphate

β -TCP (β -tricalcium phosphate) is the stoichiometrically pure form of calcium orthophosphate $\text{Ca}_3(\text{PO}_4)_2$. It can only be made by calcination, for example calcium deficient hydroxyapatite (CDHA) at temperatures above 800 °C as shown in below equation; it cannot be precipitated from solution.



It changes into the high-temperature phase α -TCP at temperatures over 1125 °C. β -TCP being the more stable phase at room temperature, it is less soluble in water than α -TCP. Biological calcifications never contain pure β -TCP. Dental calculi and urinary stones, dental caries, salivary stones, arthritic cartilage, and other soft-tissue deposits possess only the magnesium-containing form called whitlockite (chemical

formula: β -(Ca, Mg)₃(PO₄)₂) [52, 53]. Bone cements made from calcium phosphate also make use of β -TCP in the biomedical industry [13, 15, 29, 30, 33, 53, 56, 60, 62, 64, 65, 71]. As a bone-substitution ceramic, β -TCP is utilized in conjunction with hydroxyapatite (HA) to form biphasic calcium phosphate [32].

2.2.6 α -Tricalcium Phosphate (α -TCP)

Metastable at room temperature, α -TCP (α -tricalcium phosphate, α -Ca₃(PO₄)₂) is made by heating β -TCP to temperatures over 1125 °C. Hydrolysis of α -TCP produces a variety of different calcium phosphates, making it more reactive in aqueous settings than β -TCP. Rarely used in medicine, calcium phosphate cements are never found in biological calcifications [15, 30, 56, 60].

2.2.7 Amorphous Calcium Phosphates (ACP)

In the process of forming calcium phosphates in aqueous systems, the amorphous calcium phosphate (ACP) phase frequently occurs. Whenever a supersaturated solution is made by rapidly mixing solutions containing calcium cations and phosphate anions, ACP is typically the first phase to precipitate out [8, 72–75]. The mother liquors calcium and phosphate ion concentrations, as well as the solution pH, have a significant impact on ACP chemical formation. For instance, the Ca/P ratio of ACP phases has been reported to range from 1.18:1 (precipitated at solution pH 6.6) to 1.53:1 (precipitated at solution pH 11.7) and even up to 2.5:1.

Absorption bands for phosphate in the IR spectrum of ACP are quite broad and featureless. X-ray diffraction tests confirm that the compounds are amorphous. When viewed using an electron microscope, ACP often appears as round particles with diameters between 20 and 200 nm. Although X-ray diffraction tests show that ACP is amorphous (no coherent X-ray scattering data), it is likely that ACP possesses an apatitic short-range structure due to its extremely small crystal size. This is supported by extended X-ray absorption spectroscopy results on both natural and artificial samples [76–79]. On the other hand, a cluster of ions with the composition Ca₉(PO₄)₆ was postulated to be the fundamental structural unit of ACP. A model was constructed to characterize HA crystallization as a gradual assembly of these units, and these clusters were found experimentally as seed nuclei during crystallization [80]. Soft-tissue pathological calcifications (such as heart-valve calcifications of uremic patients) contain ACP (frequently comprising magnesium, carbonate, and pyrophosphate) [53]. Calcium phosphate cements are a commonplace application for ACP in the medical field [15, 58]. Bioactive composites made from ACP and polymers can be used in both dentistry and surgery because to their advantageous features [23, 25, 60, 81, 82].

2.2.8 Hydroxyapatite (HAp)

Calcium orthophosphates ranges in stability and solubility, with hydroxyapatite (HAp), $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ being the most stable and least soluble. Crystals of pure HAp form in the monoclinic $P2_1/b$ space group. However, HAp undergoes a monoclinic-to-hexagonal phase change (space group $P6_3/m$) at temperatures above 250°C [83, 84]. The hexagonal structure of HAp is stabilized at room temperature by certain impurities, such as the partial substitution of hydroxide by fluoride or chloride ions. This is why the extremely uncommon examples of natural HAp found in the form of single crystals invariably have a hexagonal space group. Apatite is a popular name for the phosphates of metals, which might be chloro, fluoro, or hydroxylated. The mineral name “apatite” originates from the Greek word “apate,” which signifies “deceit.” The word was created to describe the wide range of colors seen in crystals with the basic formula $\text{M}_{10}(\text{ZO}_4)_6\text{X}_2$, where M can stand for a number of minerals (Ca, Mg, Fe, Cd) and Z can stand for a number of other elements (P, As, V, S, C, S). X stands for F, Cl, Br, OH, etc. Calcium HAp is the most frequent apatite in the body.

Synthesis method of Hydroxyapatite (HAp), it is important to consider not only the materials expected performance, cost, precursors, solvent type, and surfactant material, but also the distribution of particles, the need for complex expensive additional steps, and the possibility of agglomerations or impurities in the crystalline structure. Most investigations aimed to change or create new synthesis pathways with the goal of manipulating these factors [10, 12]. Sol–gel, chemical precipitation, polyol, hydrothermal, sonochemical and microemulsion, solid-state technique, combustion, and thermal breakdown are only some of the ways that HAp can be produced. Biomimetic techniques and hydrothermal molten salt synthesis are just two examples of the novel approaches to synthesis that have emerged in recent years as environmental concerns have gained widespread attention [31, 42, 85–87]. The size and form of HAp particles can vary greatly depending on the synthesis strategy. Aqueous solutions of HAp can be made by combining stoichiometric amounts of calcium and phosphate containing solutions at $\text{pH} > 9$, then heating the mixture in the absence of carbon dioxide for several days, filtering it, and drying it. Solid-state reactions of other calcium phosphates (e.g. MCPM, DCPA, DCPD, OCP) with CaO, $\text{Ca}(\text{OH})_2$, or CaCO_3 at temperatures above 1200°C , in an environment of equal proportions of water and nitrogen, yield microcrystalline samples of HAp as well. Hydrothermal synthesis allows for the creation of HAp single crystals. From $\text{Ca}(\text{OEt})_2$ and H_3PO_4 , a water-free ethanol-based synthesis can be carried out [88, 89]. Pure HAp never occurs in living organism. However, HAp is widely utilized as hip-joint prosthesis and dental implants [1, 43], and a calcium phosphate cement with HAp has also been created [61] (Fig. 2).

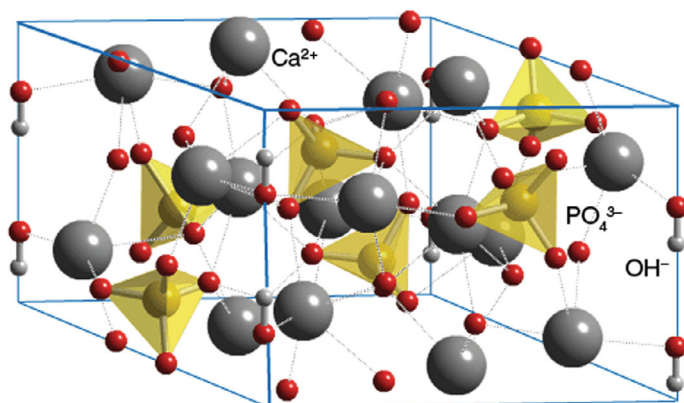


Fig. 2 Molecular structure of Hydroxyapatite $\text{Ca}_5(\text{OH})(\text{PO}_4)_3$ (The individual oxygen atoms are OH^- ions with H sitting outside of the cell. Phosphate and hydroxide ions work together with calcium ions to form a stable complex.) (Credits: ChemTube3D)

2.2.9 Substitutions of Ions in Hydroxyapatite (HAp)

Though HAp biocompatibility is high, still its bioactivity can be improved by including replacement ions into its unit cell [20, 45]. Poor mechanical qualities are one reason why synthetic stoichiometric HAp is not recommended for use on its own [90]. Depending on the substitution ions employed, a novel HAp composite can be created with enhanced properties for targeted biological applications [91]. HAp is able to accommodate a wide range of compositional structures in its sub-lattices. If we look at how the employment of different dopants has changed over time in terms of frequency, competition, and other factors, we can see that several elements from the periodic table have been successfully incorporated into its structure.

HAp hexagonal structure makes it amenable to substitution with a wide variety of cations (Sr^{2+} , Na^+ , K^+ , Mg^{2+} , Zn^{2+} , Ag^+ , etc.) and anions (CO_3^{2-} , SiO_4^{4-} , SeO_2 , F, Cl, Br, and others) [12, 49, 92]. Cations with smaller sizes than Ca atoms are favored for substitution due to the shorter distance between Ca II sites and the Ca II-O bond [93]. Despite maintaining the same hexagonal structure following substitution, HAp may experience slight variations in thermal stability, solubility, and hardness due to minute internal stresses. Mechanical performance and many biofunctionalities, including osteogenesis, adhesion resistance, and bacterial strain proliferation, can be improved through the incorporation of different doping ions into the hydroxyapatite structure [48].

2.2.10 Calcium-Deficient Hydroxyapatite (CDHAp)

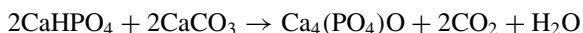
Adding solutions containing calcium and phosphate to boiling water at the same time and continuing to boil the resulting suspension for several hours yields CDHAp

(calcium-deficient hydroxyapatite). At this point, the OCP or ACP that had precipitated out of the solution (depending on its pH) has been converted into CDHAp. Above 700 °C, dry CDHAp with a Ca/P ratio of 1.5:1 will transform into β -TCP, whereas dry CDHAp with a Ca/P ratio of $1.5:1 < \text{Ca/P} < 1.67:1$ will change into a compound consisting of HAp and β -TCP (the aforementioned biphasic calcium phosphate, BCP) [4, 14, 94–98].

CDHAp is never stoichiometric, hence it always has other ions in it. The amount is determined by the counter ions of the chemicals (such as Na or Cl) employed in the process. CDHAp structures and unit cell characteristics are unknown because to a lack of direct determinations. CDHAp can be thought of as an approximation of HAp in which some ions have been removed [99]. The chemical formula for CDHAp indicates that the crystal structure of this compound contains unoccupied sites for both calcium ions (primarily Ca²⁺ sites, [16, 100] and hydroxide ions. However, little is understood regarding phosphate ion vacancies; in CDHAp, some of the phosphate ions are protonated or substituted by other ions such as carbonate. The main inorganic component of animal and human normal and pathological calcifications is called “biological apatite” or “dahllite”, and it is formed when Na⁺, K⁺, Mg²⁺, Sr²⁺ are substituted for Ca²⁺; carbonate is substituted for phosphate; fluoride, chloride, and carbonate are substituted for hydroxide; and some water is added [60]. Therefore, CDHAp is a chemical with great potential for use in the production of prosthesis bone substitutes.

2.2.11 Tetracalcium Phosphate

The simplest form of calcium orthophosphate is tetracalcium phosphate (TTCP) with empirical formulae Ca₄(PO₄)₂O. But unlike HA, it dissolves more easily in water. Since TTCP is insoluble in water, it must be synthesized in a solid-state reaction at temperatures above 1300 °C. This can be accomplished by heating homogenized, equimolar amounts of DCPA and CaCO₃ in dry air, or in a stream of dry nitrogen.



In water, TTCP slowly hydrolyzes into hydroxyapatite and calcium hydroxide. That’s why TTCP never available in any kind of biological calcification. Self-setting calcium phosphate cements are commonly utilized in the medical field, and TTCP is a key ingredient in their production [32, 101].

2.2.12 Calcium Sulphate (CS)

Plaster of Paris, or calcium sulphate hemihydrate (CaSO₄·1/2H₂O), (CS), has been utilized in the medical, dental, and orthopedic fields for well over a century. Biodegradability, biocompatibility, and osteoconductivity are three of the many biological benefits of CS, making it popular bone filler. Bone voids have been filled

with CS pellets since at least 1892 [102]. Additionally, it has been employed as a growth factor release agent [103, 104] and as a binder for HAp-ceramic particles in partially resorbable composite cements [21]. Calcium sulphate dihydrate ($\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$) paste, created when CS powder is combined with water, is widely considered to be one of the most effective bone cements due to its capacity to undergo in situ setting after filling the defects, without provoking any inflammatory response [102, 105]. CS is a soluble substance with bioactive characteristics that encourages bone growth; it is not only a gap filler that allows bone to repair passively. In fact, recent investigations have shown that CS-filled defects exhibit more angiogenesis than autograft-filled defects [104, 106].

However, CS does have some significant limitations. The first issue is the wide variety of natural materials that can be used to produce CS. Natural carbonates and silicates, as well as trace amounts of other metals, are among the impurities detected in CS [5]. These pollutants must be tested for in biomedical grade materials. The rapid disintegration rate of CS is the second major complaint of CS as a bone transplant material. In most cases, the deterioration of CS is more faster than the formation of new bone [47, 106], taking place within 4–7 weeks. There was evidence that CS pellets collapsed within days after implantation, leaving the developing bone unsupported. The rate of CS deterioration has been slowed in several ways. The creation of a calcium phosphate surface layer was beneficial in delaying the degradation when HAp particles were added to CS. The compressive strength of the modified CS pellets also fell, despite the fact that their degradation rate was reduced. Poly-L-lactic acid (PLLA) can be added to CS in minute quantities as a second method. The half-life of the granular compound in simulated bodily fluid at 37 °C was 68 days, while the half-life of neat CS granules was only 9 days.

3 Bioactive Glasses

Hench et al. [107] first developed silica-based Bioactive glasses (BG) as a kind of surface-reactive glass–ceramic biomaterials in 1969. BGs have been used successfully as a bone-substitute material for non-load-bearing applications in orthopedic and dental surgery due to their high biocompatibility, their ability to connect with bone and other tissues, and their stimulatory effects on bone cell function [108, 109]. The chemical reactivity of BG is responsible for its bonding abilities through interfacial and cell-mediated processes that break silicon bonds and generate a CP-rich layer on top of the glass, which then crystallizes to HCA [27, 28, 108, 110]. SiO_2 , Na_2O , CaO , and P_2O_5 are the main ingredients of most BGs. The traditional 45S5 BG formula, often known as Bioglass®, consists of the following ingredients in the following percentages by weight: 45% SiO_2 , 24.5% Na_2O , 24.4% CaO , and 6% P_2O_5 [27, 28, 108, 110]. The bioactivity, osteoconductivity, and bioresorbability of BG can be easily adjusted by adjusting the composition [27, 28, 108, 110]. Glass with a silica content of 54–60% takes two to four weeks to attach to bone, while

glasses with a silica content in the 42–53% range can be worn immediately. Glasses with a silica content of greater than 60% prevent BG from fusing with bone [111].

Based on their ability to stimulate bone regeneration and repair, Hench divided bioactive materials into two groups (A and B). Class A materials are those that cause fast reactions on the implant surface, leading to both osteoconduction (the formation of bone along the bone-implant interface) and osteoproduction [112]. Bone conduction is permitted in Class B materials, but bone formation is not. Since the molecular structure and chemistry of glasses are modifiable, glasses with tailored biological properties can be designed for use in bone-tissue engineering. Ectopic bone growth was observed in canines implanted with Bioglass® with holes ranging from 100 to 600 μm [113]. Bone regeneration in rabbit femoral defects was aided by silica-calcium phosphate scaffolds with varying porosities (51, 47, and 43% created by lowering the silica content) and a wide variation of pore diameters from 10 to 300 μm [114]. Because BG bioactivity declines with increasing crystallinity an amorphous structure is advantageous to BG bioactivity [87]. The amorphous, on the other hand, mechanical strength and reduces its durability due to their construction as BGs limits their application due to their low fracture toughness, particularly when porous (Fig. 3).

The first 45S5 Bioglass® was made by melting high-purity oxides at 1370 °C. A frit is made by quenching the molten mixture with water. To get the desired particle size distribution, the next procedures are drying and grinding. Moulds and rods can be made from the Bioglass, or as-cast parts can be made [108, 112]. This technique is thought to be easy and workable for larger quantities of goods. However, the evaporation of P_2O_5 at such high temperatures is a drawback of the approach. The sol-gel method has been the subject of recent research. This methodology allows for

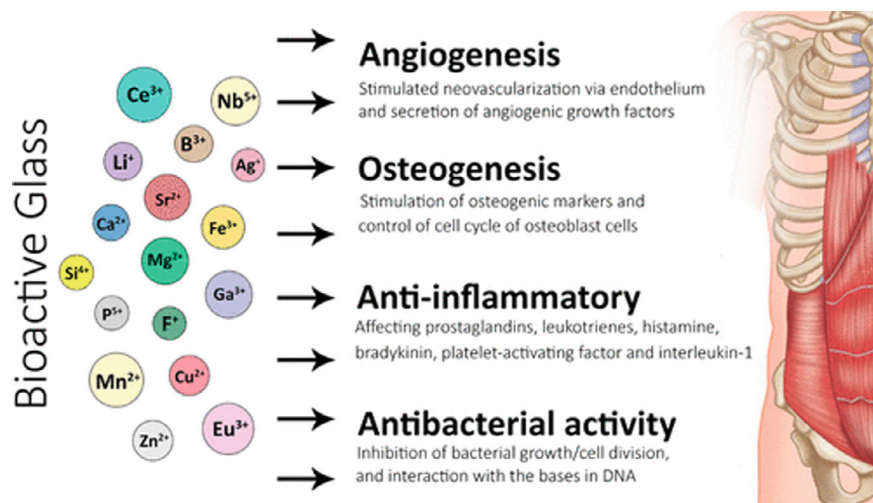


Fig. 3 Application of bioactive glass ceramics. Adapted with permission from Ref. [18]

the possibility of obtaining a homogeneous composition at a lower temperature than the conventional procedure [110]. In addition, a technique that prevents end product contamination is desired if clinical applications are being explored. Supercooled liquids, quick solidification, and suppression of heterogeneous nucleation are all benefits of utilizing the containerless technique rather than the conventional method, in which interactions between the prepared samples and the crucible wall cause internal stress [115].

3.1 Glass Ceramics

In order to meet the shortfalls of bioactive glasses, Glass ceramics were developed. Glass ceramics are glasses with improved nucleation due to the use of self-nucleating compositions or the inclusion of an external nucleating agent [27, 108, 111]. The end product is a substance that contains tiny crystals. The ultimate qualities of glass ceramics depend on a number of variables, including crystal orientation, intergranular bonding, percentage of crystallinity, crystalline phase distribution, any remaining glassy phase, and grain size. The above mentioned parameters can be managed by regulating the base composition, nucleating agent selection, and heat treatment schedule [27, 108, 111]. The Lithia-silica ($\text{Li}_2\text{O}-\text{Si}_2\text{O}$) system was the primary focus of early glass ceramics research. Alumina was used later to further disrupt the initial formula ($\text{Li}_2\text{O}-\text{Si}_2\text{O}-\text{Al}_2\text{O}_3$). In a Pyroceram-like system, β -spodumene, a polymorph of LiAlSiO_4 , is precipitated to occupy the vast majority of the glass ceramics volume. Here, Al^{3+} takes the role of Si^{4+} in the network structure, and Li^+ is kept nearby to preserve the electrostatic equilibrium. In the previous system, MgO , Al_2O_3 , and SiO_2 were used instead of Lithia. TiO_2 , ZrO_2 , and SnO_2 are the nucleation agents. Na_2O is used in place of Lithia in an alternative formula. Trade names for some GCs have been developed; examples include Mica GC (Dicor[®]), Apatite-Devitraite GC (Ceravital[®]), and Mica-Apatite GC (Bioverit[®]) [27, 108, 110]. Glasses and glass ceramics with added CaO and P_2O_5 have been studied extensively and manufactured as bioactive or surface-active biomaterials. One of the main components of bone and teeth is carbonated apatite, therefore the chemical interaction between phosphate-based materials and apatite is an advantage. Phosphate glasses and glass ceramics rely on networks of phosphate tetrahedra that share corners to form their structures. It has also been established that apatite-mullite glass ceramics based on $\text{SiO}_2-\text{Al}_2\text{O}_3-\text{P}_2\text{O}_5-\text{CaO}-\text{CaF}_2$ compositions can generate fluorapatite and mullite after undergoing a certain heat treatment process.

Apatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{O},\text{F}_2)$] and wollastonite [CaOSiO_2] are two crystalline phases in the $\text{MgO}-\text{CaO}-\text{SiO}_2$ system that have gained increased attention among GCs. The apatite-wollastonite glass-ceramic (A/W GC) system was discovered by Kokubo et al. in 1982 [2]. This materials strong mechanical properties (such as toughness and strength) are maintained for a long time in the body environment, and its biological ability to spontaneously connect to living bone (in a short duration) makes it particularly appealing [2, 25]. Wollastonites phase inhibits the linear development

of cracks and causes a reinforcing effect [108], while apatite's phase is responsible for the spontaneous bonding to natural bone. Due to its superior characteristics, Al/W GC is increasingly being employed as a substitute for real bone [27, 108, 110].

3.2 Alumina

Aluminum oxide (Al_2O_3) also commonly known as alumina is one of the most important ceramic filler for biomedical field utilized in total-hip and knee arthroplasty to repair and replace damaged bone tissue and joints. They are inert, but can be utilized to deliver medications and stimulate tissue regeneration when combined with other materials like biodegradable polymers. Alumina is anticorrosive and trustworthy in vivo behavior can be traced back to the chemical stability of the crystal lattice, a symmetrical three-dimensional structural arrangement of the constituent ions inside a crystalline solid that contributes to biocompatibility. Surfaces of implants made from these materials typically have free hydroxyl radicals ($-\text{OH}$), which interact with bodily fluids to form a lubricating layer. The first commercially available bioceramics for dental implant use and acetabular cup replacement in complete hip prostheses were alumina based materials [19, 37, 43, 116]. Because of its low surface energy and silky smoothness, alumina has the best of both things in terms of hardness and abrasion resistance. As a result, a biomimetic coating on alumina has been employed to create a bioceramic that has been successfully implemented as synthetic bone grafts or as a porous prosthetic device. Bone screws, alveolar ridge and maxillofacial reconstruction, ossicular bone substitutes, corneal replacements, segmental bone replacements, and blade and screw and post-type dental implants are just a few other clinical applications of alumina prostheses [37]. When zirconia is added to alumina ceramics (Zirconia toughened alumina), the low fracture toughness of the alumina ceramics is much increased, and the resulting composite material has improved toughness and tribological properties [43]. Zirconia toughened alumina (ZTA) combines the beneficial qualities of monolithic alumina and zirconia, since it is composed of an alumina matrix phase (70–95%) and a zirconia polycrystals (TZP) secondary phase (5–30%) [117]. The risk of impingement and dislocation is decreased, and stability is enhanced, because of ZTA ceramics low sensitivity to stress-assisted deterioration [118]. Alumina brittleness, fatigue strength, and mechanical strength are all affected by the purity, size, and distribution of its crystals, in addition to the materials density. It is utilized to make endosseous implants for use in orthopedics and maxillofacial surgery because of its strong mechanical strength [22]. Alumina implants have a low surface roughness ($R_a \leq 0.02 \mu\text{m}$) and a tiny average particle size ($\leq 4 \mu\text{m}$).

3.3 Zirconia

In the mid-1980s, research began on using zirconia ceramics as a biomaterial for total hip replacements. The goal was to create ball heads for hip replacements that could surpass the limitations of alumina ceramics. Early research focused on magnesia-partially stabilized zirconia, which had small acicular precipitates within the matrix of cubic grains. However, most developments shifted towards yttria-stabilized tetragonal zirconia polycrystal (Y-TZP), which is formed by submicron-sized grains and has become a standard material for clinical applications [119–122].

One reason for the shift to Y-TZP is that the acicular phase in MgPSZ can negatively affect the wear properties of the polyethylene used in acetabular components. Y-TZP also requires stringent process control during the aging steps, which may not be suitable for mass production. Despite these challenges, zirconia was widely used in hip joint arthroplasty until a recall in year 2 K led to its phasing out. Currently, Y-TZP ceramics are primarily used in the dental industry [25, 123, 124]. They are used as blanks for computer-aided design and computer-aided manufacturing (CAD-CAM) machining of dental crowns, bridges, implants, and abutments [125, 126].

Zirconium dioxide, commonly known as zirconia, is an oxide that can exist in different crystal structures depending on the temperature. At room temperature, it has a monoclinic structure, but it changes to a tetragonal structure at higher temperatures and then to a cubic structure at even higher temperatures. These structural changes result in volume and shape changes in the crystal cells. Zirconia was initially used as a refractory or pigment, but its properties were further explored when the stabilizing effect of certain oxides was discovered. Yttria oxide was found to stabilize the tetragonal phase, leading to the development of Yttria-Tetragonal Zirconia Polycrystal (Y-TZP) ceramics [119, 122, 123, 127]. Y-TZP is composed mainly of tetragonal grains, with minor amounts of monoclinic and cubic zirconia. The addition of stabilizing oxides allows for the transformation of tetragonal grains to monoclinic, which contributes to the materials toughness and resistance to cracking. The transformation is explained in terms of a shift in free energy, which is influenced by factors such as strain energy, chemical free energy, and surface energy. The mismatch in thermal expansion coefficients between the different phases of zirconia leads to processing challenges in sintered polycrystals. The size of the grains also plays a role in the energy shift during the phase transformation. Overall, understanding the crystal structure and phase transformations of zirconia is crucial for engineering applications, such as in the development of ceramics for various industries, including biomedical applications [3, 7, 117–119] (Fig. 4).

Zirconia is a ceramic material that possesses impressive mechanical properties, thanks to its transformation toughening mechanism. Unlike metals, zirconia does not exhibit plastic strain before fracturing, which serves as a dissipative mechanism for fracture energy. While zirconia may have a higher fracture strength than metals, it is not as tough, with a toughness of only 9–12 MPa m^{1/2} compared to 4–6 MPa m^{1/2} for high-density alpha-alumina. In terms of bending strength, zirconia performs well, with a strength of over 900 MPa in 4-point bending tests. This makes it comparable

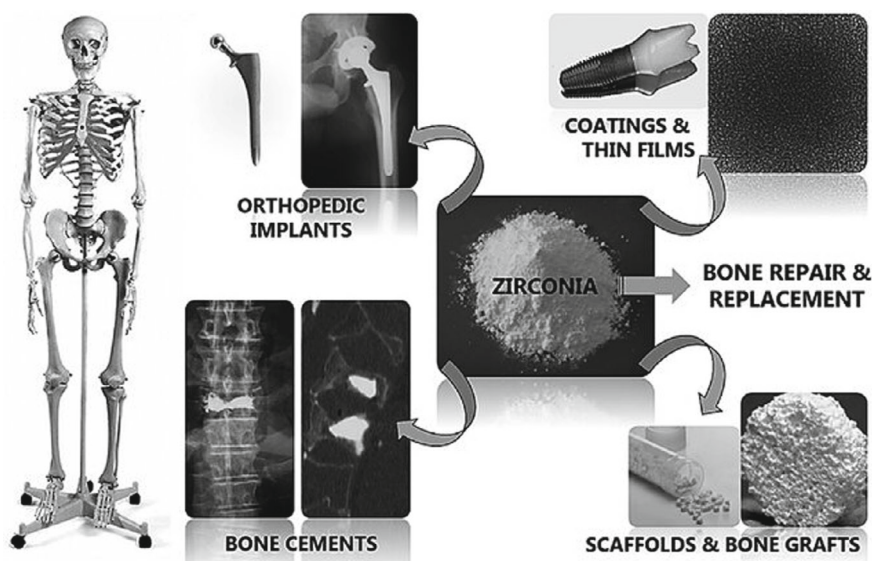


Fig. 4 Modern bone replacement and repair utilizing zirconia ceramics as a biomedical material. Adapted with permission from Ref. [3]

to several alloys. Additionally, zirconia elastic modulus of about 200 GPa is similar to that of titanium alloys, making it easier to design metal-to-ceramic connections [7, 22, 120–122, 124].

Zirconia hardness and thermal conductivity are particularly relevant for its use in structural applications in dentistry, along with its bending strength and toughness. It has a low thermal conductivity, about one-tenth of alumina, which means caution must be exercised when grinding zirconia components at high speeds. The resulting thermal spikes could degrade the materials mechanical properties over time. This is especially important to consider in situations like lubrication deprivation on the bearing surfaces of a total hip replacement. Zirconia has been avoided in ceramic-on-ceramic total hip replacement bearings due to its low hardness compared to alumina. It is important to note that zirconia behavior is highly dependent on various factors, including the selection.

3.3.1 Alumina–Zirconia Composite Fillers

The zirconia transformation kinetics are greatly slowed down when alumina is added to the material, creating an alumina–zirconia composite ($\text{Al}_2\text{O}_3\text{--ZrO}_2$). Since zirconia was deemed unsuitable for use in orthopedics, the two-phase alumina–zirconia material has been promoted for these purposes [118, 124]. When zirconia is the dominant phase, even a small amount of alumina can slow down the kinetics of the phase shift, however this explanation is not yet complete. Alumina-Toughened

Zirconia (ATZ) ceramics is a typical term for this type of ceramic composite. Instead, alumina with a trace quantity of zirconia added to it, known as zirconia-toughened alumina (ZTA) or alumina matrix composite is also very resistant to hydrothermal ageing [117]. Furthermore, the slower ageing kinetics is likely more apparent in these materials, where alumina is the dominant phase, for topological reasons. Due to its presence in the zirconia phase, which is uniformly dispersed throughout the material, the percolative pathway risk is reduced, and degradation cannot proceed deep inside the material. Since the monoclinic zirconia rises during hydrothermal treatment, the ZTA roughness remains constant. The rigid main alumina matrix also acts as a barrier to the transition.

Despite the challenges posed by hydrothermal ageing, the two approaches to design demonstrate the fundamental material strategy taken by material scientists: high-fracture toughness may be the primary characteristic in an ATZ, whereas hardness may be the dominating feature in a ZTA. Due to its superior qualities for pair bearing application in THA and, presumably, the general aversion to zirconia-based materials, ZTA has been the dominant material in this field in the previous decade.

3.3.2 Zirconia Toughened Alumina

The idea behind Zirconia-Toughened Alumina (ZTA) is to use zirconia as a reinforcing element to significantly boost the materials fracture toughness and strength by exploiting zirconia tetragonal to monoclinic phase transformation, as described earlier, while maintaining or improving the alumina properties—hardness, stiffness, and thermal conductivity—that have made it successful for more than 40 years as implantable ceramic in The goal of improving mechanical characteristics is to make alumina tabular parts last longer and be less prone to failure, while also giving designers more leeway in creating new and interesting shapes. The stabilization of the zirconia tetragonal phase at body temperature is crucial for the required toughening process, and the ability of zirconia phase transformation ($t\text{-ZrO}_2$ to $m\text{-ZrO}_2$) in ZTA ceramics is a necessary condition for their superior mechanical properties. As a result of its microstructure and grain size, Y_2O_3 is the most used tetragonal zirconia chemical stabilizer. However, stabilization must be accomplished in such a way that no material deterioration will occur in the body environment, i.e. in aqueous liquid (synovia), which is known to potentially initiate phase transformation at the surface of ceramic components [52].

3.3.3 Alumina Toughened Zirconia

A novel alumina-toughened zirconia material (ATZ) discovered by Begand et al. [124] in 2004. In 2010, Mathys Orthopedic GmbH (Mörsdorf, Germany) launched a commercially available material to the global market. Mathys ATZ ceramic composite, sold under the trade name Ceramys®, was an attempt to combine the benefits of Al_2O_3 and ZrO_2 monolithic materials while avoiding their drawbacks,

similar to CeramTec GmbH ZTA solution presented a few years before. According to Mathys, the material and its components have outstanding qualities, and in some circumstances, they even outperform the ZTA counterpart. Despite this, ATZ has not yet seen the widespread adoption of its rival, with only 30,000 components having been reported sold by Mathys in four years. The fact that Mathys is a prosthetics firm with full THA implants in its portfolio makes it difficult to offer their ceramic bearing solution to other prosthetics companies, which may be the root cause of the problem. Furthermore, alumina being a significantly cheaper raw material than zirconia could account for the pricing pressure in the THA field.

4 Conclusions

Ceramics fillers are indispensable materials for use in biomedical applications. Despite their widespread usage in orthopedic and dental implants, these ceramic fillers may also be useful in a variety of other tissue engineering. Biomaterials, growth factors/bioactive compounds, and cell combinations can all benefit greatly from tissue engineering contributions. Some of the most pressing issues in the area now involve implementing novel approaches that hold the promise of future breakthroughs. Ceramic fillers have useful properties including chemical inertness in biological media, hardness, and biocompatibility, but they also have a low resistance to traction. Improving the mechanical integrity of the ceramics upon implantation and ensuring adequate porosity for the cellular adhesion, proliferation, and differentiation is a primary focus of current research into the chemistry, composition, and micro- and nanostructure of the materials. Scaffolds, fibers, and hydrogels based on three-dimensional (3D) microstructure have been the primary focus of biomimetic techniques for tissue engineering scaffolding. In addition to being biodegradable and biocompatible, the high water content of the latter is also a major selling point. Although great progress has been made in the field of tissue engineering, more work needs to be done to make this approach clinically practical. Long-term mechanical strength, particularly the fatigue limit under periodic external load, and the underlying hierarchical structure of bioceramics should be the focus of research and development efforts.

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Different Types of Fiber in Polymer Matrices for Biomedical Engineering



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Abstract Fiber-reinforced polymers have been emerging as a promising candidate for biomedical application owing to their unique properties. Since biomedical applications mandates stringent safety aspects prior to its interaction with the human body, different types of reinforcing fibers, including bio-based fibers or synthetic ones such as carbon, glass, and aramid, have been tailored to integrate with the biological systems to ensure its compatibility. Apart from the nature of fibres and its characteristics, their interaction with the polymer matrices, significantly improve the composite's overall performance. Several surface modifications on fibers were employed to augment the fiber-matrix interfacial adhesion and to mitigate the complications due to stress transferability of the composites. With a growing interest on environmental responsibility, future market will prioritize the development of eco-friendly fiber reinforced polymer materials. Relying on sustainable practices and life cycle assessment will ensure the development of next-generation devices and implants to address the evolving needs and preferences in healthcare sector.

Keywords Natural fiber · Synthetic fibers · Fiber-reinforced composite · Biomedical application

1 Introduction

Recent advancement in science and technology embraces the potential of fiber-reinforced polymer (FRP) composites among other conventional materials. FRPs have gained considerable attention in the field of biomedical applications owing to its unique combination of properties, along with renewability and biodegradability [1]. The low fracture strength and high density of ceramic-based compounds are of great concern and have driven the evolution of FRP composites (FRPC). The fibres

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are better reinforcements in terms of low cost, light weight, abundance, and degradability. Furthermore, the foray into green materials has also explored numerous fibre-reinforced composites that render superior performance for drug delivery systems, dental and biomedical implants and tissue engineering applications. FRPs possess the advantage of tunable impact strength and modulus depending on fibre and the polymer matrix interactions. Due to the synergic physico-chemical properties, natural and synthetic fibers are extensively investigated within various polymer matrices [2]. Since FRP composites display low elastic modulus and high strength simultaneously, they are promising in biomedical applications. This chapter dwells on the prospects and viabilities of various types of fiber reinforcements in polymer matrices suitable for biomedical applications. Conventionally, carbon, glass, wood, and cellulose are explored as fibers in thermosetting polymers. Apart from the nature of fibres, their quality, orientation, composition, as well as interaction with the matrices, govern their mechanical and thermal characteristics significantly.

2 Overview of FRPs in Biomedical Application

In pursuit of efficacious biomedical devices, various bio-based and biodegradable polymer matrices are widely being used after the inclusion of fibers. Besides, numerous thermoplastic polymers such as polystyrene, polypropylene, and polyether ether ketones have also been explored as matrices because of their desirable mechanical strength, and chemical resistance. The performance of FRPs in biomedical devices is governed mainly by fibre-polymer, fibre-fibre, and polymer-polymer interactions [3]. Although synthetic fibers possess better characteristics, attributing higher strength to the composites [4, 5], natural fibers reinforced composites have become instrumental for technologically advanced biomedical applications owing to their abundance and biocompatibility. Studies reveal that the ‘go green approach for the sustainable future’ is finding its way into biomedical fields [6]. Despite its wide acceptance, the main challenge lies in its lack of dimensional stability and very high moisture absorption capacity. Since their hygroscopic property affects overall thermal and mechanical properties, it is noteworthy to attribute relevant modifications to improve the characteristics of natural fibers. Various approaches include physical and chemical treatments, essentially endow better compatibility between natural fibres and polymer matrices [7, 8]. Additionally, the tendency of aggregation of natural fibers and thereby their low degree of homogeneous distribution within the matrices lacks good adhesion between polymer and fiber restricting their use without modification [9]. Due to the stress exerted on fibers during polymer processing such as extrusion, injection moulding, and thermoforming etc., it requires careful optimization to yield composites with better fiber-polymer interfacial adhesion [10]. Besides fibers, the choice of polymer matrices also plays a vital role in the composites protecting the fibers from natural abrasion.

3 Selection Criteria of Fibers Reinforcing Agents

The properties of FRPC depend on the nature and the properties of reinforced fibers, matrix, source of components, and other parameters in line with each other. The fiber obtained from various habitats or resources differs in terms of its moisture absorption, crystallinity and consequently renders different properties in the same matrices [1, 11]. The peculiar hydrophilicity of fiber often leads to compatibility issues within hydrophobic matrices. The consequent poor adhesion hinders these composites exhibiting superior physico-chemical and mechanical properties. The selection criteria for fibers as reinforcing materials depend on their desirable properties according to their end use. The most essential parameters in fibre selection are availability, density, tenacity, tensile strength, and Young's modulus; nevertheless, biocompatibility is another key need for biomedical applications [12].

In comparison to stiff metals, FRP composites exhibit relatively fewer mechanical properties; however, a well-oriented alignment of the fibers within the polymer matrix can augment the properties substantially. Corrosion resistance is indeed a crucial factor for bio-implants, as the consequent release of metal ions can potentially cause toxic reactions such as inflammation and long term health issues [13]. Unlike stainless steel and titanium alloys, FRP-based implants can mitigate the risk of corrosion, magnetic effects, anode-cathodic reactions in the body, and other adverse effects. Ceramic fibres have strong biocompatibility and great compression resistance, but their limitations include high density, brittleness, poor fracture strength, difficulties in fabrication, and a lack of resilience. Therefore, FRPC materials have emerged as potential alternative materials.

An efficient fibre reinforced composite minimises stress localization and dissipates the stress equally in all directions. This property can be achieved merely by having a homogenous fibre distribution within the matrix [2]. Depending on the alignment of fiber distribution, two types of FRP composites are possible, anisotropic and isotropic. Anisotropic FRP is conferred by uniform or continuous distribution, and the latter belongs to the non- or discontinuous short fiber distribution [14]. Better fiber—matrix interphase interactions are achieved by improving physical and chemical adhesion, fibre-to-fibre interlocking, and friction. The overall mechanical properties of FRPC are influenced by the optimum loading ratio of fibers in composite [15]. FRP possessing high wear resistance with a low coefficient of friction is enormously desirable to prevent sliding against tissues in the body. Furthermore, various additives for antimicrobial, anti-inflammatory, antioxidant, and UV stability have been demonstrated to impart specific properties to FRPCs [6].

The evolution of the biomedical field has exposed fiber-reinforced polymer composites with superior properties and recognised various means to obtain them. Recent advancements in fabrication methods and processing have led to the exploration of FRPCs for the development of novel biomedical devices for clinical applications.

4 Properties of Polymer Fibers

FRPCs have a higher potential for structural biocompatibility than homogenous monolithic materials and are utilised for numerous biomedical applications owing to their chemical stability, cost-effectiveness, and ease of processing. Changing the volume and arrangement of reinforcing fibres has a significant impact on their qualities depending on the physiological and mechanical conditions [16]. A better matrix-reinforcement is required to ascertain their compatibility with the host body [17]. During their processing, fibers might undergo extremely high stress, and hence it is very difficult to control their shape and orientation. However, a better orientation can be achieved by incorporating fibers with a length that is close to the critical fiber length [10]. Furthermore, the strength of fiber-reinforced composites is significantly dependent on interfacial compatibility and effective stress transfer [18]. In case of biomedical devices and implants, it is essential to ensure that FRPCs do not trigger any adverse reactions within body leading to its toxicity and inflammation [12]. Figure 1 displays a schematic diagram of the natural fiber reinforced polymer matrix interphase [15].

The high water absorption capacity of natural fibres is often considered a short-coming; however, it has been found advantageous in diapers and sanitary products that require water absorption applications. Cellulose-based fibre reinforcements can effectively retain water, making them ideal for such applications. The thermal and mechanical properties of the FRP composites depend on the nature of the fibres reinforced and are governed by their loading ratio and its interfacial characteristics. Delving into the kinds of interactions and investigating the other multifarious properties necessitates adopting various testing and characterization methods. The

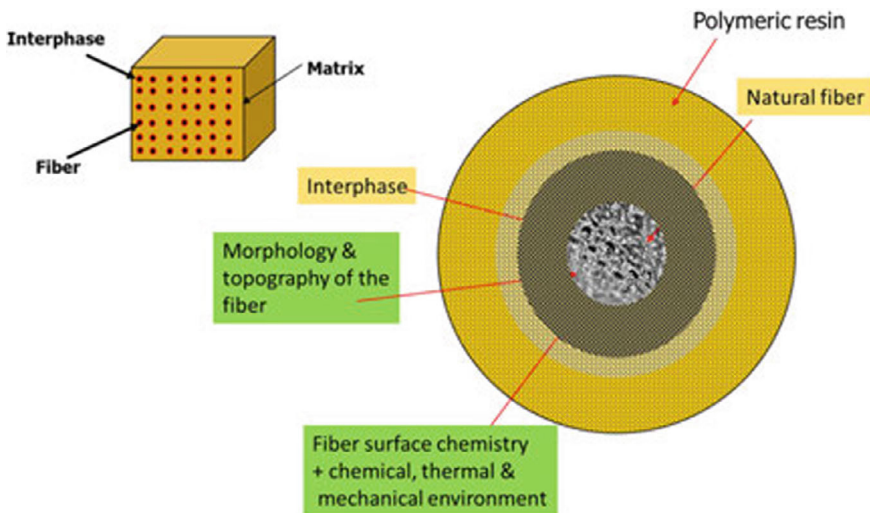


Fig. 1 Schematic of the concept of natural-fibre-matrix interphase [15]

analysis of FRPCs is done through pull-out tests, the microbond test, and single fibre fragmentation tests [19, 20]. In fragmentation tests, the embedded fibre in the matrix has to be loaded axially in the same direction as the fibre up to a certain strain, and samples are not allowed to break. The fewer the fragments, the better the quality of adhesion. Further, the critical length of the fibre, its tensile strength, and its interfacial shear strength are also very important to understand, whereas in the pull-out and microbond tests, the fibre embedded parts are being tested [20].

5 Classification of Fibers

Natural, synthetic polymers as well as ceramic fibers are being explored as reinforcements in numerous biodegradable applications.

6 Natural Fibers

Natural fibres originated from plants, animals, or microorganisms normally exist as structural or storage polymers. Recently, with the growing demand for greener composites, natural fibre-reinforced composites have garnered enormous attention and are widely accepted for biomedical applications due to their non-immunogenicity. Although the strength of plant natural fibres is typically inferior to that of synthetic fibres, the properties of a natural-fibre-reinforced polymer composite are still adequate for many domestic and household purposes. Based on their origin, various natural fibres are classified into leaf fibres (pineapple, screw pine); fruit fibres (cotton, palm); bast fibres (hemp, kenaf, jute, flax, etc.); and grass fibres (sugarcane bagasse, bamboo). Animal-based fibres such as silk, wool, and hair are suitable considering their superior strength and bioactivity; nevertheless, their use is restricted in biomedical applications due to their high cost and relatively low accessibility [21, 22].

Biofibres possess a complex 3-layered structure consisting of primary, secondary, and tertiary cell walls. The cell wall is made up of a matrix of lignin hemicellulose-embedded cellulose microfibrils. The lignin enhances the rigidity, whereas hemicellulose functions like cement between cellulose fibrils. Components such as pectin and wax present in natural fibres need to be removed prior to their inclusion as reinforcing agents in polymer matrices to ensure better interaction with the matrix. Therefore, the pristine bio-fibres are not preferable due to their poor adhesion with the matrices [21, 23]. Natural fibres provide an uneven distribution of fibres within the matrix, contributing to increased moisture retention and increasing the processing problems [15]. The water retention in fiber-reinforced composites depend on numerous factors such as temperature, orientation, and permeability [24]. In this context, different approaches have been attempted for the modification such as physical, chemical or physico-chemical treatments to enhance the properties of reinforced composites. The

modification methods such as solvent extraction, heat treatment, corona and plasma treatments, laser, γ -ray and UV bombardment are commonly used to accomplish physical modification [15]. The chemical modification process such as alkali, silane, acrylation, acrylonitrile grafting, iso-cyanate includes treatments (Table 1). Apart from that, maleated coupling treatment using maleic anhydride is found to be an effective method to augment the interaction between the fibre surface and the polymeric matrix. These surface-treated natural fibres exhibited superior characteristics in terms of dimensional and mechanical strength to the composites in comparison to the pristine ones [25].

In general, the properties of the FRPs are primarily influenced by factors such as their morphology, dimensional stability, microstructure, aspect ratio, hydrophilicity, or hydrophobicity. Additionally, the microfibrillar angle, which represents the angle between the fibre axis and the microfibrils within the material (up to 30 nm in size), also plays a pivotal role in determining the mechanical properties of these reinforced composites. The greater the fibrillar angle, the better the ductility, while a lower angle indicates stiffness. Natural fibres with greater mechanical qualities often have

Table 1 Chemical modification of plant-based fibers for FR polymer composites

S. No	Fiber	Process	Result	Reference
1	Jute	Cellulose alkalization	Improved crystallinity, hydrophobicity	[30]
2	Sisal		Crystallinity, mechanical properties	[30]
3	Flax		Roughness, thermal properties	[8]
4	Henequen	Silane-coupling treatment	Better interfacial load transfer	[27]
5	Sisal		Improved mechanical and hydrophobic properties	[28]
6	Palm	Acetylation	Decrease hydrophilicity	[31]
7	Kenaf	Peroxide treatment	Increase in crystallinity index and surface roughness	[32]
8	Sisal	Benzoylation treatment	Increase hydrophilicity and other properties	[33, 34]
9	Banana	Potassium permanganate treatment	Increase hydrophilicity and other properties	[35]
10	Banana	Stearic acid treatment	Increase hydrophilicity and other properties	[35]
11	Flax	Isocyanate coupling treatment	Increase hydrophilicity and other properties	[36]
12	Banana	Maleated coupling	Increase hydrophilicity and other properties	[37]
13	Pine	Acrylation and acrylonitrile grafting	Increase hydrophilicity and other properties	[38]

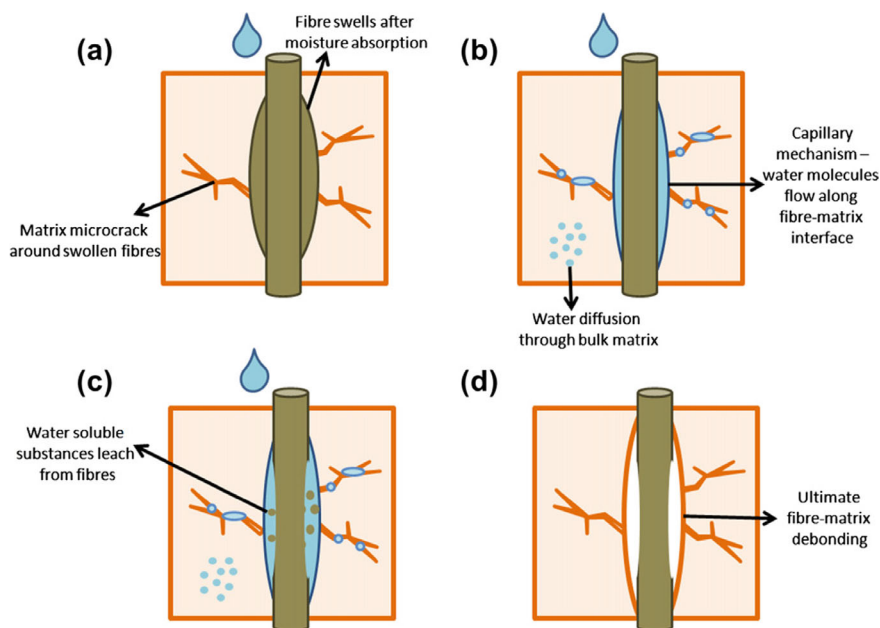


Fig. 2 Schematic diagram on the effect of water on fiber-polymer interface [6]

a higher cellulose content, a longer cell length, and a smaller microfibrillar angle [25]. Figure 2 displays the effect of water on fibre-polymer interface [6].

6.1 Cellulose Fibers

Cellulose is the most essential structural component in plant-based biofibers and one of the most commonly used reinforcing agents. It encompasses almost 10,000 D-pyranose units linked together by 1,4-glycosidic connections. They are hygroscopic and linear, with hydrogen bonding and van der Waals forces. These intermolecular forces impart crystallinity in addition to high chemical stability and mechanical strength; however, solubility can be achieved only when inter- and intra-molecular hydrogen bonding is effectively disrupted [26]. The degree of crystallinity mainly depends on the habitat, source, and processing method. The fibres obtained from cotton, algae, and bacteria exhibited 40%, 93%, and 75% crystallinity, respectively [23]. In general, more cellulose increases tensile strength and Young's modulus; nonetheless, it can also cause excessive moisture absorption due to the degree of voids [27]. Hence, to comprehend the modification of the cellulose, several approaches attempt to improve its microstructure, wettability, surface morphology, and adhesion to the matrix. Furthermore, hydrophilicity in cellulose was controlled by lowering the number of hydroxyl groups through grafting with acrylonitrile or triazine [28].

Different chemical modification processes attribute different properties, and hence the suitable method is chosen according to the application.

Cellulose from various sources has exhibited promising characteristics for biomedical applications; however, the fibre from hemp demonstrated superior reinforcement in terms of tensile strength when compared to kenaf, sisal, and jute fibre composites. Among various fibres, the lowest strength was rendered by the coir-fibre-reinforced composites. Additionally, studies revealed that hollow fibres would weaken the net cross-sectional area and consequently decrease the strength of composites [29]. The cotton or ramie fibres demonstrated relatively high moisture absorption and retention in their composites, which completely disturbs the integrity of the composites. This absorption of moisture is attributed to the presence of micro cracks at the interface. Therefore, controlling various parameters during the manufacturing process, such as low humidity or vacuum conditions, followed by the drying process, is very crucial. Another parameter is the fibre percolation threshold within the matrix, which ensures better fibre-polymer interface interactions.

Furthermore, nanotechnology has devoted fibres to smart biomedical applications owing to their enhanced surface area and superior properties. The fabrication of nanofibers of cellulose, chitosan, and silk mainly depends on techniques such as electrospinning and self-assembly methods [39]. The nanofiber-reinforced composite offers superior mechanical strength, flexibility, thermal stability, controlled water uptake, controlled release, and excellent skin adhesion properties [40].

7 Animal Fibers

Unlike plant fibres, animal fibres such as silk, wool, and hair are principally composed of structural proteins. These fibres are being chemically modified by coupling (glutaraldehyde, cyanuric chloride-activated) amino acids (sulfated tyrosine or azo-modified tyrosine) or grafting (polymethyl methacrylate, tyrosine-catalysed) reactions [4, 12, 41]. These modifications significantly contribute to the functionalization of fibres by enhancing physicochemical properties or incorporating novel properties. One of the major components of hair, nails, feathers, or skin is a structural protein, namely keratin, which can function as a synthetic extracellular matrix owing to its unique properties. It also functions as a scaffold for cell proliferation. Over the last decade, a considerable number of studies have reported various isolation methods for a broad range of biomedical functions and applications [42, 43]. The brittleness of keratin-reinforced composites is diminished by incorporating additives, making them suitable for biomedical applications such as cell growth, wound dressing, and drug delivery [3]. Furthermore, a keratin fibre derived from sheep and chicken feathers with appropriate modifications is being investigated for potential biological applications.

7.1 *Silk Fibroin*

Among various animal-based fibres, silk obtained from silkworms or spiders stands out among the family of structural fibrous proteins [16]. The most prevalent and widely used silk is obtained from silkworms and is comprised of monomeric units of self-assembled amino acids in the sequence [44]. They possess exceptional physico-chemical and mechanical properties endowed by strong hydrogen bonding and weak van der Waals interactions find application in biomedical fields, especially sutures [3]. The silk fibre spun from cocoons has an approximate length of 1000–1500 m and is conglutinated by an outer and inner layer of sericin and fibroin in the ratios of 25% and 75%, respectively. Sericin is an envelope that has antibacterial, UV-resistant, and moisture-controlling properties; however, it has a few drawbacks in terms of its biocompatibility and hypersensitivity. Therefore, removing sericin from silk is an important step prior to their application.

Although the silk fibres have a non-uniform cross-sectional geometry with respect to their shape and size, their resemblance to a block polymer consisting of both hydrophilic and hydrophobic regions is highly advantageous. Amino acid coupling and grafting processes are the primary means of achieving these chemical changes. The reinforcement with polymer matrices is greatly facilitated by their reactive functional groups and is an appropriate candidate for tissue engineering scaffolds owing to their ease of processability, morphological flexibility, well-regulated proteolytic biodegradability, and interconnected porous structure, which is greatly desirable for tissue engineering scaffolds. Silk fibres demonstrate high tensile strength in comparison to glass fibres or many other synthetic fibres. Additionally, they are stable at physiological temperatures and resist failure under compression [45]. It exhibits a high rate of bone repair, ligament repair, and tendon repair. Depending on applications, they can also be processed into foams, films, fibres, and meshes. Overall degradation of silk *in vitro* and *in vivo* marks its utility as a biodegradable scaffold for the slow ingrowth of tissues. Silk, which was reinforced with polylactic acid, has displayed better elasticity, ductility, and controlled re-absorbability in the human body [46].

Owing to their territorial and predatory nature, spider silks are difficult to obtain in sufficient quantities as compared to silk from silkworms. Spider silk, when combined with other polymers, is found to be a potential material for tissue engineering, drug delivery, etc. The recombinant spider silk protein has no cytotoxic or inflammatory responses. Noteworthy, these fibres augment the secretion of insulin and hence blood glucose levels [47]. Furthermore, the self-assembly of nanosilk on polycaprolactone in conjunction with a high-porosity and durable ceramic substrate is desirable for bone regeneration [48]. Reinforcing with nylon fillers, it displayed higher hardness but lower flexural and tensile strength than jute and spider silk reinforcements [49].

7.2 *Chicken Feather Fiber*

The feather fibre from chicken has gained tremendous interest as a reinforcing material due to its viability for product design and industrial applications. The average diameter was observed to be in the range of 5–50 m, which comprises 91% keratin, 1% lipid, and 8% water. A higher Tg (235 °C) indicates the strong intermolecular interaction between fibres [31]. The key factor influencing the impregnability of the polymer matrix to synthesise reinforced composites would be the aspect ratio of the fibres. As a result, the stress transferability and shear strength of the composites would be affected by the short- or long-range order. It can also act as a barrier to the flexibility of the polymer chain, enhancing thermal characteristics and fracture toughness. The adhesion of chicken fibre within polyethylene and polypropylene matrices was significantly improved by maleated polyethylene and maleated polypropylene additives [50].

7.3 *Chitosan/Chitin Fiber*

Chitosan or chitin fibres are observed as biocompatible wound healing agents in human beings or other animals. It requires a modification process to yield better properties since they are not structural components in animal tissues [51]. One of the most effective methods of modification was by employing tropocollagen, a triple-helical peptide found in connective tissues with chitosan fibres [52].

7.4 *Collagen Fiber*

In the last decade, soft tissue engineering has garnered huge interest, and collagen has been identified as a promising scaffold material [2]. The collagen fibres revealed a unique hyper-elastic behaviour along with prominent mechanical properties similar to those of natural human tissue. Hence, these fibres are considered highly promising materials for biomedical fields, especially for tissue regeneration and healing processes [45].

8 *Synthetic Fibers*

Synthetic fibre reinforcement has received a lot of interest in the quest for high-performance biomaterials. The fundamental advantage of synthetic fibre over natural fibre is that it holds less water and consequently exhibits more stability in complex

physiological conditions. Their adaptability in terms of composition, surface modification, and production technique makes them acceptable for certain biomedical applications. Among synthetic fibres, carbon fibre, fibre glass, aramid fibres, high-performance polyethylene fibres, and basalt fibres are most commonly used. These fibres improve mechanical properties such as strength, stiffness, and impact resistance. By integrating Kevlar, carbon, and PPMMA fibres, which considerably reduce tissue necrosis, concerns about bone cement or implant failure that would occur *in vivo* have been alleviated [53, 54]. The fibre reinforcement helps to lower the temperature during cement polymerization, which in turn helps to prevent tissue necrosis. These synthetic fibre-reinforced cements have not yet been recognised for application in clinical practises despite experimental evidence of greater mechanical strength. This is because of their limitations, including increased viscosity and a corresponding decline in workability.

8.1 Carbon Fiber

Carbon fibres are widely used in high-performance biomedical applications due to their exceptional strength, stiffness, and low weight. They are noted for their superior mechanical and conductivity qualities and are light-weight with a density of $1.6\text{--}2.2\text{ g/cm}^3$ in comparison to compact bones (2.0 g/cm^3) [55]. Due to their high strength-to-weight ratio, light weight, and radiolucence, CFRP-based materials have displaced conventional metal-based medical implants. The radiolucent property of the material explains its efficacy for fluoroscopy, X-ray, or computed tomography (CT) imaging, which is essential in clinic applications [56]. Despite their advantages, CFRPs could be leveraged for widespread biomedical applications, and hence the issues related to their manufacturing and processing must be addressed. These carbon fibre-reinforced composites have been explored in molecular recognition, neurology, and regenerative medicine. It serves as a scaffold to improve support and speed up the healing of both soft and hard wounds. Although there are numerous debates around the use of carbonaceous materials in the medical profession, fascinating findings on their biocompatibility and clinical acceptance promises its scope. The biocompatibility of CFRP composites is seen as being improved by surface modifications or by using biocompatible coatings [46]. Carbon fibre polymer-filled composites rendered better adhesion in comparison to a metal [57]. The percent bone area was found to be significantly greater for the composite implants in the tibia bone marrow in comparison to titanium-6-4 alloys. CFRP composites are employed in the fabrication of prosthetic limbs and orthotic devices due to their light weight and high strength. They are also utilised as scaffolds in tissue engineering applications, as they can mimic the mechanical properties of natural tissues and deliver a suitable environment for cell attachment, proliferation, etc.

With the growing interest, the development of novel materials for tissue engineering, drug delivery, and gene therapy, is achieved with the intervention of carbon nanotubes [41]. Such nanocomposites provide a greater opportunity to tailor the

properties of matrix and biological properties. Chitosan filled with MWCNT reinforced hydrogels synthesized by free radical mechanism using *N,N* methylene bis acrylamide as a cross linker is also a promising material [48]. The progress in mechanical and thermal properties for as-synthesised composites exhibited antibacterial properties against *Staphylococcus aureus*. A scaffold which is highly porous has been fabricated by MWCNT-reinforced poly 3-hydroxybutyrate-chitosan on a silk microfiber knitted substrate was investigated for tissue engineering [49]. Other advantages over metals include non-corrosiveness, superior bonding characteristics, and ease of repair, particularly in dental applications [29].

8.2 *Steel Fibers*

Unlike other biodegradable materials, steel fibers are stable possessing low degradability, which can be advantageous in long-term applications such as implants where consistent mechanical performance is required. These fibers are potentially used for orthopaedic implants, screws and rods, nonetheless, their desirability as biomaterial is highly important. In case of spinal implants, where retaining proper spinal alignment is crucial. Furthermore, it has also been explored for dental applications. Apart, nano-coated steel was also investigated for biomedical application to enhance the surface characteristics [58].

8.3 *Polyester Fibers*

Polyester fibers have found diverse biomedical application and many medical products based on polyester are commercially available in the market signifies their potential. The manifestation of electrospun fibers of poly (lactic-co-glycolic) (PLGA) grounds good mechanical strength and integration demonstrated better cell behaviour [49]. They exhibit high load bearing capacity and hence find suitable for implantable devices owing to their high surface to volume ratio and better interaction with biological tissues. By leveraging the advantages of electrospun PLGA fibers, its potential has been explored for drug release biomedical applications and tissue regeneration applications. Nanocomposite comprising PLGA/gelatin electrospun fibers have also been produced to mimic cardiac tissues [59]. Polymerization of polyethylene glycol hydrogels on the surface of electrospun fibers of polycaprolactum with tunable properties were successfully prepared by immobilizing trithiocarbonate-based chain transfer agent [60].

8.4 Polyethylene Fibers

The texture of the microfibers provides enhanced mechanical strength for the tissue engineering applications. Polyethylene-fiber reinforced polyolefins are utilized for ligament and tendon implant applications. Another example, fiber reinforced ultra-high molecular weight polyethylene possess superior creep and fatigue resistance than the unreinforced ones [53]. These properties are desirable in total knee and hip joint replacement [54].

8.5 Glass Fiber

Glass fibers are silica-based fibers extruded with required diameter and the most conventionally used glass fibers are E-Glass and S-glass fibers [14]. Glass reinforced polymer composites renders high mechanical strength and its light weight nature is desirable for the applications such as limbs, braces and orthopaedic devices. They also find very useful for surgical instrument and devices due to the resistance to corrosion. Glass fiber is the most frequently used filler in dentistry as a result of its chemical resistance and relatively much low cost and hence it is being accepted for clinical practices [55]. The main challenge while utilising a fiber reinforced composite is the compatibility issue due to the shrinkage during polymerization which indirectly influences the tissues. Biostable glass fibers- reinforced composites render antimicrobial properties manifested by the dissolution of the bioactive glass particles that support bone-bonding.

9 Polyamide Fibers

Variety of polyamide fibres exhibit their applications in the immobilisation of proteins, biomedical implants, orthopaedic devices, and antimicrobial agents. Aramid-based reinforcement is utilised for the applications where exceptional mechanical strength and resistance to degradation are required. Orthopaedic implants such as plates, screws, and rods for fracture fixation or spinal stabilisation need high stiffness and compatibility with the tissues. The prosthodontic frameworks comprising an aramid-reinforced composite framework have been meticulously investigated for dental restoration [56]. Typical polyamide, i.e., nylon, reinforced composites with superior mechanical strength are used in implants, which play a vital role in the engineering of dentures and suture materials.

10 Summary and Future Prospects

Fibre-reinforced polymer composites are promising for biomedical applications and hold a range of opportunities for advancing healthcare and medical technology. They possess remarkable mechanical strength and stiffness, making them suitable candidates for load-bearing biomedical applications. They also serve as structural supports for tissue scaffolds, aiding in the regeneration of damaged or diseased tissues. Apart from biodegradable or resorbable characteristics, providing scaffolds is more favourable. Incorporating drug-delivery functionalities within fibre-reinforced polymer composites can enable the localised and controlled release of therapeutic agents. They have the potential to revolutionise treatment strategies by providing targeted therapies directly at the site of interest.

Although several reports are incorporating nanofibers, there is a plenty of room for the development of FRPC with novel properties. The advantages of nanotechnology and the scope of surface modification can be further explored. Integrating stimuli responsive sensor technology would be more advantageous for the development of smart implants and devices. By integrating 3D printing technology, these FRPC can enable complex structures for synergising therapeutic utilization with specific applications. Forthcoming developments in biodegradable FRPC and advanced manufacturing methods will drive the progress for innovative biomedical applications. As current research continues to address the encounters and unravel new possibilities, these fiber-reinforced composites embrace the potential to reorganise the biomedical engineering and contribute considerably to the betterment of human health.

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Synthesis, Properties, and Characterization of Fibrous Filler



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Abstract Creating a complete material that satisfies criteria like durability, manufacturability, low cost, and lightweight is the current goal for material scientists and researchers. At this moment, composites based materials have been come to the forefront which satisfies the demand of society. To fabricate any type composite materials, the reinforcing materials (i.e. fillers) are one most important component which is responsible for achieving the characteristic properties in composite materials. Among various filler materials, fibers have mostly been employed in composite materials as reinforcing materials for the past ten years to give lightweight materials with increased stiffness, modulus, and strength. This chapter points out both natural and synthetic fibers used as fillers in the fabrication of composites for various applications. In addition, the synthesis, characteristic properties, and characterization techniques of both natural and synthetic fibers have been elaborated here. Finally, the chapter concluded with a summarization of future prospects of the fibrous fillers with respect to their application in various sections of society.

Keywords Composites · Reinforcing materials · Lightweight · Natural and synthetic fibers · Future prospects

1 Introduction

The final cost and manufacturing process of construction materials is rising regularly as a result of a shortage of raw materials and the high cost of energy. Alternative components in wood-based building materials and non-biodegradable materials are currently a global concern for energy efficiency, resource conservation, and ecosystem health. Worldwide attempts are being made to develop high-performance products with desirable features and achieve sustainable economic growth [1]. When

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compared to particulate fillers, which provide isotropic properties for the material, using high aspect ratio fillers in the composite may drastically alter the physical properties of composites. Fillers with a high aspect ratio have a large length to cross-sectional diameter ratio. High aspect ratio fillers in composites include fibers, however shorter filament like fillers such as whiskers can also be termed high aspect ratio fillers [2]. The increasing interest in lightweight composite materials with high mechanical properties has moved attention towards fibrous fillers (natural and synthetic) owing to their special characteristic features. There is a strong contest between natural and synthetic fiber in the commercial market but synthetic fiber has a significant advantage over natural ones owing to their high strength and inertia. On the other side, as natural fibers are more environmentally friendly, they are used instead of synthetic fibers [3]. It has been found that the majority of natural fiber composites lack some mechanical properties when compared to composites constructed with synthetic fibers. This is due to the significantly inferior mechanical properties of natural fibers compared to synthetic fibers. In addition, natural fibers are incompatible with various matrices such as polymers, which results in poor fiber/matrix interface adhesion, poor dimensional stability, unreliable characteristics, and high susceptibility of natural fiber composites to moisture absorption. A practical resolve to these problems is to combine natural fibers with another synthetic fiber in the same matrix. Synthetic fibers are especially useful in minimizing these restrictions because of their uniform properties, low moisture absorption, compatibility with polymer matrices, and substantially improved mechanical capabilities. The synthetic fiber most typically used for this purpose is glass fiber, however, aramid and carbon fibers are also being used increasingly regularly. This is due to the cheaper price and characteristics of glass fibers, which are comparable to those of natural fibers. The biodegradability of the composite is decreased by the addition of synthetic fibers, but this is compensated for by the composite's improved mechanical properties and other advantages [4]. Though lots of research articles have been published based on the comparison, but in this chapter we have focused only on commercially important natural and synthetic fibers used as filler/reinforcing materials and discuss their synthesis/extraction, and characterization techniques. The chapter has come to a close with an overview of the fibrous fillers' potential facets in the near future.

2 Synthesis and Properties of Fibrous Fillers

2.1 Natural Fibers

On the basis of origin, natural fibers are divided into three categories: Plant, animal, and mineral. Plant-based fibers are widely employed because they are readily available and recyclable. Depending on the plant portion from which fibers are derived, there are other divisions of plant fibers, including: bast, leaf, seed, fruit, and wood. Cotton, flax, kenaf, jute, bamboo, sisal, hemp, and abaca are the most often used plant

fibers [5]. On the other side, animal fibers such as silk, wool, and hair are mainly composed of proteins. Mineral fibers are seldom favoured in techno-commercial applications owing to their carcinogenic characteristics [6]. Based on this priority, we discussed here the most commercially important natural fibers extraction process with their significant properties.

2.1.1 Cotton

The cotton plant belongs to the Malvaceae family's *Gossypium* genus. Only four of the around 50 species of shrubs and small trees in the genus *Gossypium* are farmed on a large-scale commercial basis globally: namely *G. hirsutum*, *G. barbadense*, *G. herbaceum*, and *G. arboreum*. These four species are distributed worldwide in tropical and subtropical regions [7]. After pollination, these plants' fruits, known as bolls, start to form. Cotton seeds are contained in the boll. Individual cells on the surface of the seeds begin to develop after the flowers have shed, and these fibers develop, inside the boll to produce a hollow cotton fiber [8].

Cotton fiber is a type of natural hollow fiber. This is recognized as breathable fibers as it is very much soft and cool. Cotton fiber can also act as an excellent adsorbent. Water may be held in the cotton fibers 24–27 times their own weight. This fiber is robust, dye-absorbing, resistant to abrasion wear, and temperature-resistant. Cotton fibers are often blended with other fibers (such as nylon, flax, wool, and polyester) to enhance each fiber's greatest qualities because cotton wrinkles easily [9]. Cotton fiber is usually used to manufacture a variety of textile products and cotton reinforced composites are also applied in various automobile applications [10].

2.1.2 Flax

The botanical name of flax is *Linum usitatissimum*, which is a member of the Linaceae family. An annual herbaceous plant called flax is produced largely for its seeds, oils, and fiber. Different flax types have been created for oilseed and fiber. Various retting techniques, such as water, dew, and enzyme retting, have been employed to extract flax fibers. The goal of the retting methods is to separate technical fiber bundles from woody tissue [11].

Flax fiber bundles resemble strands of blonde hair because it is silky, glossy, and flexible. Flax fiber is an extremely breathable fabric that absorbs moisture efficiently. Flax is a very strong fiber owing to the fact that flax's very crystalline polymer system allows its extraordinarily long polymers to make more hydrogen bonds than cotton fiber. Excellent heat resistance is a property of flax. Thus, flax sheets are extremely cool in the summer [12]. The flax fiber's availability, renewability, and biodegradability broaden its range of applications. Along with its more common uses in carpets, towels, ropes, and fabrics, flax fiber also has more advanced uses in the form of composites in various load-bearing structural applications. In all of its

forms, flax is used in the manufacture of food, cosmetics, animal feed, fiber, and a variety of other industrial products [12, 13].

2.1.3 Kenaf

The botanical name of kenaf is *Hibiscus cannabinum*, which is a member of the Malvaceae family like cotton and it is a warm-season yearly cane-like bast fiber crop. The kenaf plant is made up of 74% stalks and 26% leaves, with an average kenaf stalk consisting of 65% woody core and 35% bark [14]. The stalks have consisted of two different types of fiber: an inner fiber (i.e. called as a core) that is short and placed in the ligneous zone and an outer fiber (i.e. called as a bast) that is long and positioned in the cortical layer. Fibers from kenaf stalks are often removed using water retting or dew retting. The amount of fiber obtained from this process varies with changing of stalks [15].

Kenaf fiber has a soft handle and is also robust. The breaking strength of kenaf fiber is comparable to that of low-grade jute, and it only slightly weakens when wet. Since, kenaf fibers contain a long staple, very strong and fine yarn can be spun from them. Very little flexibility can be found in kenaf fiber. This fiber can be broken down chemically. Kenaf is both hydrophobic in nature and the most absorbent natural fiber known to humankind [16]. Sacking, canvas, and rope are commonly produced by kenaf fibers. In order to prevent the depletion of forests, the plant has also been employed as a substitute raw material in the paper and pulp industries [17].

2.1.4 Jute

Jute fibers rank with cotton as one of the most significant fibers. Two domesticated genera of the genus *Corchorus* in the family Malvaceae are *C. capsularis* and *C. olitorius* which are known as white jute and dark jute respectively [18]. Jute plant stalks with specific height and diameter are picked and the most commonly used method is water retting which has been engaged to extract the fibers. Around 4–4.5% of the green crop is made up of dry fibers that have been extracted using this method [19].

Jute fiber is completely biodegradable, recyclable, and therefore eco-friendly. It is a natural fiber with a silky, golden luster. It promotes enhanced fabric breathability and has high tensile strength and minimal extensibility. In addition to being exceptionally robust and resilient, jute cloth is also resistant to tearing, stretching, and abrasion. This makes it perfect for items like purses, carpets, and shoes that need to be made of a robust, long-lasting material. It also has good insulating qualities and is naturally UV resistant, making it appropriate for usage in a variety of climates. Jute fiber has a moisture recovery of around 11–13%, which is a little greater than cotton fiber (7–8%). It is a hygroscopic fiber, and wet filaments can swell in diameter by up to 23%. Due to its coarseness and inelastic structure, jute fiber has fairly high flexural and torsional rigidities, and for this reason the jute fabric wrinkles and

creases quickly [20]. Jute fibers are appropriate for usage in a variety of industries, including fashion, travel, luggage, furnishings, carpets, and other floor coverings because of their biodegradability, fire resistance, and heat resistance [21].

2.1.5 Bamboo

The botanical name for bamboo is *Bambusa vulgaris*, and it is a member of the Poaceae (grasses) family. Bamboo is the most significant plant fiber because it is environmentally beneficial, has a rapid growth rate, and absorbs carbon dioxide from the atmosphere. More than 1000 species of bamboo and about 70 species have been identified to naturally grow in a range of climatic conditions [22]. Based on diverse process flows and methods, bamboo fiber is divided into two categories: natural original bamboo fiber and bamboo pulp fiber (more particularly, bamboo viscose fiber or regenerated cellulose bamboo fiber). In general, mechanical processing and chemical processing are the two forms of processing used to obtain bamboo fibers. Bamboo strips are first split in both methods, and depending on the way the bamboo fibers will be used later, either mechanical processing or chemical processing is then applied. Alkali hydrolysis (such as NaOH, KOH, etc.) is a preliminary step in chemical processing that produces cellulose fibers. Then, using a multi-phase bleaching process, the alkali-treated cellulose fibers are passed through carbon disulphide (CS₂). The majority of manufacturers employ this method since it produces bamboo fibers in a short span of time [22, 23].

The bamboo fiber is distinguished by its superb color impact of pigmentation, soft feel, great permeability, and good hydrophilicity. Bamboo fiber provides substantially greater moisture absorption and breathability due to the numerous micro-gaps and micro-holes that make up its cross-section. Bamboo fiber has twice the moisture absorption capacity of cotton fiber, with exceptional dirt absorption. Numerous scientific studies demonstrate the natural antibacterial properties of bamboo fiber owing to the presence of an antimicrobial bio-agent named as “bamboo Kun”. Bamboo fiber’s anti-ultraviolet properties have made them appropriate for summer clothes, especially for protecting people from the effects of ultraviolet radiation. Bamboo fibers are mostly employed in the textile sector for clothing, towels, and bathrobes due to their adaptable qualities. It is used to make bandages, masks, nurse wear, and sanitary napkins because of its antimicrobial properties. To decrease the impacts of microorganisms and the harm caused by ultraviolet radiation on human skin, bamboo fibers are also used to make television covers, wallpaper, curtains, and many other products [24].

2.1.6 Sisal

The botanical name for sisal is *Agave sisalana*, and it is a member of the Asparagaceae family [25]. Generally, a sisal plant provides 200–250 leaves, and each leaf yields roughly 1000 bundles of fiber. A traditional method of mechanical decortication, hand

decortication involves first pounding the leaf, and then scraping the pulp away with a knife. Since, the invention of mechanical decorators, this labor-intensive procedure has been abandoned. To create the automated decoration, a rotating wheel beats, and crushes leaves with blunt knives until only the fibers are left. This type of leaves are good for the extraction of fibers because they do not contain any woody parts [26].

The fibers of sisal are very much smooth, straight, and yellow color. The fiber is extremely durable and requires little maintenance due to its low wear and tear. This fiber is anti-static in nature, does not hold dust particles on its surface, and the moisture adsorption is very low. The fiber has excellent sound and impact absorption properties. This fiber is very much tough and inflexible and the modulus of the fiber is increasing with increment of fiber length. It demonstrates high tensile strength and the strength of this type of fiber is maximum at the middle of the yarn and least at the edge. Among all the other natural fibers, this fiber has the greatest variety of dyed colors owing to the texture of the fiber, which makes it easy to dye. Sisal fiber is frequently employed in the marine sector for lashing, cargo handling, and securing small ships. Surprisingly, it is also utilized as the steel wire cables' core fiber in elevators. This fiber is also used in paper industries, cordage industries, carpet, and agriculture industries [27].

2.1.7 Hemp

The botanical name of the hemp plant is *Cannabis sativa L.*, which belongs to the Cannabaceae family. The plant needs to be harvested 70–90 days after planting in order to produce fiber [28]. The plants can reach heights of 2–4 m, and their typical fiber yield ranges from 15 to 25%. Dew retting is the most popular and affordable method for obtaining hemp bast fibers and for this retting technique, hemp stalks are left for up to 5 weeks in the field [29].

Hemp fiber varies in color from deep brown to yellowish grey. The porous structure of the hemp fibers permits the air to circulate inside and also furnishes a protective insulating layer. Owing to this the garment made of hemp fibers keeps the human body cool in summer and hot in winter season. The tensile strength of this hemp fiber is very high but elongation at break is in the low region. The hemp fiber has very poor elastic recovery. It has very high moisture adsorption capability and excellent heat resistance properties. The fiber is very much resistant to alkali and organic solvents. It has enough ability to prevent harmful radiation from the sun but it can not dye [30]. Hemp fibers are utilized in a variety of products, including paper, carpeting, home furnishings, building and insulation materials, auto parts, composites, fabrics, and textiles [31].

2.1.8 Abaca

Abaca (also known as *Musa textilis*), a plant related to the banana, produces some of the strongest natural fibers utilized by humans in its leaves, which is a member of the

Table 1 Chemical composition of various natural fibers [35, 37, 38]

Fibers	Cellulose (wt%)	Lignin (wt%)	Hemicellulose (wt%)	Pectin (wt%)	Wax (wt%)	Moisture content (wt%)
Cotton	82.7	—	5.7	—	0.6	—
Flax	71.0	2.2	18.6–20.6	—	—	—
Kenaf	31–39	15–19	21.5	—	—	—
Jute	61–71.5	12–13	13.6–20.4	0.4	0.5	12.6
Bamboo	26–43	21–31	30	—	—	—
Sisal	67–78	8–11	10–14.2	10	2	11
Hemp	70.2–74.4	3.7–5.7	17.9–22.4	0.9	0.8	10
Abaca	68.32	12–13	19	—	—	10–11

Musaceae family [32]. Until harvesting, an abaca plant will generate 12–20 stems (leaves). The inner leaves of abaca are finer, less fibrous, and narrower than its outer leaves. Typically, the stalks are harvested 18–24 months after the first buds appear. Depending on the extraction method, the amount of fiber produced ranges from 1.5 to 3.5%; for example, the mechanical decortication method produces 3.0–3.5% of fiber, whilst the spindle stripping method only produces 1.5–2.0% [33, 34].

Abaca fiber is known as the strongest natural fiber. The fiber's colors vary from light and dark brown to ivory white. Abaca is considered as an excellent fiber because of its high tensile and folding strength, buoyancy, dense porosity, and resistance to saltwater degradation. Fibre has a higher intrinsic acidic content and a higher propensity for acidic breakdown due to its higher lignin concentration. It is easily condensable with phenol, soluble in hot alkali, and easily oxidized. The dyeing of abaca fiber exhibits outstanding results without any shine loss. It is applied as a raw material for making cordage, fiber crafts, and pulp for specialty paper goods such as cigarette papers, tea bags, meat casings, and security papers [35, 36].

For comparison purposes, the composition of extracted natural fibers and properties are summarized in Tables 1 and 2 respectively.

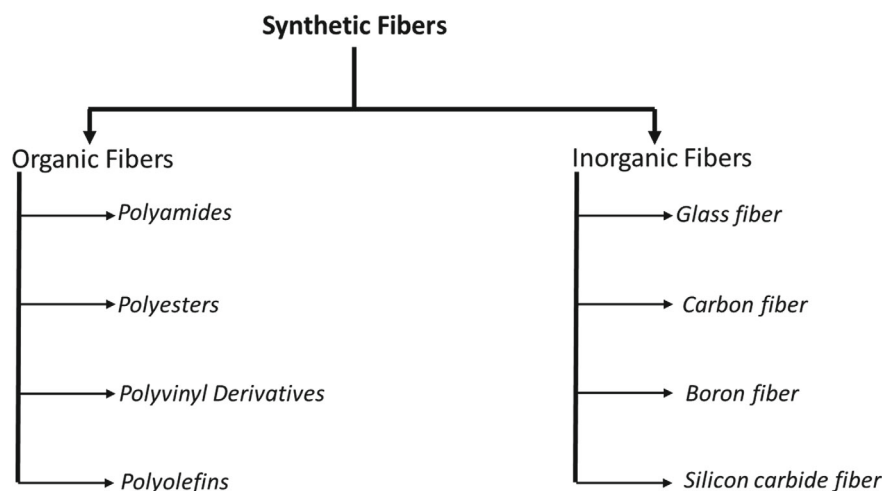
2.2 Synthetic Fibers

Organic fibers and inorganic fibers are the two major groups of synthetic fibers, which are further sub-classified based on their origin. The classification of synthetic fibers is summarized in Fig. 1.

Synthetic fibers are prepared from polymer (not naturally occurring) on the lab scale through various methods such as spinning (melt, wet and dry spinning), polymerization, and filament processing [40]. Depending on the preparation method, synthetic fibers can be manufactured in a variety of grades. In comparison to other fibers with the same mass, organic synthetic fibers have a lower density, which results

Table 2 Mechanical properties of natural fibers [37, 39]

Fibers	Density (g/cm ³)	Diameter (μ m)	Tensile strength (MPa)	Young's modulus (GPa)	Elongation at break (%)
Cotton	1.5–1.6	–	287–800	5.5–12.6	7–8
Flax	1.5	–	345–1100	27.6	2.7–3.2
Kenaf	1.45	–	930	53.0	1.6
Jute	1.3–1.45	25–200	393–773	13–26.5	1.16–1.5
Bamboo	0.974	–	1430–1690	32–34.6	4.3–9.7
Sisal	1.45	50–200	468–640	9.4–22.0	3–7
Hemp	1.47	–	690.0	70.0	2–4
Abaca	1.5	–	980	41.0	1.1

**Fig. 1** Flow chart of synthetic fibers classifications

in a higher volume percentage in the fabrication of composites. In comparison to inorganic fibers, organic synthetic fibers often have a low modulus of elasticity and high elongation qualities. Synthetic organic fibers have a low Young modulus, which reduces the stiffness and increases the ductility of the composite, preventing failure of the material when subjected to significant deformation [41]. Here we are paying attention to the synthesis and important properties of the commercially significant inorganic and organic synthetic fibers.

2.2.1 Organic Fibers

The synthetic organic fibers as a filler have been gain attention in the fabrication of composites owing to their good mechanical and thermal properties, good resistance to abrasion, and enhanced bonding capability with respect to other fillers [42]. Large numbers of organic fibrous fillers are available. But in this chapter, we are focusing on synthetic organic fiber which is potentially employed as a filler material in the fabrication of composites for various applications.

Polyamides Fibers

Polyamide (PA) (nylon) is the first synthetic polymeric material that has been used as a fiber. PA is a type of material in which the repeating units are connected to each others through an amide linkage. The PAs are classified into two categories: (1) aliphatic and (2) aromatic polyamide. PAs are synthesized either by condensation or ring opening polymerization. Due to the decreased reactivity of aromatic amines compared to aliphatic amines and the difficulty of synthesizing aromatic PAs utilizing diacids and diamines, aromatic PAs are often synthesized from diamine and diacid chloride. Based on the length of the diamine and diacid monomer employed during synthesis, aliphatic polyamides can be further divided into a number of categories. They can be referred to as PA-x or PA-xy, where x and y denote the distance between nitrogen atoms and carbon atoms, respectively. The PA fibers are manufactured by either spinning (melt, wet, and gel) or drawing method by which low strength semi-crystalline polymers are converted into highly oriented high strength fibers [43].

PA fibers have a very low density and thickness, making them an extremely lightweight material. These fibers have a high level of wear and abrasion resistance. It is especially durable in high-contact zones because of this characteristic properties. With regard to corrosive substances, it has excellent corrosion resistance and this property makes it suitable for adverse circumstances that would corrode metals in a short period of time. Flexural strength is the fundamental characteristic of polyamides. It can bend and fix to any place with its assistance. Additionally, it facilitates assembly and installation in areas inaccessible to solid metal structures. Even after prolonged exposure to the greatest temperatures, polyamides maintain their flexibility. In addition to their flexibility and density, polyamides have the best tensile strength and excellent impact strength. For example, polyamide can easily defend against the piercing of insulation and can withstand intense forklift pressure with dimensional stability, according to the strength tests. PAs can withstand a wide variety of temperatures; aliphatic polyamides, for example, have a melting point of roughly 500–550 K, giving them amazing heat tolerance. They offer thermal characteristics including fire resistance and smoke reduction, and some PAseven have self-extinguishing flames when they are on fire. Although intense ultra-violet light can damage some materials, polyamide resists its brittle effects and also for a considerable amount of time, it can function properly in the sunlight [44].

Polyesters Fibers

The standard description of polyester fiber is manufactured fiber in which the fiber forming substance is any long chain synthetic polymer composed at least 85% by weight of an ester of dihydric alcohol (HO-R-OH) and terephthalic acid ($\text{p-HOOC-C}_6\text{H}_4\text{COOH}$). The most abundant synthetic fiber manufactured globally is polyester fiber, specifically poly (ethylene terephthalate) (PET) fiber. The following are the causes of PET fiber overwhelming success: (1) Low price, (2) easy to process (3) blending with cotton and other natural fibers is very simple (4) convenience in recycling, and (5) excellent performance that can be customized [45]. The polyester fiber is manufactured from polyester (which is synthesized via condensation polymerization) using the melt spinning process.

The polyester fibers are mostly white in color and they have brilliant lustre. It has a good ability to reflect light. The physical characteristics of polyester fibers include durability, outstanding wash and wear performance, good elasticity, shape retention, and wrinkle resistance. As a result, polyester fiber is being used more frequently in clothing textiles of all types. Polyester fiber also quickly generates static electricity, which results in clothing accumulating dust and adhering to the body, which in turn results in poor comfort. Polyester fiber also performs poorly at absorbing perspiration, making the wearer feel hot and sticky while wearing it. Additionally, polyester performs exceptionally well during the dyeing process. The polyester fibers have good resistance to both acid and alkali under room temperature but it degrades at high temperature [45].

Polyvinyl Derivatives Fibers

There are a large number of polyvinyl groups containing fibers such as polyacrylonitrile (PAN) fiber, polyvinyl alcohol (PVA) fibers, polyvinyl chloride (PVC) fibers, etc. But among them most commercially important fiber is PAN fiber owing to its excellent characteristic properties which expands its applications in different sections. Based on this significance the chapter has discussed only PAN fibers among those polyvinyl derivatives based fibers.

Polyacrylonitrile Fibers

Acrylic fibers are spun from polymers that include at least 85% by mass of acrylonitrile in the monomer chain. The French chemist Moreau produced acrylonitrile and polyacrylonitrile in 1894, but the first polyacrylonitrile (PAN) based fibers were developed in 1938 [46]. PAN polymers were not employed industrially until just before World War II because they could not be melted without degrading them and because the solvents needed for solution processing were not known at that time [47]. PAN fibers are manufactured by solution spinning and melt spinning process. The solution spinning can be of two types: (1) wet spinning and (2) dry spinning. Wet spinning is the method most frequently used for producing PAN fibers out of those

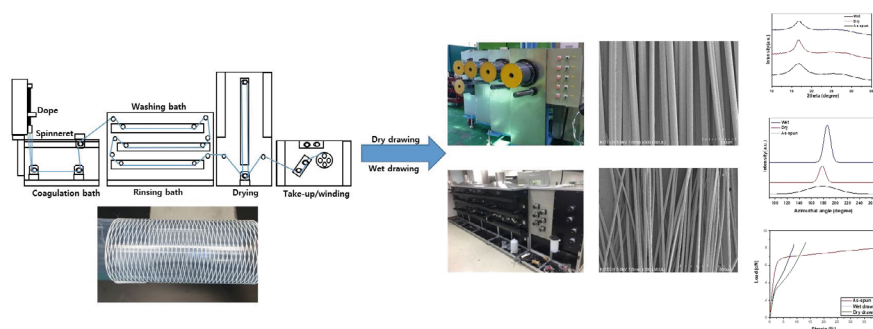


Fig. 2 Schematically presentation of the manufacturing process of Polyacrylonitrile fibers [48]

mentioned above. Above all, techniques like wet spinning are used to create this fiber by combining chemicals and solvents in a coagulation bath at the proper ratio. When compared to other spinning techniques like dry and melt, this procedure takes longer to generate fibers. The fabrication of the wet spinning process is presented in Fig. 2 [48].

PAN fiber has a density above one and it is high crystalline in nature. This fiber is an essential material for textile and high technology applications because of its unique qualities, which include low density, thermal stability, high resistance, and elasticity modulus, good impact strength, low creep resistance, good fatigue resistance, resistance to UV radiation degradation, non-melting, and chemical resistance. Insects, microorganisms, and mildew have also no effect on this fiber. Due to the presence of active polar groups on the PAN fibers, it can be easy to be dyed by various chemical agents. PAN fiber has replaced wool in many winter clothing items, including sweaters, faux fur, gloves, socks, hoodies, coats, and pants. This is because it is inexpensive and readily available. It also serves as a knitting yarn. This fiber is also used to create household textiles including rugs, curtains, carpets, and blankets [46, 49].

Polyolefins Fibers

Polyolefin fibers are mostly made of macromolecules of saturated aliphatic hydrocarbons. Among various polyolefin fibers, Polypropylene (PP) and polyethylene (PE) are by far the most common commercial polyolefin fibers.

Polyethylene Fibers

The simple and adaptable polyethylene molecule serves as a basis for the ultra-strong, high-modulus fibers known as gel-spun PE fibers. High-performance polyethylene (HPPE) fibers, high-modulus polyethylene (HMPE) fibers, or occasionally extended chain polyethylene (ECPE) fibers are designations given to them. These high performance PE fibers are manufactured by a gel-spinning process. The process consists

of the following primary steps: (1) Extrusion of high molecular weight polyethylene (2) Spinning the solution, crystallization, and gelation of the polyethylene solution and this can be done by cooling, extraction or evaporation methods and (3) finally drawing and removal of the excess solvent to obtain fibers. Besides, others steps are also very much significant to obtain good fibers [50].

The densities of the PE fibers are less than one and the strength and modulus of the fibers are very high. But its elongation at break is very less compared to others organic fibers. These fibers have also the ability to adsorb high amount of energy which make them a suitable candidate for ballistic applications. The fibers are the high-performance fibers with high tenacity as well as tension and bending fatigue properties comparable to PA and polyester which are commonly used in various types of ropes. The fibres produced from high molecular weight PEs have the high abrasion resistance and due to this reason, it is engaged in biomedical applications. These fibers are hydrophobic in nature and it does not contain any porosity in its structure. So, the property of the PE fibers is significantly not affected by moisture. As the fibers are manufactured from highly crystalline and high molecular weight PE and it does not contain any groups such as hydroxyl, aromatic, etc. which are susceptible to attack by various aggressive chemicals. The fibers are very much resistance to attack by different chemicals [51].

Polypropylene Fibers

Polypropylene (PP) fibers have consisted of stereoregular crystalline and amorphous polypropylene molecules. In the PP fibers, the macromolecular PP molecules can be arranged into three different configurations namely: isotactic (methyl groups of PP chains arranged in the same direction), syndiotactic (methyl groups of PP chains arranged in alternative direction), and atactic (methyl groups of PP chains placed randomly). The PP fibers are manufactured by melt spinning process starting from PP and as per desired properties of PP fibers six different types of melt spinning are applied: (1) Short air quench melt-spinning process (engaged in the production of high tenacity fibers) (2) Long air quench melt-spinning process, (engaged in the production of staple fibers) (3) Spin-draw process (employed in the production of coarser high tenacity yarns), (4) Spin draw texturing process (used in the production of bulked continuous filaments), (5) Water quench melt-spinning process (used in the preparation of heavy denier microfilaments) and (6) Tape yarns from slit film (used in the manufacture of high tenacity yarn from films) [52, 53].

PP fibers are the lowest density synthetic fiber and it is also hydrophobic in nature like polyethylene fibers. So, its properties are also not affected by moisture. As per the requirement of the market, PP fibers are manufactured in a range of kinds with various tenacities. The elasticity and abrasion resistance of the PP fibers are also quite good. The fibers also exhibit low temperature flexibility. But its thermal conductivity is very low compared to the others synthetic fibers. The fiber made of PP resists acids, bases, and organic solvents well. It has excellent thermal and electrical insulation which can hold onto heat for a longer period of time. In the presence of sunlight and UV rays, the PP fibers gradually degrade with time. As this fiber has no

polar groups like polyethylene fibers it can not be easily to be dyed by chemicals. PP fibers have some properties that make them an acceptable complement when used for building projects, more specifically when added to concrete, to get certain benefits. The applications of PP fibers include industrial pavements, highly resistant concrete, industrial grounds, tunnels, special mortars, and precast concrete [54, 55].

2.2.2 Inorganic Fibres

Inorganic fibers are becoming more and more common in modern society. Glass, carbon, boron, silicon carbide, alumina, potassium titanate, and ceramics are the most popular inorganic materials used to make fibers [56]. The three main categories of inorganic fibers are amorphous, polycrystalline, and monocrystalline fibers. Amorphous fibers have a high strength and a moderate elasticity modulus owing to a lack of grain boundary. Small crystals are responsible for the excellent thermal stability of polycrystalline fibers while monocrystalline fibers have extraordinarily high levels of strength and resemble extremely fine fibers [57].

Glass Fiber

Glass is a non-metallic fiber that is frequently utilized in industry today. Glass yarn spinning for use in fabrics is a very old technique that started in 1713. The glass fibers (GFs) were too stiff to drape, making them too heavy to be worn. GFs are made from silica, primarily in the forms of sand, limestone, stone ash, and borax. According to the composition of GF, this can be classified into several categories such as: (1) A-glass, (2) C-glass, (3) D-glass, (4) E-glass, (5) AE-glass, (6) ECR-glass, and (7) AR-glass. A-glass fiber is also known as alkali glass and it is resistance to various chemicals. C-glass fiber is known as chemical GF and it has higher chemical resistance than A-glass fiber. D-GF has a low dielectric constant and is employed in electrical applications. E type of glass combines the qualities of C-glass with excellent electrical insulation properties which is also known as electrical glass. AE-GF is also a type of alkali resistance fiber. ECR-GF is known as electronic GF and it has much better properties than E-GF. AR-GF is identified as alkali resistance GF and this type of fiber is specially designed for concrete construction [58]. Nowadays, there are various phases involved in the large-scale manufacture of continuous glass filaments. These procedures consist of batch material weighing and mixing. (such as finely ground silica, sand, clay, limestone, and boric acid), reaction and melting of the mixed batch around 1500 °C, typically in a gas-fired or electrically-boosted gas-fired furnace, homonization of the melted glass, cooled the molten glass in the forehearth, and followed by the drawing of fibers around 1250 °C (as presented in Fig. 3) [59]. On the other for making staple GFs, jets of air quickly cool the filaments as the glass runs through the bushings. The filaments are also cut into lengths by turbulent airbursts. Later, these filaments land on a rotating drum after passing through a lubricating

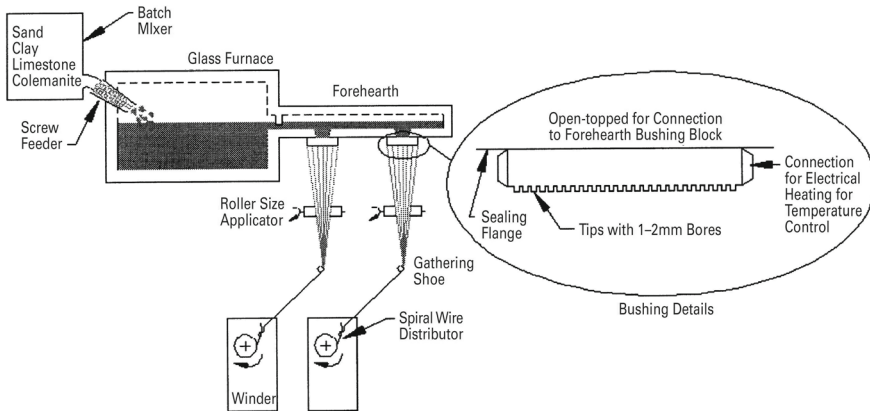


Fig. 3 Schematic presentation of continuous glass fiber manufacturing process [62]

spray and forming a thin web. The web is pulled out of the drum and formed into an uninterrupted string of loosely woven fibers [60, 61].

GFs are a widely preferred material in high-performance composite applications due to their attractive physical and mechanical characteristics, ease of manufacture, and comparably low cost to carbon fibers. GFs is almost as strong as aramid fibers in terms of strength and strength fibers depends upon the ratio of silicon (Si) and oxygen (O) and other components present in the fibers. As the GFs are water-repellent, water cannot affect this material and it is unlikely to shrink it. GFs are lighter and have a higher tensile strength than steel wire of the same diameter. GFs have high heat resistance. For example, GFs maintain 50% of room temperature tensile strength at 370 °C while retain 25% tensile strength at 480 °C. It is not sensitive to changes in humidity or temperature and owing to this reason; its linear expansion coefficient is very small. GF is incombustible by nature because it is a mineral substance. It does not help a flame grow or continue and when it is heated under a flame, it doesn't produce smoke or hazardous substances. GFs are not affected by most of chemicals and are also very much resistance to ultra-violet radiation and bacteria. But strong alkaline chemicals, heated phosphoric acids, and hydrofluoric acid can only affect GFs. High dielectric strength and low dielectric constant are characteristic property of glass fiber and even at low thicknesses; it is an excellent electrical insulator [63]. GFs are a superior material in applications where high strength and light weight are required because of their high strength-to-weight ratio. This strength can be unidirectional or bidirectional in textile form, providing versatility in design and budget. The automotive industry, civil construction, sporting goods, aviation and aerospace, boats and the marine industry, electronics, the home, and wind energy all make substantial use of it. Additionally, they are employed in the production of printed circuit boards, structural composites, and a variety of other products with unique uses [64].

Carbon Fiber

Carbon fiber (CF) is a special material in that its thermo-physical characteristics may be tailored to the specific use, allowing for a broad spectrum of material attributes. According to the mechanical characteristics of CFs, they can be divided into four groups: ultra-high modulus (UHM) (> 500 GPa), high modulus (HM) (> 300 GPa), intermediate modulus (IM) (> 200 GPa), and high strength (HT) (> 4 GPa). CF PAN is the most significant precursor on the market, and pitch is used to make the majority of other forms of CF. The once-used precursor rayon is no longer of any commercial significance. Different approaches are needed for the processing of carbon fibers from various precursors to produce high-quality end products [65]. CFs are manufactured using a combination of mechanical and chemical processes. The production of CF is schematically presented in Fig. 4 [66]. In the first step, The precursor is gathered into long strands or fibers and heated to an extremely high temperature without exposing it to oxygen. The fibers can not burn in the absence of oxygen. Instead, because of the high temperature, the fibers molecules vibrate erratically until the majority of the non-carbon atoms are ejected. This procedure, known as carbonization, results in the formation of a fiber made up primarily of long, intricately linked chains of carbon atoms with very few non-carbon atoms. The fibers must undergo chemical modification before carbonization in order to change their linear atomic bonding to a more thermally stable one. To achieve this, the fibers are heated around $200\text{--}300$ °C. After carbonization the fibers are oxidized to get better bonding with other materials to fabricate composites. The oxidation treatment should be controlled in such a way that there is no such defect formation in the fiber. The fibers are coated after the oxidation treatment to protect them from abrasion during winding or weaving. This procedure is known as sizing. The materials used for coatings are chosen so that they work well with the adhesive that is used to create good composite products [67, 68].

CF is a substance made of carbon atoms linked together in long chains to form thin, strong crystalline filaments. The fibers are utilized in numerous processes to produce exceptional materials for construction since they are incredibly stiff, robust, and light. In contrast to aramid fiber and GFs, CFs have a high tensile strength and a low coefficient of thermal expansion (CTE). Fibers often have lower CTE values than steel, which is one of the main materials used in structural applications. The lowest magnitude of CTE among commercially available fibers has been observed in CFs. In addition to these, CF is a strong option for other applications like energy harvesting, EMI shielding, and heat sinks due to its excellent high-temperature stability, chemical resistance, and thermal and electrical conductivity. Although the compressive strength of CFs is lower than that of inorganic fibers, it is considerably greater than that of polymeric fibers [69].

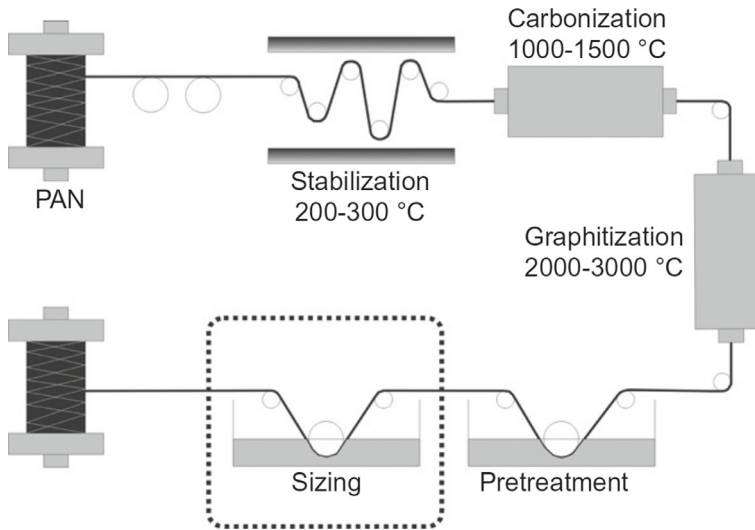


Fig. 4 Schematic representation of carbon fiber production [66]

Boron Fiber

Boron fiber (BF) having outstanding mechanical qualities and low density make them appealing for use in fiber reinforced composites, particularly lightweight construction. BFs were created to increase the rigidity of composite materials at a time when glass fibers were mostly employed to strengthen composites. Following in the footsteps of high-modulus carbon fibers with higher rigidity and cheaper cost, BFs presently have fairly limited applicability. The initial attempts were made to create a continuous BF, however, the fiber was so brittle that it was useless. Later, fibers with more usefulness were produced by vapor-deposition coating of boron onto a tungsten core [57]. Now, the boron fibers are manufactured via chemical vapour deposition (CVD) of boron onto the core of either tungsten or carbon wire having a diameter of $\sim 12 \mu\text{m}$. For this reason, the diameters of the BFs are much larger in the range of 100–200 μm . These fibers are exceedingly brittle and easily damaged on the surface [70].

BF has very low density, high tensile strength, and high modulus of elasticity which make them a potential candidate for lightweight structural applications. It has much higher compressive strength than any other fibers. The main limitation of boron fibers is that it has a very large diameter in comparison to that of other inorganic fibers. To solve this issue, when the diameters of fibers are reduced, its density increases (i.e. its weight increase), and specific strength also decreases [71].

Silicon Carbide Fiber

Silicon carbide (SiC) fibers, like boron fibers and carbon fibers, are potentially important continuous inorganic reinforcing materials with high modulus; they are particularly well suited for structural elements requiring high rigidity. SiC fiber is a high-performance ceramic material composed mostly of silicon carbide molecules and owing to its superior performance characteristics, recently SiC fiber is in high demand. Two different types of SiC fibers exist: one is substrate based SiC fiber and the other one is fine ceramic SiC fiber. In the case of substrate based SiC fibers, either tungsten (W) or carbon (C) are used as a substrate to produce fiber having a thickness in the range of 100–150 μm through chemical vapour deposition while fine ceramic fibers with a diameter in the range of 15 μm are manufactured by pyrolysis of polycarbosilane $(-\text{R}-\text{Si}-\text{R}-)_n$ [72].

SiC fibers offer distinct properties as compared to organic and some ceramic fibers, including high tensile strength, stiffness, modulus, chemical resistance, low weight, low thermal expansion, and high temperature tolerance. SiC fibers are far more durable than other fibers such as carbon, glass, alumina, and alumina silicate. Because the remarkable fiber intensity is maintained up to 1200 °C in an inert gas environment, these fibers do not react with standard matrix alloys [73, 74]. It is capable of exhibiting robust behaviour in high-temperature and oxidative environments.

3 Characterization of Fibrous Fillers

Given their extraordinary texture, fibers demand for specialized procedures to characterize them. Although fibers have been utilized since the beginning of time, controlled experiments and fiber observations have only recently been made possible. But now that highly specific knowledge can be gathered about the interlink between structure and properties by using methods like electron microscopic techniques and spectroscopic method, it is possible to optimize fibers and better understand their full potential in various applications field. The chapter has explored important characterization techniques which have a significant impact on the academic as well as industrial research and development section.

The linear density, a measurement of the mass of the fibers per unit length, is used by fiber producers as an indicator of fineness. The most used units are the denier, which is the traditional unit for which the weight of the fiber, in grams, is normalized to a length of 9000 m, and the tex, which is a commonly used measurement standardized to a length of 1000 m. On the other side, to investigate their physical qualities and chemical contents, the dried natural fibers were cut into various lengths. Before investigating the mechanical properties of the fibers, physical properties such as diameter, cross-sectional area, water absorption, and density were measured and the physical appearance of the fibers has been observed. Generally, the diameter of the natural fibers has been determined using the Fresnel diffraction method using a monochromatic light source (He–Ne laser light). The image of the fiber surface

was used to generate the diffraction pattern of the fiber peripheries. The apparent density, bulk density, apparent porosity, and water absorption behaviour of the fibers were determined according to American Society for Testing and Materials (ASTM) C830-00. For these measurements, the fibers were dried overnight in a vacuum oven, and the dried fiber mass (D) was weighed immediately after being removed from the oven. After immersing each fiber in an aqueous medium in a vacuum chamber overnight, the saturated weight of the fibers (W) was weighed in air. Finally, the suspended weights of fibers (S) were determined while submerging the fiber in an aqueous medium. The above mention properties of fibers were calculated by the following equations [75]:

$$\text{Apparent density}(\text{gm/cm}^3) = \frac{D}{D - S} \times \rho_{\text{Medium}} \quad (1)$$

where ρ_{Medium} indicates the density of the displacement medium.

$$\text{Bulk Density}(\text{gm/cm}^3) = \frac{D}{W - S} \quad (2)$$

$$\text{Apparent Porosity}(\%) = \frac{W - D}{W - S} \times 100 \quad (3)$$

$$\text{Water Absorption}(\%) = \frac{W - D}{D} \times 100 \quad (4)$$

Specific surface area is another important parameter for fibers for acting as a filler which is defined as the total surface area of fibers per unit mass. This property plays a very crucial role in determining the strength of the materials as well as their interaction with other materials. In industries the specific surface area has been measured by BET (Brunauer, Emmett, and Teller) adsorption isotherm method. By this method, the amount of nitrogen gas adsorbed at a very low temperature ($\sim -196^\circ\text{C}$) on the materials to form a monolayer of gaseous nitrogen has been considered as a specific surface area [76]. Both natural and synthetic fibers are cut into small pieces and investigated under various electron microscopies to study surface morphology, diameter, porosity, and internal defects. To analyse the surface groups such as hydroxyl, carboxyl, carbonyl etc. present in the fiber surfaces, Fourier transform infrared spectroscopy (FTIR) is engaged. The determination of surface groups is very much important in interaction with other materials for its modification to fabricated modified materials for use in different applications. X-ray diffraction (XRD) analysis is performed to examine the percent of crystallinity and crystallite size of the fibers. This study is very much significance as the crystallinity of the fibers determines the strength of fibers. To examine the stability and thermal degradation of fibers, thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) have been applied. TGA analysis of fibers provides information about moisture content, decomposition temperature, resistance to oxidation, and thermal stability whereas DSC analysis accounts for any phase transition such as glass transition temperature,

melting temperature, polymorphism, crystallization temperature, etc., transitional enthalpy, specific heat, oxidation induction time and temperature of the fibers. To determine the mechanical properties of the fibers various tests such as tensile testing, relaxation, creep, and fatigue testing has been performed. The tensile property of the fibers has been measured according to ASTM C 1557-14. In this method, fibers are extracted from the bundle of fibers and placed into the testing machine. The mounted fibers are then stressed until they failure. From this test, the tensile strength, Young modulus, and elongation at the break of the fibers have been examined. The creep test is a technique for determining how a fiber deforms over time under a constant force while the stress relaxation test is a technique to assess how a material release stress in the fibers with time under a steady strain. In fatigue testing, the fibers are deformed under cyclic loading and the test measures the numbers of cycles in which the materials are undergone failure. The above mention characterization methods are mostly used for the fibers to employ in various applications.

4 Summary

There is a wonderful chance to concentrate on the study of fibers in order to create more technologies with higher technical and safety aspects. Additionally, the integration of beneficial modifications in fibers that have little to no negative environmental impact needs to receive significant attention. To encourage decision-makers and customers to increase their use of in various composites and have a better substitute in the future for other reinforcing materials in different applications, the interaction between economic impacts and environmental impacts of various composites should be investigated, evaluated, and compared to conventional materials. In-depth research on the current state of the industrialization of high-performance and high-value-added fiber based composite products is also required, as is the advancement of the industrialization of key technologies, the deployment of high-tech in advance, and the promotion of the green, intelligent, and high-performance production of such composites.

Abbreviations

CS ₂	Carbon disulphide
PA	Polyamide
HO–R–OH	Dihydric alcohol
<i>p</i> –HOOC–C ₆ H ₄ COOH	Terephthalic acid
PET	Poly (ethylene terephthalate)
PAN	Polyacrylonitrile
PVA	Polyvinyl alcohol
PVC	Polyvinyl chloride

PP	Polypropylene
PE	Polyethylene
HPPE	High-performance polyethylene
HMPE	High-modulus polyethylene
ECPE	Extended chain polyethylene
GF	Glass fiber
CF	Carbon fiber
UHM	Ultra-high modulus
HM	High modulus
IM	Intermediate modulus
HT	High strength
CTE	Coefficient of thermal expansion
BF	Boron fiber
CVD	Chemical vapour deposition
SiC	Silicon carbide
W	Tungsten
C	Carbon
(-R-Si-R-) _n	Polycarbosilane
ASTM	American Society for Testing and Materials
D	Dried fiber mass
W	Saturated weight of the fibers
S	Suspended weights of fibers
BET	Brunauer, Emmett, and Teller
FTIR	Fourier transform infrared spectroscopy
XRD	X-ray diffraction
TGA	Thermogravimetric analysis
DSC	Differential scanning calorimetry

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Structural, Mechanical, In-Vitro, and In-Vivo Characterization Biocomposites



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Abstract The natural fiber and fillers loaded composites and biocomposites are developed through injection molding, compression molding, electrospinning, and additive manufacturing techniques with many available natural fillers and fibers throughout the world and it was utilized in many applications including medical and transport, naval, defense, and sports, etc. Since the composites are developed using a new combination of natural and synthetic matrix and natural and synthetic reinforcement and must be evaluated for structural, mechanical, thermal stability, in-vitro, and in-vivo properties to use the composites in most relevant applications. Hence the structural, mechanical, in-vitro, and in-vivo characterization of the biocomposite composite specimens is to be prepared as per ASTM standards to carry out the studies. The prepared specimens were carried out Fourier-transform infrared spectroscopy (FTIR), X-ray powder Diffraction (XRD), Differential Scanning Calorimeter (DSC), Thermogravimetric Analysis (TGA), Field Emission Scanning Electron Microscope (FESEM), Energy-Dispersive X-Ray (EDX), Tensile, compressive, Flexural, shore D hardness, direct cytotoxicity, indirect cytotoxicity, trypan blue staining, cell attachment through MG 63 cell line. Then the specimen was carried out SBF analysis to find the apatite formation on the surfaces of the composite. This chapter discussed the various techniques to identify the properties of the composites and biocomposites such as structural, mechanical, and thermal stability, in vitro, and in vivo.

Keywords Structural · Mechanical · Thermal stability · In-vitro · In-vivo

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1 Introduction

Natural Fiber composites have been utilized more in recent years due to their low density, excellent performance, biodegradability, and biocompatible. Many fillers and fibers were loaded in vinyl ester matrix and epoxy and developed the polymer composites through an open, hand lay-up, compression molding process. The composite exhibited better tensile, flexural strength, hardness, and impact strength [1]. The fillers such as HAp, ZO, GO, and CaCO_3 , loaded in HDPE composite for implant applications [2–8]. The short fiber-loaded polymer composites revealed better impact and flexural strength [9].

Sugarcane fibers loaded bio-composites with the tamarind seed fillers revealed improved compressive strength and flexural strength [10]. A sandwich composite improves the rigidity of the skin, and it would be used in roof panels [11]. The impact and compressive strength of the Juliflora-loaded composite revealed improved properties than the GFRP composite [12]. The chemical treatments of fibers and the addition of coupling agents enhance mechanical properties [13]. A polyester with palm-loaded composites exhibited better mechanical properties and improved thermal stability [14]. The Luffa fiber-loaded composite exhibited improved flexural strength and flexural modulus [15].

NFC possesses low weight, biodegradable, renewable, and high strength, and offer specific properties [16]. Luffa fiber loaded with ground nut filler composites revealed better mechanical properties [17]. The Coccinia fiber reinforced with epoxy composites revealed good wear resistance [18]. The incorporation of GO in composites enhanced flexural strength and improved bonding between the fillers and the matrix [19–23]. Since the hydrophilic nature fiber and bonding with the hydrophobic nature matrix is very weak [24–26].

Hence, there is a need to modify the fibers to enhance their hydrophobic nature, as suggested by Rajkumar Srinivasan et al. [27]. Thermoplastics are chosen for their exceptional biocompatibility and mechanical properties, as emphasized by Zhiltsova et al. [28]. Ultra-High Molecular Weight Polyethylene (UHMWPE), known for its chemical resistance, very low friction coefficient, and high impact strength, is widely utilized in total joint replacements, as indicated by Xiong et al. [29], Saikko and Shen [30], Xue et al. [31]. The fabrication processes of UHMWPE, including blow molding, extrusion, and injection molding, are outlined in studies by Sauer and Anthony [32], and Chen et al. [33]. These thermoplastics exhibit superior wear and creep resistance, resulting in an improved wear rate, as highlighted by Brown [34]. To further enhance the properties of Polyethylene (PE), various fillers such as carbon, glass fiber, graphite, talc, and hydroxyapatite have been incorporated, as explored in research by Huang et al. [35], Dangsheng [36], and Sui et al. [37]. Additionally, composites loaded with wood flour, kenaf fiber, barley husk, cellulosic fibers, abaca fiber, cordenka and flax, soy protein isolate, and ramie fibers have been successfully developed, as evidenced by the work of Liang et al. [38].

The objectives of this work are to discuss the different characterization techniques such as FTIX, XRD, DSC, TGA, FESEM, EDX, tensile, compressive, flexural, and

shore D hardness. Then direct cytotoxicity, indirect cytotoxicity, trypan blue staining, and cell attachment through the MG 63 cell line. Then the specimens were carried out SBF analysis to find out the apatite formation on the surfaces of the composite. This chapter discussed various techniques to identify the properties of the biocomposites such as structural, mechanical, thermal stability, in-vitro, and in-vivo.

2 Characterization Techniques

2.1 Structural Characterization

2.1.1 FTIR Spectral Analysis

FTIR is utilized for the identification of various functional groups present in the organic and inorganic fillers, as well as fibers in loaded composites. This technique allows for the recognition of functional groups like water OH stretch, alcohol OH stretch, carboxylic acid OH stretch, N–H stretch, =C–H stretch, –C–H stretch, –C–H aldehydic stretch, CH₂ bend, CH₃ bend, C–O–C stretch, C–OH stretch, NO₂ stretch, C–F, C–Cl, C–Br, C–I, C=O aldehyde, C=O anhydride, C=O ester, C=O ketone, C=O amide, C=C alkene, and C=C aromatic [39], through the FTIR spectrum. The FTIR spectrum exhibits distinctive peaks following the absorption or emission of various materials, including solids, liquids, fibers, powders, thin films, coatings, or gases. An FTIR spectrometer captures spectrum data across a broad range, typically measured in the mid and near IR regions (5000–400 cm^{−1}) [40]. This analytical approach proves particularly valuable for determining water content in relatively thin plastic and composite components.

2.1.2 XRD

XRD is an analytical method primarily employed for identifying the phases in crystalline materials and obtaining information on unit cell dimensions. The XRD analysis of particles covered a 2θ range spanning from 20° to 70°, offering valuable insights into the crystalline planes and orientations of various materials, including solids, liquids, fibers, powders, thin films, and coatings. The determination of the average grain size of fillers through Debye–Scherrer’s relation peak:

$$D = 0.9\lambda / \beta \cos \theta$$

where,

D denotes the average grain size,

β represents the full width at half maximum of the peak,

λ is the diffraction wavelength (0.154059 nm),

θ signifies the diffraction angle [41].

This XRD method was applied to estimate the average crystallite size of the fillers incorporated in the polymer matrix composites.

2.1.3 Thermogravimetric Analysis (TGA)

TGA involves subjecting the polymer sample to controlled heating in various environments such as CO₂, He, air, N₂, and Ar at a specified rate. The alterations in the weight of the polymer sample are meticulously recorded concerning temperature or time, providing a measure of mass changes relative to temperature changes. This analytical method yields valuable information about phase transitions, absorption, adsorption, and desorption phenomena [42]. For the examination of thermal stability in new polymer samples, TGA proves useful, particularly as these samples typically undergo melting before entering the decomposition stage. The TGA analysis spans a temperature range from 30 to 1200 °C. Notably, the majority of polymers exhibit melting or degradation before reaching 200 °C [43–46]. The analysis quantifies the rate of mass degradation in a composite. TGA was conducted under a nitrogen environment (300 ml/min) using the Q600 SDT instrument from TA Instruments in the USA, covering the temperature range from atmospheric to the specified maximum (650–1200 °C or 1200 °C).

2.1.4 Differential Scanning Calorimeter (DSC)

DSC serves to identify the glass transition (T_g), crystallization (T_c), and melting temperature (T_m) of polymer composites [47]. With increasing temperature, amorphous solid samples exhibit reduced viscosity, allowing molecules to achieve sufficient freedom of motion for spontaneous crystalline formation at the crystallization temperature (T_c). The transition from amorphous solid to crystalline solid is characterized by an exothermic process. As the temperature further rises, the polymer sample undergoes the melting process, manifesting as either endothermic or exothermic peaks in the DSC curve obtained [48]. The reference sample needs to possess a well-defined heat capacity across the analyzed temperature range. DSC analysis was carried out using a Q600 SDT instrument from TA Instruments in the USA, with the polymer sample analyzed in a nitrogen environment (Nitrogen 50.0 ml/min).

2.1.5 FESEM

FESEM studies the surfaces of materials, particles, and fibers to quantify and assess minute features. It can provide a plethora of knowledge to support research into materials, chemicals, or life. Using the image of FESEM studies the surfaces of

materials, particles, and fibers to quantify and assess minute features. The FESEM is currently the most crucial piece of hardware in research for obtaining highly sharp images. To increase the conductivity of the samples, a gold-sputtered composite $\approx (3 \text{ mm} \times 3 \text{ mm} \times 3 \text{ mm})$ was placed on stubs. Using the FESEM, the surface morphology of the gold-sputtered composite specimens was directly examined, and found the surface morphology and dispersion of fillers and fibers in the matrix [49].

2.2 Mechanical Characterization

The Universal Tester Machine (UTM) was employed to assess the tensile, compressive, and flexural strengths of the polymer matrix composite. The composite specimens were prepared following the guidelines set by ASTM standards. Six distinct composite specimens, each with identical weight percentages of fillers or fibers, underwent testing, and the resulting average values for the strengths were documented.

2.2.1 Evaluation of Tensile Strength

The ultimate tensile strength (UTS) of the polymer matrix composite is the maximum stress that a new polymer material can withstand when it is stretched or pulled before its breaking of polymer composite samples as per ASTM standards. In the brittle nature of the polymeric materials the UTS is closer to the yield point, whereas in the ductile nature of polymeric materials, the UTS can be higher. ASTM D638 followed for testing the tensile strength of composites and for computing their mechanical properties. Figure 1a–b shows the tensile strength specimens as per ASTM D638 standards.

Also, ASTM D3039 is used as a standard test method for finding the tensile properties of fiber-reinforced composites. ASTM D638 (Plastics) or ASTM D3039 (Composites) should be used. An ASTM D638 Deepak Poly Plast (Gujarat, India) Universal tester was used to conduct tensile testing at room temperature at a rate of 2 to 5 mm/min. The grip length of 65 mm, gauge length of 25 mm, thickness of 3.2 mm, and breadth of 6 mm were entered into the Deepak Poly Plast software. The grip length of the wedge clamp used to hold the composite specimens was 65 mm. ASTM D638 suggests speeds between 2 and 5 mm/min using the lowest speed that ruptures the specimen within 12 and 5 min as the benchmark. The Fig. 2a–d shows the different failure locations of the tensile failure of the different fiber-loaded and fiber mat-loaded epoxy composites specimens and Fig. 2e shows the failed locations of the specimens in the UTM fixture. The most tensile failure occurs in the middle of the specimens and fibers were elongated and disintegrated from their positions after failures which are observed in the failed specimens. Only a few samples failed at the neck positions of the specimens were observed in the failed specimens as shown in Fig. 2.

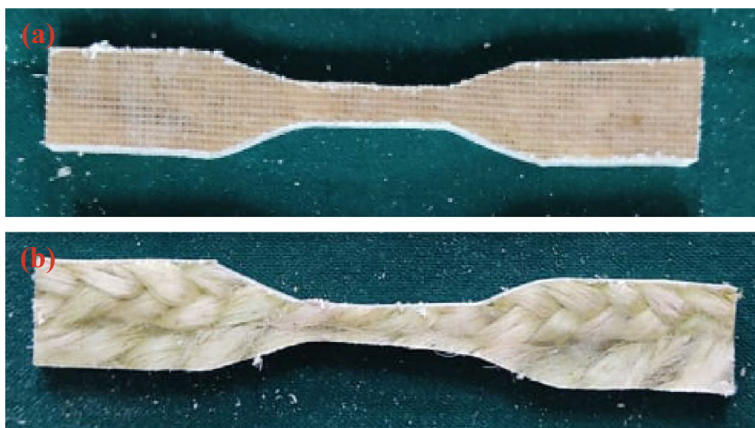


Fig. 1 a, b Tensile strength specimens as per ASTM D638 standards

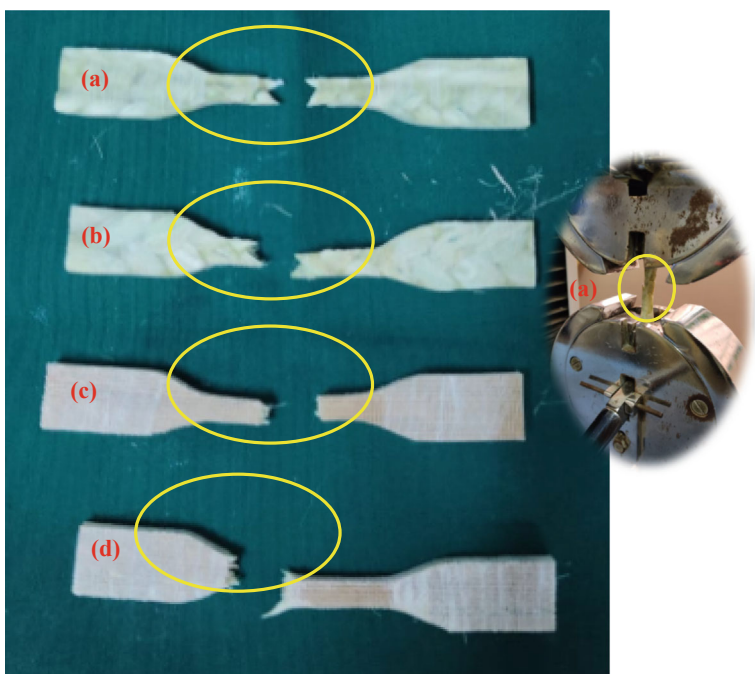


Fig. 2 a–d Different failure locations of the tensile failure of the specimens and e failed locations of the specimens in the UTM fixture

Table 1 Tensile strength results

S. No	Results	Units
1	Area	cm ²
2	% strain at yield	%
3	Tensile stress at yield	MPa
4	Tensile stress at break	MPa
5	% strain at break	%
6	Yield force	N
7	Break force	N
8	% Elongation	%
9	Tensile stress at max	MPa
10	% strain at max	%
11	Modulus of elasticity	GPa

The following Table 1 shows the detailed results obtained from the UTM software after extracting the results. The incorporation of 400 GSM E-glass fiber in composites resulted in a substantial increase in tensile strength, measuring 26.5 ± 0.5 MPa, as reported by Rajak et al. [50] in their 2021 study. The noteworthy improvement in tensile strength was attributed to the strategic placement of E-glass fiber on both the upper and lower surfaces of the PLSFC (Presaturated Laminated Sheet-Foam Core).

The decision to use 400 GSM E-glass fiber was motivated by its cost-effectiveness, offering an economical solution while concurrently enhancing the overall strength of the composite material. This cost-efficient approach, combined with the observed strengthening effects, highlights the practical and effective nature of incorporating E-glass fiber in reinforcing composite materials [3–6].

2.2.2 Evaluation of Compressive Strength

The compressive strength of a polymer material is its ability to withstand forces aiming to reduce its size by resisting compression and preventing buckling [51, 52]. For ASTM D695 standard compression testing, a universal tester from Deepak Poly Plast in Gujarat, India, was utilized at room temperature and a speed of 2 mm/min. The testing involved ASTM blocks with dimensions of $12.7 \times 12.7 \times 25.4$ mm, where each cylinder had a diameter of 12.7 mm and a length of 25.4 mm. While ISO recommends different specimen dimensions ($10 \times 10 \times 4$ mm and $50 \times 10 \times 4$ mm) for strength testing, the analysis used ASTM blocks. The specimen was securely held between parallel plates and subjected to regular crushing as shown in Fig. 3. Throughout this process, the maximum load was recorded, along with data on strain and stress. The modulus was calculated using an extensometer attached to the fixture's front (Table 2).

The application of microwave radiation to composites resulted in a significant 22% improvement in compressive strength, attributed to the enhanced interfacial

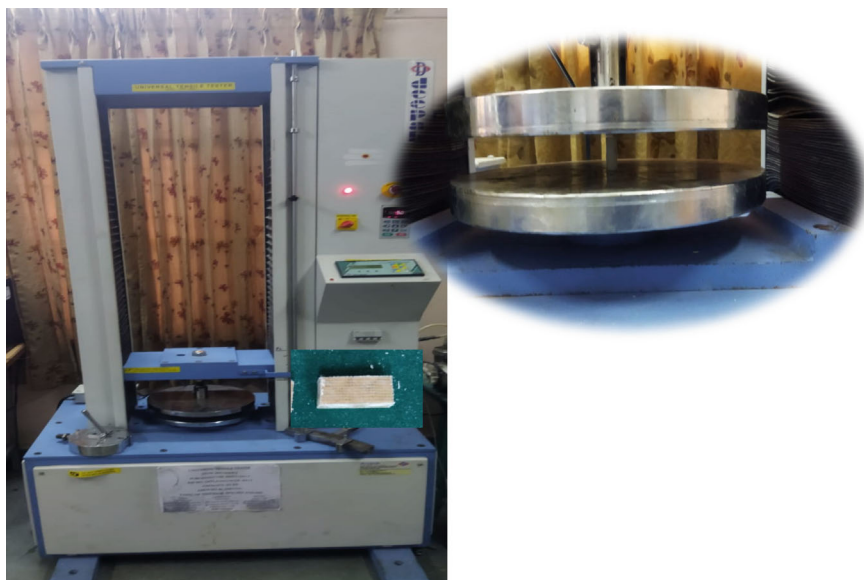


Fig. 3 a Compressive strength testing setup b specimens fixed in the fixture

Table 2 Tensile compressive results

S. No	Results	Units
1	Max. force	N
2	Max. deflection	mm

bonding between fibers and the matrix, as reported by Xu et al. [23]. Furthermore, the observed increase in compressive strength was also linked to the higher quantities of fillers incorporated into the matrix, as noted by Kulkarni et al. [21].

2.2.3 Evaluation of Flexural Strength

Flexural strength is used to find out the bending strength in a polymeric material just before it yields in a flexure test [53] as shown in Fig. 4. The resulting stress of the polymeric sample under a load in a three-point bending [54].

$$s = \frac{3FL}{2bd^2}$$

where,

F is the axial load (N), (b) is the width (mm), and (d) is the depth or thickness (mm) of the composite specimens respectively.

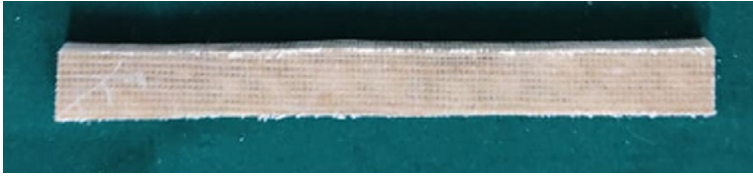


Fig. 4 a Flexural strength specimens as per ASTM D790 standards

The ASTM D790 flexural test was carried out at room temperature at a rate of 2 mm per minute using a universal tester produced by Deepak Poly Plast (Gujarat, India). The Deepak Poly Plast algorithm used the following inputs: span length = 48 mm, width = 12 mm, and thickness = 3.2 mm. The speed was set to 1–5 mm/min for the experiment as shown in Fig. 5. The highest force just before the break was recorded. The applied force versus deflection curves were measured for this experiment. The flexural stress, flexural strain, and flexural modulus were found from the flexural test.

$$\sigma_f = \frac{3Fl}{2bd^2}$$

where l is the span length (mm), F is the maximum force in (N), σ_f is the flexural strength (in MPa), and b and h are the specimen's breadth and thickness in (mm) respectively (Table 3).

To augment the properties of the composites, Wu et al. [26] recommend incorporating 0.1 wt% of graphene oxide (GO). The enhancement is attributed to the improved interfacial adhesion between the natural fillers and the matrix. This, in turn, results in an overall improvement in the mechanical properties of the composites, as proposed by Irawan et al. [24].

2.2.4 Shore D Durometer

The material under the Shore D hardness (ASTM D2240) test is a minimum of 6 mm as shown in Fig. 6. Rubbers, elastomers, and polymers can all have their hardness determined using the Shore D durometer. The higher the numbers on the scale, the stronger the resistance to indentation and, thus, the harder the materials. As the number decreases, the material becomes more resilient. The thickness of the test specimens is 6.4 mm on average. Even if it is possible to reach the required thickness of 6.4 mm, using just one specimen is advised. The addition of rigid reinforcing elements (SiO_2 and TiO_2) into the matrix improves the hardness of the composites [25].

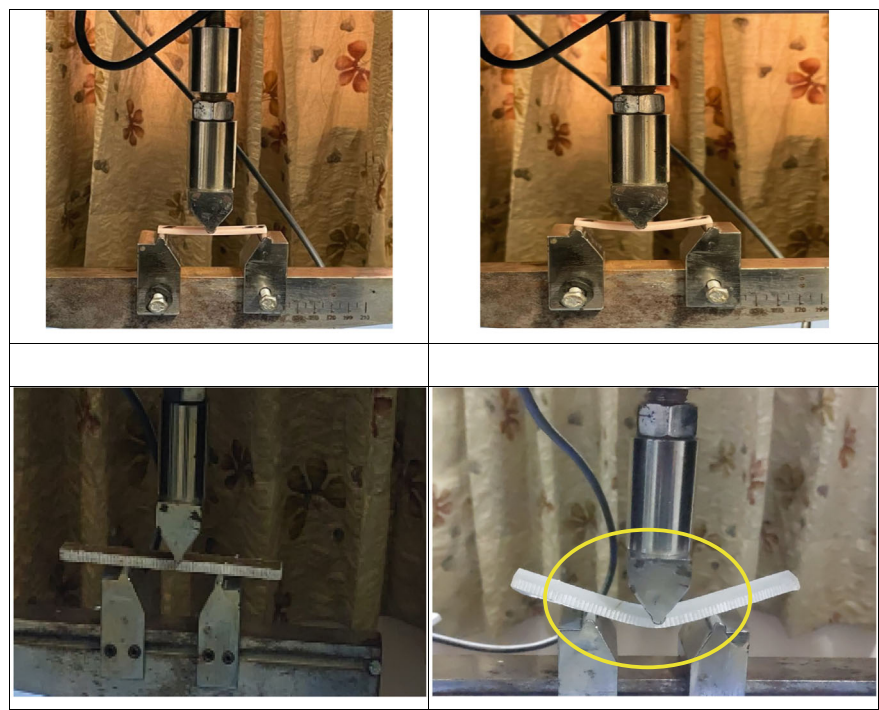


Fig. 5 Flexural strength thermoplastic specimens **a** before bending **b** after bending, flexural strength thermosetting specimens **c** before bending **d** after bending

Table 3 Flexural compressive results

S. No	Results	Units
1	Force at 1%	N
2	Deflection at 1%	mm
3	M (SLOP)	N/mm
4	Flexural modulus at 1% secant	MPa
5	Max. force	N
6	Flexural strength	MPa

Fig. 6 Shore D hardness specimens as per ASTM D2240 standards



3 In-Vitro Characterization

Characterization of Biomaterials

To estimate the cell/tissue interactions of biomaterials, certain experiments have to be followed.

- (i) The primary step is the development of new polymer composites and their characterization.
- (ii) After estimating the structural, and mechanical properties of new polymer composites goes to the microbiology department, where the new polymer composites are sterilized by ethanol or other most suitable techniques. The new polymer composites were carried out in-vitro direct cytotoxicity, in-vitro indirect cytotoxicity, cell proliferation, and cell adhesion [55] to find out the level of toxicity presence in the new polymer composites and cell growth, Cell proliferation, and cell attachments.
- (iii) The new polymer composites go to an in-vivo toxicity laboratory. Then liquid extract from the new polymer composites is injected into small animals or the material is placed in the animal body. Then it goes to the histopathology laboratory, where the new polymer composites interacted with animal tissues are primed for microscopic analysis to check the morphology of the cells.
- (iv) An ethical committee decides the number of animals and the type of animal for carrying out the particular in-vivo experiments [56].
- (v) After satisfying all the tests above which goes to the implant biology section to shape the new polymer composites for final use.
- (vi) The testing laboratory environment should be free from dust, and microbes, and sterilized [57].

3.1 Evaluation of Biocompatibility

The assessment of biocompatibility is vital for determining how well a new polymer composite implant will interact within a biological environment. It aims to investigate potential adverse physiological effects that may arise from the use of these new polymer composites, as discussed by Mihai et al. Safety evaluations, encompassing both in-vitro and in-vivo studies, are routinely conducted on various medical devices, biomaterials, and related products to detect any toxic or harmful effects. In the evaluation of biocompatibility, in-vitro cytotoxicity is a key method that involves tissue culture and various cell culture assays. This approach employs cultured and isolated cells to assess the impact of a material or liquid extract on both living and non-living cells. In-vitro cytotoxicity tests are conducted using prepared assays to examine the potential effects on cell viability. Li et al. [58] specify procedures for in-vitro cytotoxicity testing, which include direct or indirect contact with devices, examination of extracts from devices, and filter diffusion. Essentially, biocompatibility refers to the capacity of a newly developed material to perform specific functions without

compromising the fundamental immunological functions of the body. The thorough evaluation of biocompatibility is critical to ensuring the safety and efficacy of medical implants and devices within a biological context.

3.1.1 Cell Culture

The MG-63 cell line is widely recognized for its established and well-documented characteristics, ensuring consistent outcomes. The cell culture medium used for MG-63 is formulated through the Minimum Essential Medium (MEM) process, with the addition of fetal bovine serum. Fetal bovine serum is selected for its appropriateness, featuring minimal antibody levels and an abundance of growth factors. This serum's versatility makes it ideal for various cell culture applications, providing optimal support for the growth and health of the MG-63 cell line.

3.2 Evaluation of Direct Cytotoxicity of the Composite

The composites underwent a comprehensive assessment through direct in-vitro cytotoxicity studies involving the MG-63 cell line to determine the potential cytotoxicity within the samples. Liquid extracts from the sterilized composite were directly applied to the MG-63 cell line at varying concentrations (10, 20, 30, 40, and 50 μ l). Cultivated in Minimum Essential Medium (MEM) supplemented with 10% Phosphate Buffered Saline, approximately 10,000 freshly trypsinized MG-63 cells were seeded per well in a 96-well plate and allowed to incubate for 24 h. Subsequently, the culture medium was replaced with a fresh medium before introducing liquid extracts of the composite at five different concentrations, each in triplicate. Following an 18-h incubation at 37 ± 1 °C, MTT (1 mg/1 ml) was added to all wells and incubated for an additional 4 h. Post-incubation, Dimethyl Sulfoxide was introduced, and the morphology of the cells was examined using a 570 nm photometer, indicating cell viability by dark purple colors as shown in Fig. 7. The percentage of cytotoxicity and cell viability was then calculated using the provided formula. Cytotoxicity percentage was determined using the direct cytotoxicity method, and the obtained results were compared with a standard reference, as detailed in Table 4.

$$\text{Cytotoxicity} = [(\text{Control} - \text{Treated}) / \text{Control}] * 100$$

$$\text{Cell viability} = (\text{Treated} / \text{Control}) * 100$$

Fig. 7 MG-63 cell morphology living and non-living cells direct cytotoxicity

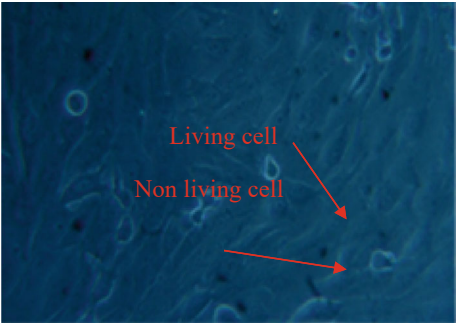


Table 4 Evaluation criteria of the direct cytotoxicity

S. No	Grade of cytotoxicity (%)	Reactivity
1	0	None
2	1–20	Slight
3	21–50	Mild
4	51–70	Moderate
5	> 71	Severe

3.3 Indirect Cytotoxicity

The ETO-sterilized composite specimens underwent an in-vitro evaluation for indirect cytotoxicity using the MG-63 cell line. The liquid extract obtained from the sterilized new polymer composite was applied to MG-63 cells through the agar diffusion method, a form of indirect cytotoxicity assessment. The objective was to analyze and determine the grade of cytotoxicity exhibited by the new polymer composite specimen.

3.3.1 Agar Diffusion

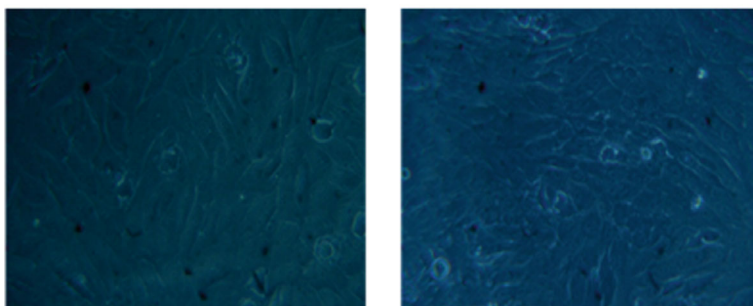
A thin layer of agar solution was added to the MG 63 cells. After the agar solidified, liquid extract from the new polymer composite was added to this layer, incubated, and checked under the spectrometer microscope.

3.3.2 Evaluation of Indirect Cytotoxicity

The assessment of indirect cytotoxicity involving the MG-63 cell line was conducted for the new polymer composite. Through the indirect cytotoxicity method, the extent and grade of cytotoxicity were determined and subsequently compared with predefined evaluation criteria presented in Table 5. In this assessment, the new polymer

Table 5 Evaluation criteria of the indirect cytotoxicity

S. No	Level of cytotoxicity	Reactivity	Grade of cytotoxicity
1	0	No detectable zone	None
2	1	Some malformed or degenerated cells	Slight
3	2	Zone limited to the area under the composite	Mild
4	3	Zone extending specimen size up to 1 cm composite	Moderate
5	4	Zone extending farther than 1 cm beyond the composite	Severe

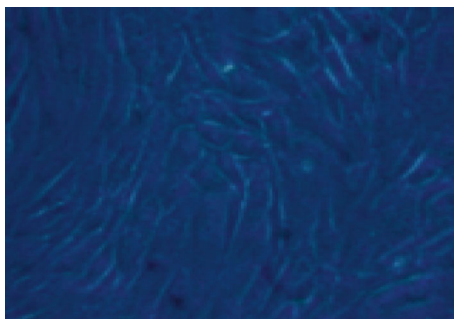
Control**Fig. 8** MG-63 cell morphology living and non-living cells trypan blue assay

composite specimens, particularly at a 50 μ l volume of the extract, were introduced to a fresh culture medium using the indirect method is shown in Fig. 8. The evaluation revealed a maximum cytotoxicity score of 1 for the liquid extract of the composite specimen when interacting with the fresh medium. This assessment was then cross-referenced with the criteria outlined in Table 5, indicating that the observed cytotoxicity level fell within reactivity level 1. Although the reactivity level was slightly low, it remained within an acceptable range.

3.4 Trypan Blue Assay—Test Procedure

One of the often used techniques for determining the percentage of live cells is the trypan blue assay test. Trypan blue is an azo dye that only enters cells with damaged membranes because its cell membrane is impermeable. Trypan blue strongly binds to the proteins inside the cells, giving them a blue tint when cells with damaged cell membranes enter the cell as shown in Fig. 9. The fraction of living cells, unstained, and blue-colored dead cells in a particular cell sample are identified and counted

Fig. 9 Control (before trypan blue staining)



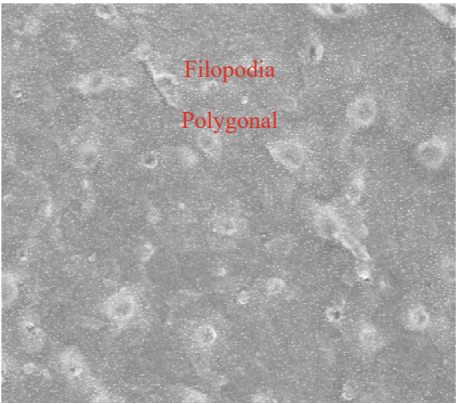
using the trypan blue assay. This approach simply involves adding trypan blue, an azo dye, to the supplied population of cells. The cells are then analyzed visually to determine whether they contain or do not contain dye [59].

To ensure that the cells had completely separated, the cells were cultured in a MEM medium that had 10% FBS added to it. The well was seeded with the cells (5×10^5) and incubated at 37 °C for 24 h. Duplicate samples were introduced, and control cells were those without any samples. For 24 h, the plate was incubated. The medium was withdrawn following incubation. Each well received a 0.4% trypan blue stain, which was then examined under an inverted phase-contrast microscope. The formula can be used to determine the percentage of alive cells. Viable cells (%) are calculated as follows: [59] (Total Number of Viable Cells)/(Total Number of Cells) * 100.

3.5 Cell Adhesion—Test Procedure

Because it involves numerous molecular interactions, including the binding of a receptor and a ligand and the modification of cytoskeletal assembly, cell adhesion is significant. A cell's contact with its extracellular adhesion proteins as well as information on other cellular activities are measured using a cell adhesion assay. It is mostly used to examine a cell line's capacity to adhere to particular adhesive substrates. Typically, 10% FBS is added to the MEM medium to supplement cell growth. Following trypsinization, the cells are counted using a cell hemocytometer. The sample must be covered with MG-63 cells (10^5), which must then be incubated at 37 °C for 24 h. The medium must be thoroughly removed after incubation and treated with glutaraldehyde (0.25%). After four hours at 0 °C, the composite sample should be inspected using a FESEM is shown in Fig. 10.

Fig. 10 Tensile strength specimens as per ASTM D638 standards



3.6 Preparation of SBF Solution

Kokubo has developed the concentration of an ion in SBF as given in Table 6.

An ion’s concentration is comparable to the concentration of human blood plasma. To match the ionic concentration of a mixture of inorganic ions similar to blood plasma, the appropriate quantities of reagents such as CaCl_2 , Na_2SO_4 , KCl , $\text{K}_2\text{HPO}_4 \cdot 3\text{H}_2\text{O}$, NaCl , NaHCO_3 , $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$, and $\text{CH}_2\text{OH}_3\text{CNH}_2$ were liquified in 1 L of distilled water. One liter of distilled water was added with the reagents one at a time, gradually. The SBF was created in a lab with an ionic concentration that was almost identical to blood plasma. To determine the bioactivity, in-vitro SBF experiments were performed on HDPE composite specimens packed with 30-weight percent FS particles that were $3 \times 3 \times 3$ mm in size. The composite specimens were submerged in SBF solution kept at 37°C and cultured for 7, 14, 21, and 28 days while being refreshed or supplemented with new SBF solution. The composite specimens were removed from the SBF solution after a specific amount of time of incubation, as shown in Fig. 11, and allowed to dry at room temperature. The potential to

Table 6 Ion concentrations of SBF and human blood plasma

S. No	Ionic concentration (mmol/dm ³)	Simulated body fluid	Fluid blood plasma
1	Na ⁺	142	142
2	K ⁺	5.0	5.0
3	Mg ⁺	1.5	1.5
4	Ca ⁺	2.5	2.5
5	Cl [−]	147.8	103.0
6	HCO ₃ [−]	4.2	27.0
7	HPO ₄ [−]	1.0	1.0
8	SO ₄ [−]	0.5	0.5

Fig. 11 FESEM image composite immersed in SBF after 14 days

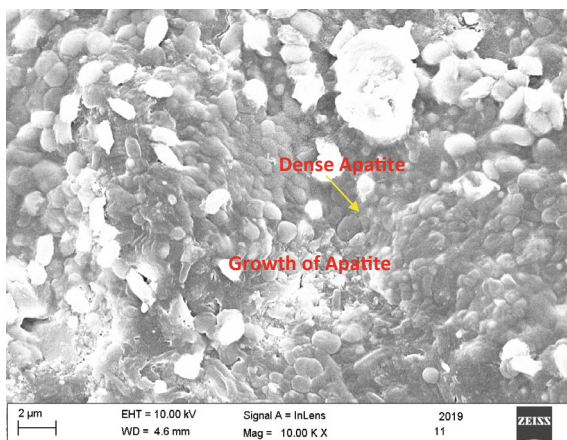


Table 7 Reagents used for preparing SBF solution

S. No	Reagent	Amount (g/l)
1	NaCl	7.996 g
2	NaHCO ₃	0.350 g
3	KCl	0.224 g
4	K ₂ HPO ₄ ·3H ₂ O	0.228 g
5	MgCl ₂ ·6H ₂ O	0.305 g
6	1M-HCl	40 ml
7	CaCl ₂	0.278 g
8	Na ₂ SO ₄	0.071 g
9	(CH ₂ OH) ₃ CNH ₂	6.057 g

generate apatite was also determined by FESEM analysis of the composite specimens is shown in Fig. 11. Then, it was made sure that Table 7 contained a complete list of each reagent's dissolution.

To match the ion concentration, the proper amount of reagents should be added and dissolved in distilled water. The pH of the solution is kept at 7.4 by adding the HCl gradually. For a second SBF analysis of the composite, the produced SBF solution was maintained in the refrigerator at a temperature of 37 °C [60].

3.7 In-Vivo Characterization

Animals used as in vivo models provide a wealth of information on how wounds heal. Studying the internal cellular and metabolic processes that go on within an animal's body paves the way for this. Wound healing is one of the most frequently studied

topics in vivo, and polymeric composite is frequently used in these investigations. Rats, mice, rabbits, and pigs are among the species utilized as models for in vivo studies [54].

4 Conclusion

The natural-based composites are developed from many available natural resources throughout the world and it was utilized in many applications including transport, naval, defense, sports, and medical, etc., Since the composites are developed new combinations of matrix and reinforcement must be evaluated structural, mechanical, in-vitro, and in-vivo properties. This chapter discussed various techniques to identify the properties of the composites.

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Silica-Polymer Composites for Biomedical Applications



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Abstract This chapter goes into detail about how silica polymer composites can be used in different biomedical fields. Silica polymer composites have gotten a lot of attention because they have a unique set of properties, such as being biocompatible, having pores that can be changed, and being easy to add functions to. This chapter starts by talking about how polymers, nanoparticles, and functional moieties are used in the design and synthesis processes used to make these composites. The chapter then talks about specific uses of silica polymer composites in biomedicine, such as drug delivery systems, scaffolds for tissue engineering, contrast agents for bioimaging, and biosensors. The pros and cons of each application are talked about, giving an

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idea of how these composites might be used in the future and where they could be improved. At the end of the chapter, we talk about new ideas and directions for the future, such as stimuli-responsive systems, 3D printing, and bio-inspired materials. Overall, this chapter is a thorough guide for researchers and scientists who want to use silica polymer composites to make biomedical applications better.

Keywords Silica · Polymer composites · Biocompatible · Bioimaging · Biosensors

1 Introduction

Silica-polymer composites have been identified as multifaceted materials with a wide range of applications in different domains, including the field of biomedicine. The composites under consideration amalgamate the distinctive characteristics of silica nanoparticles and polymers, thereby yielding substances that manifest amplified mechanical robustness, biocompatibility, and regulated drug liberation potential [1].

Drug delivery systems have emerged as a prominent area of interest for silica-polymer composites. The high drug-loading capacity of silica nanoparticles is attributed to their porous structure, which is complemented by the stability and controlled release properties of the polymer matrix [2]. The integration of these elements facilitates the creation of drug delivery systems that are both enduring and specific, thereby reducing adverse reactions and enhancing the effectiveness of treatment [3]. The adjustability of pore size and surface properties of silica nanoparticles facilitates the encapsulation of diverse drug types, such as proteins, nucleic acids, and small molecules. The utilisation of silica-polymer composites has been observed in the field of tissue engineering. The integration of silica nanoparticles into polymer scaffolds can yield a substantial improvement in the mechanical characteristics of the scaffolds, rendering them appropriate for applications that require the ability to bear loads. The composites exhibit biocompatibility, thereby facilitating cellular adhesion, proliferation, and differentiation, which in turn fosters the regeneration of tissues [4]. Furthermore, the regulated discharge of bioactive molecules from the composite material can offer stimuli for cellular response and tissue proliferation, thereby promoting the advancement of operative tissue structures [5]. Silica-polymer composites have exhibited considerable potential for diverse applications in the realm of bioimaging. Silica nanoparticles have the potential to function as carriers for imaging agents, including but not limited to fluorescent dyes [6], quantum dots [7–16], or magnetic nanoparticles [17–20]. The aforementioned agents have the capability to be enclosed within the permeable configuration of the silica or affixed to its exterior, leading to the production of imaging probes that are augmented in contrast [21]. The utilisation of a polymer matrix in in vivo imaging and in vitro applications guarantees safe administration due to its ability to provide stability and biocompatibility. The capacity to integrate various imaging agents within the composite material

facilitates multimodal imaging, a technique that employs diverse imaging modalities to enhance diagnostic precision [22].

Silica-polymer composites have demonstrated usefulness in the field of biosensing and diagnostics. Silica nanoparticles possess a considerable surface area and porosity, which facilitates the immobilisation of biomolecules, including enzymes, antibodies, or DNA probes [23]. This immobilisation enables the detection of target analytes with high specificity and sensitivity. The polymer matrix confers stability and safeguards the immobilised biomolecules, thereby ensuring the durability and dependability of the biosensing platform and other applications [24–33]. The amalgamation of silica-polymer composites with microfluidic devices or portable sensing platforms exhibits significant potential for point-of-care diagnostics and rapid screening assays. Apart from the previously mentioned applications, the utilisation of silica-polymer composites as coatings for implants has also been investigated [34]. The application of these composites in the form of thin films on medical implants has the potential to enhance osseointegration and mitigate the likelihood of implant-associated infections. The composite coating's ability to release antimicrobial agents or growth factors in a controlled manner can effectively hinder bacterial colonisation and facilitate bone regeneration, ultimately enhancing the implants' long-term efficacy [35]. In the field of biomedicine, silica-polymer composites have been found to provide numerous benefits, including but not limited to facilitating progress in drug delivery, tissue engineering, bioimaging, biosensing, and implant coatings. The amalgamation of silica nanoparticles and polymers yields improved mechanical characteristics, regulated drug liberation, and biocompatibility. Sustained exploration and advancement in this domain possess significant prospects for the creation of innovative biomedical technologies and enhanced patient welfare.

The primary objective of this study is to furnish a thorough evaluation of the various techniques utilised for the production of silica-polymer composites, emphasising their strengths and weaknesses. The second aspect pertains to the examination of characterization techniques employed for the assessment of the structural, morphological, and physicochemical attributes of said composites. The chapter is dedicated to expounding upon the mechanical properties of composites made of silica and polymer, with a particular emphasis on their heightened strength and durability. Additionally, the chapter delves into the diverse array of biomedical implementations of said composites, encompassing drug delivery modalities, tissue regeneration, bioimaging techniques, biosensing mechanisms, and implant coatings. The text provides an analysis of the distinctive benefits and possible obstacles linked to each utilisation, furnishing valuable perspectives for scholars and professionals operating in the domain. The chapter endeavours to enhance the knowledge base and promote the progress of silica-polymer composites in the field of biomedical applications by addressing these objectives.

2 Silica-Based Materials

Silica-based materials are a diverse group of materials that are predominantly comprised of silicon dioxide (SiO₂), which is more commonly referred to as silica. Diverse manifestations of silica-based substances are observable, encompassing amorphous silica, crystalline silica, silica nanoparticles, silica gels, and mesoporous silica [36]. The exceptional characteristics of these materials, including their elevated chemical stability, thermal resilience, biocompatibility, and optical transparency, render them versatile and applicable across diverse domains. Various types of silica based materials/composites have been depicted in Fig. 1.

Silica based materials	Potential uses
Amorphous silica	Filler in rubber and plastics, abrasives, dental materials
Silica nanoparticles	Coatings, paints, catalyst supports, optical materials, drug delivery
Silica aerogels	Wound dressings, tissue engineering, drug delivery systems
Silica nanocomposites	Reinforcement in polymers, composite materials
Crystalline silica	Silica glass production, ceramics, refractory materials
Silica nanowires	Sensors, nanoelectronics, energy storage devices
Silica-based membranes	Gas separation, water purification, filtration
Silica-based sensors	Chemical sensing, environmental monitoring
Silica-based scaffolds	Tissue engineering, regenerative medicine
Silica gel	Column chromatography, desiccants, humidity control
Mesoporous silica	Drug delivery systems, catalysis, bioengineering
Silica fibers	Optical fibers for telecommunications and data transmission

Fig. 1 Different types of silica based materials and their potential uses

Silica-based materials have been observed to have significant utility in the realm of catalysis. The utilisation of silica-supported catalysts is prevalent in chemical processes due to their notable characteristics such as high surface area, customizable porosity, and capacity to secure catalytically active species. The aforementioned catalysts have been utilised in various fields such as organic synthesis, petroleum refining, and environmental remediation. Silica-based materials are widely employed in the domain of chromatography [37]. The porous variant of amorphous silica, known as silica gel, is frequently employed as a stationary phase in column chromatography to effectuate the separation and refinement of diverse compounds. Due to its elevated surface area and capacity to adsorb analytes, it is a highly suitable option for separation methodologies [38]. Silica-based materials are of significant importance in the electronics sector. Silicon dioxide plays a crucial role in semiconductor devices by serving as an insulating layer and gate dielectric in integrated circuits. Accurate manipulation of the thickness and characteristics of silica-derived thin films is imperative in the production of sophisticated electronic apparatus.

Silica-based materials are extensively employed in the manufacturing of optical fibres within the domain of optics [39]. Silica fibres possess desirable optical properties and exhibit low transmission loss, rendering them well-suited for applications such as long-distance telecommunications, data transmission, and sensing. The utilisation of silica-based materials in the biomedical field holds considerable importance [40]. The utilisation of silica nanoparticles and mesoporous silica in drug delivery systems has garnered significant interest owing to their expansive surface area, substantial drug-loading capability, and regulated release characteristics. Targeting ligands and imaging agents can be utilised to functionalize them, enabling the delivery of drugs to specific sites and facilitating theranostic applications. In addition, materials that are based on silica have been utilised in various fields such as biosensing, bioimaging, and bioengineering. The optical transparency, biocompatibility, and facile functionalization render them as optimal substrates for biosensors, fluorescent probes, and scaffolds for tissue engineering [41]. To summarise, materials that are based on silica exhibit a wide spectrum of properties and have numerous applications in diverse fields. The versatility of these materials for various applications such as catalysis, chromatography, electronics, optics, and biomedical applications is attributed to their chemical stability, thermal resistance, biocompatibility, and optical transparency [42]. Further exploration and innovation in this domain possess significant prospects for additional progressions and innovative utilities of materials based on silica.

3 Silica and Its Properties

Silica-based materials are a diverse group of materials that are predominantly comprised of silicon dioxide (SiO_2), which is more commonly referred to as silica. Diverse manifestations of silica-based substances are observable, encompassing amorphous silica, crystalline silica, silica nanoparticles, silica gels, and mesoporous

silica [43]. The exceptional characteristics of these materials, including their elevated chemical stability, thermal resilience, biocompatibility, and optical transparency, render them versatile and applicable across diverse domains. Silica-based materials have been observed to have significant utility in the realm of catalysis [44]. The utilisation of silica-supported catalysts is prevalent in chemical processes due to their notable characteristics such as high surface area, customizable porosity, and capacity to secure catalytically active species. The aforementioned catalysts have been utilised in various fields such as organic synthesis, petroleum refining, and environmental remediation. Silica-based materials are widely employed in the domain of chromatography [45]. The porous variant of amorphous silica, known as silica gel, is frequently employed as a stationary phase in column chromatography to effectuate the separation and refinement of diverse compounds. Due to its elevated surface area and capacity to adsorb analytes, it is a highly suitable option for separation methodologies. Silica-based materials are of significant importance in the electronics sector. Silicon dioxide plays a crucial role in semiconductor devices by serving as an insulating layer and gate dielectric in integrated circuits [46]. Accurate manipulation of the thickness and characteristics of silica-derived thin films is imperative in the production of sophisticated electronic apparatus. Silica-based materials are extensively employed in the manufacturing of optical fibres within the realm of optics. Silica fibres possess desirable optical properties and exhibit low transmission loss, rendering them well-suited for applications such as long-distance telecommunications, data transmission, and sensing. The utilisation of silica-based materials in the biomedical field holds considerable importance [47]. The utilisation of silica nanoparticles and mesoporous silica in drug delivery systems has garnered significant interest owing to their expansive surface area, substantial drug-loading capability, and regulated release characteristics [48]. Targeting ligands and imaging agents can be utilised to functionalize them, enabling the delivery of drugs to specific sites and facilitating theranostic applications. In addition, materials that are based on silica have been utilised in various fields such as biosensing, bioimaging, and bioengineering. The optical transparency, biocompatibility, and facile functionalization render them as optimal substrates for biosensors, fluorescent probes, and scaffolds for tissue engineering. To summarise, materials that are based on silica exhibit a wide spectrum of properties and have numerous applications in diverse fields. The versatility of these materials for various applications such as catalysis, chromatography, electronics, optics, and biomedical applications is attributed to their chemical stability, thermal resistance, biocompatibility, and optical transparency. Further exploration and innovation in this domain possess significant prospects for additional progressions and innovative utilities of materials based on silica.

4 Types of Silica Materials Used in Composites

Silica-based materials are of paramount importance in the advancement of composite materials, as they provide a diverse array of distinctive characteristics that augment the overall performance and functionality of the composites [49]. The aforementioned materials find application in diverse industries such as aerospace, automotive, electronics, and biomedical sectors. The present article aims to investigate the various categories of silica materials that are frequently employed in composites, emphasising their distinctive features and practical uses [50].

Silica nanoparticles refer to particles of silica that are at the nanoscale level and can exist in either amorphous or crystalline form. Nanoparticles exhibit a significant surface-to-volume ratio and are amenable to facile functionalization, rendering them highly adaptable for diverse applications [51]. Silica nanoparticles serve as reinforcing fillers in composites, thereby enhancing mechanical characteristics such as strength, stiffness, and toughness [52]. The high aspect ratio and uniform dispersion of the reinforcement within the composite matrix result in an improved load transfer between the two components. Silica nanoparticles have been utilised in polymer composites to augment the mechanical robustness and thermal endurance of the materials. Additionally, they are employed in electronic composites due to their dielectric characteristics and in coatings for their ability to act as a barrier. The integration of silica nanoparticles into composites has the potential to substantially improve their functionality, rendering them appropriate for employment in lightweight structural elements, packaging materials, and high-performance coatings.

Silica microspheres refer to spherical particles composed of amorphous or crystalline silica, characterised by diameters that span from a few micrometres to several hundred micrometres. The microspheres exhibit distinctive characteristics including regulated porosity, elevated surface area, and reduced density [53]. Fillers are frequently employed in polymer composites to enhance their mechanical characteristics, decrease their weight, and regulate their thermal expansion. The incorporation of silica microspheres into composites has been found to have a positive effect on their impact resistance, thermal conductivity, and dimensional stability [54]. Furthermore, these substances are utilised as rheology modifiers and thickeners in various industrial applications such as paints, coatings, and adhesives [55]. The incorporation of silica microspheres into composites facilitates the creation of materials that are lightweight and possess enhanced mechanical and thermal characteristics, rendering them appropriate for utilisation in various industries such as automotive, aerospace, and construction.

Silica fibres are a type of high-strength fibres that are composed of silica or glass and are characterised by diameters that typically range from a few micrometres to several tens of micrometres. The fibres exhibit remarkable thermal stability, chemical resistance, and minimal thermal expansion, rendering them highly suitable as reinforcements in composite materials. Silica fibres are frequently utilised in high-performance composites for aerospace and automotive purposes, owing to their ability to offer improved strength, stiffness, and high-temperature resistance [56].

Their electrical insulation properties make them useful in electrical and electronic composites. The integration of silica fibres into composites facilitates the creation of materials that are both lightweight and possess high strength, making them well-suited for use in structural applications that necessitate resistance to thermal and chemical factors [57].

Silica aerogels are a type of highly porous material characterised by low density. These materials are produced by subjecting a gel to supercritical conditions, which effectively removes the liquid phase. The material in question exhibits an open-cell structure, possesses a high specific surface area, and demonstrates low thermal conductivity [58]. Silica aerogels have been utilised as lightweight additives in polymer composites, thereby enhancing their thermal insulation characteristics. In addition to their primary applications, these materials are utilised for acoustic insulation, vibration attenuation, and energy dissipation purposes [59]. Silica aerogels have significant utility in the aerospace and construction sectors, as they are crucial for achieving weight reduction and thermal insulation. The integration of silica aerogels into composites facilitates the creation of materials that are both lightweight and possess thermal insulation properties, rendering them appropriate for utilisation in various fields such as aerospace, building insulation, and thermal packaging.

Silica mats refer to nonwoven membranes or mats that are composed of silica fibres. The mats exhibit exceptional thermal stability, chemical resistance, and significant porosity. Tai documented the production of a carbon-based composite nanofibrous membrane with exceptional flexibility through the incorporation of a SiO_2 precursor. The membrane's physical characteristics, such as its bulk mechanical strength and thermal stability, were also evaluated (Fig. 2) [60]. The whole process was initiated by sol-gel proceed silica synthesis followed by physical blending of the components to make an electrospinning mix.

Reinforcing layers, separators, or filtration media are common applications of these materials in composite materials. The incorporation of silica mats into composites results in enhanced mechanical characteristics, including heightened impact resistance and dimensional stability. Polymeric membranes find widespread applications in battery separators, fuel cell membranes, and filtration systems. The integration of silica mats within composites facilitates the creation of materials that possess heightened structural robustness, superior separation efficacy, and augmented longevity [61].

Silica gels are characterised as porous substances that exhibit notable adsorption capabilities and superior moisture regulation properties [62]. Fillers or additives are frequently utilised in composites to regulate moisture absorption and enhance dimensional stability. Silica gels are utilised in electrical and electronic composites for the purpose of managing moisture levels, which is of utmost importance in order to avert electrical deterioration or corrosion. The integration of silica gels into composites facilitates the production of materials that exhibit enhanced resistance to moisture, rendering them appropriate for deployment in electronic gadgets, outdoor settings, and regions characterised by elevated humidity levels.

To conclude, the distinct varieties of silica materials utilised in composites provide distinctive characteristics and advantages. The incorporation of various forms of

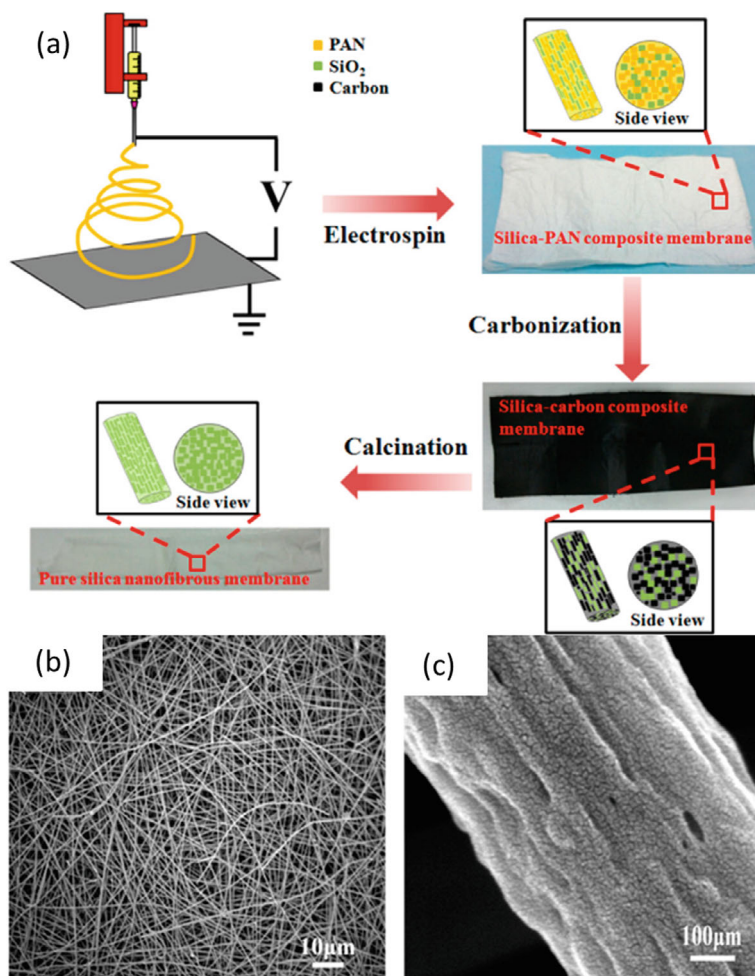


Fig. 2 **a** Electrospinning of silica-PAN, carbon, and nanofibrous to fabricate nanocomposite membrane **b** top view of electrospun composite nanofibrous mat from SEM **c** surface morphology of a single composite nanofiber from SEM. Reproduced with the permission from Ref. [60] © 2014 American chemical society

silica, including nanoparticles, microspheres, fibres, aerogels, mats, and gels, has been found to improve distinct properties of composites, such as mechanical strength, thermal stability, low weight, insulation, and moisture regulation. The integration of silica materials within composites facilitates the creation of sophisticated materials that are appropriate for a diverse array of applications, such as aerospace, automotive, electronics, and multiple industrial domains.

5 Synthesis Methods for Silica Nanoparticles and Mesoporous Silica

5.1 Common Synthesis Methods of Silica Nanoparticles

5.1.1 Stöber Method

The Stöber method is a commonly employed approach in the production of uniform silica nanoparticles. The process entails the hydrolytic and condensational reactions of tetraethyl orthosilicate (TEOS) or alternative silane precursors while a surfactant or stabiliser is present [63]. The customary procedure involves conducting the reaction within an aqueous solution of alcohol, while regulating the pH and temperature parameters. The dimensions of the nanoparticles can be modulated through the manipulation of reaction parameters, including precursor concentration, reaction duration, and surfactant concentration.

5.1.2 Sol–Gel Method

The sol–gel method is a multifaceted approach utilised for the production of silica nanoparticles. The process entails the hydrolysis and condensation of silane precursors, namely tetraethyl orthosilicate (TEOS) or tetramethyl orthosilicate (TMOS), in a liquid medium, which is then succeeded by the creation of a gel network. Subsequent to gel formation, the nanoparticles are acquired through either desiccation or calcination processes [64]. The manipulation of precursor concentration, pH, solvent composition, and drying conditions can regulate the dimensions and structure of the nanoparticles.

5.1.3 Microemulsion Method

The microemulsion method employs a microemulsion system comprising water, oil, and surfactant phases to regulate the nucleation and expansion of silica nanoparticles. The silane precursor is solubilized within the oil phase, and subsequently, the hydrolysis and condensation reactions take place at the interface of the water–oil phases. The aforementioned technique facilitates the production of nanoparticles possessing a limited range of sizes and regulated structure.

5.1.4 Template-Assisted Method

The template-assisted method involves the synthesis of silica nanoparticles through the utilisation of pre-existing templates, including micelles, polymer spheres, or biological structures. The templates serve as a structural scaffold for the silica's

development. Following the synthesis of silica, the templates are extracted, resulting in the desired silica nanoparticles. This technique facilitates the regulation of the dimensions, morphology, and permeability of nanoparticles.

5.2 Common Synthesis Methods of Mesoporous Silica

5.2.1 Sol–Gel Method with Templating

The sol–gel method can be combined with a templating approach to synthesize mesoporous silica materials. The present methodology involves the integration of a surfactant template into the solution of the silica precursor. Subsequently, the initial solution that precedes the formation of the desired product undergoes hydrolysis and condensation processes, leading to the creation of a silica matrix that envelops the surfactant micelles. After the template is eliminated through calcination or extraction, a mesoporous silica substance with a clearly defined pore structure and a large surface area is obtained.

5.2.2 Solvent Evaporation-Induced Self-Assembly (EISA)

The EISA technique is a process that entails the self-assembly of surfactant molecules and silica precursors within a solvent system [65]. Subsequent to the solvent evaporation process, there is a resultant development of well-organized mesostructures. The mesoporous silica with controlled pore size and structure can be obtained by subjecting the resulting silica material to further treatment aimed at removing the surfactant template.

5.2.3 Nanocasting

Nanocasting is a replication methodology that involves the use of a sacrificial template, such as a mesoporous material or biological structure, which is infused with a solution of silica precursor [66]. Following the processes of gelation and calcination, the template is eliminated, resulting in a silica replica that exhibits a comparable pore structure. The aforementioned technique enables the production of mesoporous silica substances featuring intricate pore geometries and customised surface chemistry [67].

5.2.4 Hard Template Method

The Hard Template Method involves the application of a rigid material, such as silica or alumina, as a template, which is subsequently coated with a solution of silica

precursor [68]. Subsequent to the coating process, the template undergoes hydrolysis and condensation, and subsequently, the removal of the template is carried out through chemical or thermal methods [69]. The mesoporous silica material obtained exhibits a preserved pore structure from the template material, rendering it suitable for diverse applications. The aforementioned methods are most frequently adopted techniques for synthesising silica nanoparticles and mesoporous silica materials. Every technique presents distinct benefits and permits the regulation of particle dimensions, shape, porosity, and surface characteristics, facilitating the creation and production of silica-derived substances with customised features for particular uses.

5.3 *Polymer-Silica Composites*

Polymer-silica composites are materials that are created by combining the properties of polymers and silica. The resulting hybrid material exhibits improved mechanical, thermal, and electrical properties. Composite materials are extensively utilised across diverse industries such as aerospace, automotive, electronics, and biomedical sectors. The incorporation of silica into the polymer matrix in polymer-silica composites serves as a filler or reinforcement mechanism, thereby conferring distinctive attributes to the resultant material [70]. This portion aims to examine the advantages, manufacturing techniques, and potential uses of polymer-silica composites.

The advantages of applying polymer-silica composites are:

- The mechanical properties of composites can be improved by incorporating silica nanoparticles or fibres into polymer matrices, resulting in enhanced tensile strength, stiffness, and toughness. The incorporation of silica as a reinforcing filler in composites leads to an improvement in the load transfer mechanism between the polymer matrix and the reinforcement [71]. This results in an increase in the composite's resistance to deformation and an enhancement of its structural integrity.
- Silica is highly suitable filler for enhancing the thermal properties of polymer matrices due to its exceptional thermal stability and low thermal expansion. The addition of silica to polymers results in enhanced thermal resistance, improved dimensional stability, and decreased coefficient of thermal expansion [72].
- The incorporation of silica nanoparticles into polymer matrices has been shown to enhance their electrical properties, specifically in terms of dielectric constant and insulation resistance. Polymer-silica composites exhibit favourable characteristics for utilisation in the electronics sector, encompassing printed circuit boards, insulators, and electrical encapsulants.
- The surface properties of composites can be regulated by functionalizing silica nanoparticles with diverse organic compounds [73]. The process of modifying the surface of silica results in improved compatibility with polymer matrices, enhanced dispersion, and interfacial bonding, ultimately leading to superior mechanical performance and stability.

Polymer-silica composites have been observed in various fields such as:

- Polymer-silica composites have been identified as a viable material for use in various automotive components, including but not limited to bumpers, body panels, and interior parts. Composite materials provide enhanced mechanical durability, impact resilience, and reduced weight, thereby promoting fuel economy and ensuring vehicular safety.
- Polymer-silica composites have been employed in aerospace applications due to their lightweight characteristics, high strength-to-weight ratio, and ability to withstand elevated temperatures [74]. Their employment is in the domain of aircraft components, encompassing structural elements, interior panels, and materials for thermal insulation.
- Polymer-silica composites have been utilised in various electronics and electrical engineering applications such as circuit boards, connectors, insulating materials, and encapsulation. The composites provide excellent electrical insulation properties, thermal stability, and dimensional accuracy.
- Polymer-silica composites have been utilised in various biomedical applications, including tissue engineering scaffolds, drug delivery systems, and biosensors [75]. The composites offer biocompatibility, controlled release properties, and mechanical strength suitable for various biomedical devices and implants.

6 Fabrication Methods for Silica-Polymer Composites

The techniques employed in the production of silica-polymer composites are contingent upon the targeted composite architecture, characteristics, and proposed utility. In this discourse (also showed in Fig. 3), we shall deliberate on prevalent techniques employed in the production of silica-polymer composites. The Sol–Gel method is a process that involves the conversion of a colloidal solution (sol) into a solid or gel-like material through a series of chemical reactions.

The sol–gel process is a prevalent methodology employed in the production of silica-polymer composites. The process entails the hydrolysis and condensation of silica precursors, namely tetraethyl orthosilicate (TEOS) or tetramethyl orthosilicate (TMOS), while a polymer matrix is present [76]. The process commences by blending the silica precursor with a solvent to generate a sol, which is a colloidal suspension comprising of silica particles. Subsequently, the polymer is introduced into the sol, and the resultant amalgam undergoes gelation and desiccation procedures, culminating in the production of the composite substance [77].

The sol–gel technique presents various benefits, such as the capacity to regulate the dimensions, dispersion, and incorporation of silica particles into the polymer matrix. The sol–gel process facilitates the inclusion of functional groups or additives, thereby enabling the alteration of the composite's characteristics [78]. In addition, the sol–gel technique exhibits compatibility with diverse polymers and facilitates the generation of composite coatings, films, or bulk materials.

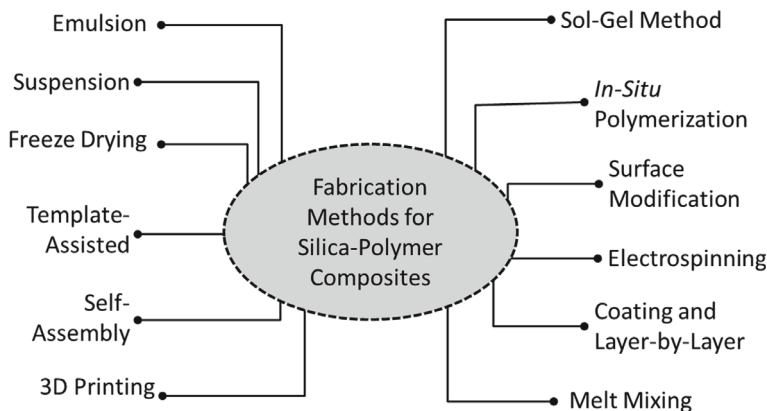


Fig. 3 Different methods for fabrication of silica-polymer composites

The process of in situ polymerization involves the concurrent polymerization of monomers and the hydrolysis/condensation of silica precursors to create the polymer matrix. This methodology facilitates the in-situ generation of silica nanoparticles or networks within the polymer matrix [79]. The procedure commences by blending the silica precursor, monomers, and additional additives within an appropriate solvent [4]. The polymerization reaction is initiated by the addition of initiators or catalysts, while the hydrolysis and condensation of the silica precursor take place concurrently.

The utilisation of in situ polymerization presents certain benefits, including the achievement of superior interfacial adhesion between the silica and polymer phases, leading to enhanced mechanical characteristics. The technique additionally enables the regulation of the dimensions, arrangement, and structure of the silica component [80]. The properties of a composite can be customised to a greater extent by selecting appropriate monomers and optimising the reaction conditions. This can lead to improvements in various aspects such as thermal stability, biocompatibility, and electrical conductivity.

Surface modification is a method employed to improve the compatibility and adhesion between the polymer matrix and silica particles. The functionalization of silica nanoparticles or fillers involves the utilisation of coupling agents or surface modifiers that exhibit an affinity for both silica and polymers [81]. The process of modification generally entails the interaction between the functional groups present on the surface of silica and the molecules of the modifier, leading to the formation of either covalent or physical bonds.

The dispersion of silica particles within the polymer matrix is improved, interfacial adhesion is enhanced, and aggregation is reduced through surface modification. Moreover, it enables the regulation of surface characteristics, such as hydrophobicity or hydrophilicity, to correspond to the intended attributes of the composite. The methods employed for surface modification encompass silanization, which entails the utilisation of organosilane compounds as coupling agents, along with chemical grafting and physical adsorption techniques.

Electrospinning is a multifaceted methodology employed for the production of nanofibrous composites that possess a substantial surface area. The production of silica-polymer composites entails the dispersion of silica nanoparticles in a solution of polymer [82]. Subsequently, the solution is exposed to a potent electric field, leading to the emergence of a stream of the solution that experiences elongation and solidification during its transit towards a grounded collector.

The utilisation of electrospinning technique facilitates the generation of composite mats or membranes that are comprised of ultrafine fibres that are embedded with silica nanoparticles. The approach presents numerous benefits, such as the capacity to regulate the fibre diameter, porosity, and surface area of the resultant composite. The presence of a fibrous structure is known to augment mechanical properties, facilitate cell adhesion, and enable the encapsulation of bioactive agents. The technique of electrospinning finds extensive application in the fields of tissue engineering, drug delivery, and filtration.

The application of coating techniques entails the process of depositing a layer of silica onto a substrate made of polymer or coating a substrate made of silica with a layer of polymer [83]. Frequently employed techniques for coating are dip coating, spin coating, and chemical vapour deposition. The dip coating process involves submerging the substrate into a solution that contains either silica nanoparticles or precursors. Subsequently, the composite coating is formed through a process of drying or curing. The spin coating technique entails the even distribution of a solution onto a substrate, followed by rapid rotation at elevated velocities to attain a homogenous coating.

Layer-by-layer assembly involves the sequential deposition of alternating layers of polymers and silica through electrostatic interactions or chemical bonding. This methodology facilitates accurate manipulation of the layer thickness and chemical makeup. Layer-by-layer assembly can be achieved through the utilisation of diverse techniques, including electrostatic self-assembly and surface-initiated polymerization [84].

The utilisation of coating and layer-by-layer assembly techniques presents certain benefits, including the capacity to produce thin films or coatings with regulated thickness and composition. The utilisation of these techniques enables the creation of complex structures that possess customised attributes, such as heightened mechanical durability, superior barrier capabilities, or regulated release properties [85]. The selection of the coating technique is contingent upon the nature of the substrate and the intended usage.

The process of melt mixing is a widely employed technique for the manufacture of silica-polymer composites, particularly in scenarios involving extensive production. The process entails the dispersion of silica nanoparticles or fillers within a molten polymer matrix via techniques such as melt extrusion, injection moulding, or compression moulding. The procedure commences with the amalgamation of the polymer and silica particles at temperatures that surpass the melting point of the polymer.

The process of melt mixing involves the generation of shear forces by the mixing equipment, which facilitates the dispersion and distribution of silica particles within

the polymer matrix. Subsequently, the composite material is subjected to a cooling process, resulting in its solidification and the attainment of the ultimate product. The process of melt mixing presents several benefits, including ease of implementation, potential for expansion, and the capacity to generate large quantities of composite materials with a uniform dispersion of silica particles. Optimisation of process parameters such as temperature, shear rate, and mixing time can lead to the attainment of the desired dispersion and composite properties.

The aforementioned fabrication techniques offer a diverse set of methodologies for producing silica-polymer composites that possess customised properties and structures. The selection of a particular technique is contingent upon the particular demands of the application, including the preferred composite morphology, the suitability of the polymer and silica constituents, the potential for expansion, and the processing circumstances. Scholars and practitioners persist in investigating and advancing novel fabrication techniques to augment the characteristics and capabilities of silica-polymer composites for diverse applications in the field of biomedicine and beyond.

7 Characterization Techniques

In the context of biomedical applications, the characterization of silica polymer composites involves the utilisation of particular methodologies to evaluate their biocompatibility, drug release kinetics, and plausible interactions with biological entities [86]. The present study outlines fundamental methods for characterising silica polymer composites in the context of their biomedical applications.

The assessment of cytotoxicity is a crucial step in determining the effect of composites on the viability and proliferation of cells. The methodology entails subjecting cells to the composite material and evaluating their subsequent reaction. The MTT assay is a frequently employed method for assessing cellular metabolic activity. Furthermore, the ISO 10993-5 standard offers directives for evaluating the *in vitro* cytotoxicity of medical devices, encompassing composite materials.

The process of biocompatibility assessment involves evaluating the compatibility of a composite material with living tissues and fluids to ensure its suitability for use in biological systems. Cell adhesion assays, such as the cell attachment assay or cell spreading assay, are employed to assess the capacity of a composite material to facilitate or impede cell attachment and proliferation. Hemocompatibility assessment evaluates the compatibility of a composite material with blood by analysing parameters such as hemolysis, platelet activation, and coagulation. Immunological evaluations are conducted to assess immune responses elicited by the composite, encompassing immune cell activation or inflammatory reactions.

Silica polymer composites have been frequently employed in drug delivery applications for drug release profiling purposes. Comprehending the drug release behaviour of composites is of utmost importance. Dissolution studies can be employed to evaluate the kinetics of drug release from the composite material under

simulated physiological conditions. The analysis of release kinetics is a valuable tool for determining the release profile of a substance. This can be achieved through the application of different mathematical models, including the zero-order, first-order, or Higuchi model. The concentration of the drug that is released over a period of time can be quantified using analytical techniques such as HPLC.

Surface characterization techniques offer insights into the surface chemistry, functional groups, and topography of the composite. The Fourier-transform infrared spectroscopy (FTIR) technique is utilised to examine the infrared absorption spectrum of the composite, thereby identifying the existence of particular chemical bonds and functional groups. X-ray photoelectron spectroscopy (XPS) is a technique that enables the identification of the elemental composition and chemical states of a given surface. The utilisation of Atomic Force Microscopy (AFM) enables the attainment of high-resolution imaging, thereby facilitating the visualisation of the surface topography and roughness of the composite.

The evaluation of mechanical properties is of paramount importance in the context of biomedical applications. The process of tensile testing involves the application of tension to a composite material until it reaches its point of failure, thereby enabling the determination of its strength and elasticity. The process of compression testing involves the evaluation of an object's ability to withstand compressive forces [87]. The utilisation of nanoindentation can facilitate the determination of the hardness and elastic modulus of a composite material at a microscopic level. The aforementioned tests offer valuable information regarding the mechanical properties of the composite material as well as its capacity to endure physiological stresses.

The process of degradation evaluation involves the examination of the degradation of biodegradable silica polymer composites as they undergo natural deterioration over a period of time. The analysis of weight loss entails monitoring the alterations in the weight of the composite material during the process of degradation, thereby furnishing valuable insights into the rate of degradation [88]. The utilisation of scanning electron microscopy (SEM) enables the observation of alterations in the surface morphology of the composite material throughout the process of degradation. The technique of Differential Scanning Calorimetry (DSC) is employed to quantify the heat flow that is linked with the degradation mechanisms, thereby enabling the assessment of thermal characteristics such as the glass transition temperature or melting temperature.

The interaction of composites with biological fluids and tissues is significantly influenced by their surface wettability. Therefore, surface wettability is a critical factor to consider in the evaluation of composites. The assessment of contact angle measurements pertains to the extent of droplet spreading or beading on the surface of the composite material. A reduced contact angle is indicative of enhanced wettability, which suggests that the composite material is more prone to exhibiting favourable interactions with biological constituents.

The aforementioned techniques furnish significant insights into the physical, chemical, biological, and mechanical attributes of silica polymer composites, thereby facilitating researchers to assess their appropriateness for biomedical applications and refine their configuration for particular objectives.

The assessment of silica polymer composites' effectiveness and appropriateness in biomedical applications necessitates the use of mechanical and thermal characterization methods. The following are prevalent methodologies employed for the purpose of mechanical and thermal characterization:

The mechanical properties of a composite material can be evaluated under tension through the use of tensile testing. The parameters that are assessed include tensile strength, elongation at break, Young's modulus, and yield strength. Compression testing is a method used to assess the reaction of a composite material when subjected to compressive forces. The aforementioned data pertains to the compressive strength, compressive modulus, and deformation behaviour. Flexural testing, which is also referred to as three-point bending, is a method utilised to evaluate the capacity of a composite material to withstand bending forces. This aids in the determination of both the flexural strength and flexural modulus. Nanoindentation is a method utilised to determine the mechanical properties of materials at small scales, specifically the hardness and elastic modulus. The process entails the creation of surface indentations on the composite material through the utilisation of a pointed indenter, followed by the quantification of the corresponding force–displacement correlation. Dynamic Mechanical Analysis (DMA) is a technique that evaluates the mechanical characteristics of materials with respect to changes in temperature and frequency. The aforementioned parameters, namely storage modulus, loss modulus, and damping behaviour, can be evaluated through this method. Thermal analysis involves the use of various techniques to study the behaviour of materials under different thermal conditions. One such technique is Differential Scanning Calorimetry (DSC), which is utilised to measure the heat flow associated with thermal transitions, including but not limited to melting, crystallisation, glass transition, and curing. The aforementioned statement furnishes insights into the thermal characteristics of a system, encompassing the identification of transition points and alterations in enthalpy.

Thermogravimetric Analysis (TGA) is a technique utilised to determine the alteration in the mass of the composite in response to temperature. This technique is employed to ascertain the thermal stability of a substance, its decomposition temperature, as well as the existence of volatile components or residual solvents. Dynamic Mechanical Analysis (DMA) is a technique that can yield significant insights into the thermal characteristics of composites. This includes the temperature-dependent viscoelastic behaviour and the glass transition temperature, as previously noted. The utilisation of mechanical and thermal characterization techniques facilitates the evaluation of the mechanical properties such as strength and elasticity, deformation behaviour, thermal stability, and transitions of silica polymer composites intended for biomedical applications. Their contributions aid in comprehending the performance of the material, enhancing its design, and verifying its appropriateness for particular biomedical applications such as implants, scaffolds, drug delivery systems, or tissue engineering.

8 Surface Analysis of Silica-Polymer Composites

The distinctive characteristics and versatile applications of silica-polymer composites have rendered them a subject of considerable interest in the realm of biomedical research. The examination of the surface properties, interactions, and efficacy of these composites in biomedical environments is of paramount importance. Several conventional methods are employed for the surface analysis of silica-polymer composites.

The Scanning Electron Microscopy (SEM) is a prevalent method utilised to investigate the surface morphology of materials at a significant magnification. The provided data furnishes comprehensive insights into the surface topography, particle size, and distribution of silica particles embedded in the polymer matrix.

The Atomic Force Microscopy (AFM) technique is a highly effective method for surface imaging and characterization, providing exceptional resolution. The silica-polymer composite's nanoscale surface roughness, topography, and mechanical properties can be determined through its utilisation.

X-ray Photoelectron Spectroscopy (XPS) is a highly surface-sensitive analytical technique that facilitates the determination of the elemental composition and chemical bonding states of the surface [89]. The utilisation of this technique facilitates the detection of silica particles and their interplay with the polymer matrix, alongside any alterations in surface chemistry that may arise from surface modifications or treatments.

The Fourier Transform Infrared Spectroscopy (FTIR) technique is employed for the purpose of examining the molecular structure and chemical composition of various materials. The utilisation of this technique enables the examination of the interplay between silica and the polymer matrix, the determination of functional groups, and the detection of any chemical alterations or reactions taking place at the surface [90].

The assessment of wetting properties of a material surface can be conducted through the utilisation of contact angle measurement. The composite's hydrophilicity or hydrophobicity can be evaluated and its interaction with biological fluids or tissues can be analysed through the insights it offers.

The determination of surface energy and surface tension of composite materials can be achieved through the utilisation of surface energy analysis techniques, such as the Owens–Wendt method or the van Oss–Chaudhury–Good model [91]. The aforementioned parameters play a pivotal role in comprehending the composite's interactions with its ambient milieu, encompassing biological fluids.

The profiling of surface roughness is a crucial factor that can exert a substantial impact on the interactions between the composite and its surrounding environment. Methods such as stylus profilometry and optical profilometry are viable options for the measurement and quantification of roughness parameters, including but not limited to R_a (average roughness) and R_q (root mean square roughness) [92].

The utilisation of these methodologies can furnish significant insights into the surface characteristics, morphology, chemical composition, and interfacial

phenomena of silica-polymer composites, thereby facilitating the enhancement of their configuration, functionality, and suitability for diverse biomedical implementations.

8.1 *Drug Delivery Systems*

Silica-polymer composites exhibit considerable potential as drug delivery systems due to their ability to provide a high drug-loading capacity, controlled release, stability, and biocompatibility. The composites operate through the process of drug encapsulation within porous silica particles or mesoporous silica nanoparticles. The polymer constituent functions as a safeguarding framework, impeding untimely drug discharge and deterioration [93]. The regulated discharge of the enclosed medication can be accomplished by manipulating variables such as aperture dimensions, polymer constitution, and drug-polymer interplays. Surface modifications with ligands or functional groups can facilitate interactions with specific cells or tissues, enabling targeted drug delivery [28]. The utilisation of biodegradable polymers and biocompatible coatings is essential to ensure compatibility with biological systems [94–97]. Furthermore, the integration of external stimuli can facilitate the achievement of drug release as needed and enable control over the spatial and temporal aspects of the process. In general, silica-polymer composites offer a flexible framework for customised drug administration, rendering them appropriate for diverse biomedical implementations.

8.2 *Silica-Polymer Composite Carriers for Drug Delivery*

Taking advantage of silica-polymer composite carriers presents a potentially advantageous strategy for the effective administration of pharmaceuticals [98]. The carriers exhibit a core-shell architecture, wherein a core of silica nanoparticle is enveloped by a polymer shell. The utilisation of a silica core offers both stability and a notable surface area for drug loading, whereas the polymer shell guarantees biocompatibility, controlled release, and targeted delivery [99]. It is possible to design composite carriers with accurate dimensions, morphology, and surface characteristics to enhance drug entrapment, safeguarding, and discharge kinetics [21]. Furthermore, the permeable characteristics of silica facilitate the integration of remedial agents, such as proteins, peptides, or nucleic acids, thereby conferring adaptability in the realm of pharmaceutical transportation implementations. The composite carriers that incorporate both silica and polymer materials exhibit a synergistic effect that has the potential to enhance the specificity and efficacy of drug delivery systems. This advancement in drug delivery technology has the potential to enable personalised medicine and ultimately improve patient outcomes.

The initial stage of the process entails the incorporation of the drug into the carriers composed of silica-polymer composites. The porous structure of the carrier's silica component results in a significant surface area [100]. Drug molecules can be immobilised onto the surface of silica particles via either adsorption or chemical bonding. Furthermore, the porous architecture facilitates the entrapment of drug molecules within the pore network, affording safeguarding and regulated liberation [101].

The process of encapsulation and protection involves the confinement of the drug within a polymer shell subsequent to its loading onto the silica component [102, 103]. The polymer shell functions as a safeguarding barrier, safeguarding the drug molecules against degradation and impeding untimely discharge. The selection of the polymer material is conducted with great care to ensure both biocompatibility and stability, thereby creating an appropriate milieu for the drug that has been loaded. The composite carriers have been engineered to achieve controlled release of the drug [104]. Diverse mechanisms can be employed to accomplish this objective. Diffusion-controlled release is a frequently employed strategy in which the drug molecules diffuse slowly through the polymer matrix. The diffusion rate is subject to various factors, including the polymer matrix's size and structure, as well as the drug molecule's characteristics. Degradation-controlled release is an additional mechanism that involves the gradual release of the drug due to the degradation of the polymer shell over time. It is possible to customise the degradation rate of the polymer in order to attain the intended release kinetics. Furthermore, the attainment of stimuli-responsive release can be accomplished through the integration of stimuli-responsive polymers into the composite carriers [104]. Polymers exhibit alterations in their structure in reaction to particular stimuli such as temperature, pH, or enzyme activity, leading to the discharge of the medication at the intended time or location. The composite carriers possess the potential for additional functionalization to attain drug delivery that is targeted [105]. The surface of the carriers can be modified by attaching ligands or antibodies that exhibit specificity towards particular cells or tissues. The ligands or antibodies have the ability to identify and attach to receptors or antigens that are present on the target cells, thereby enabling the precise administration of the drug to the intended location [106]. The implementation of a focused strategy has been shown to augment the effectiveness of drugs while simultaneously mitigating unintended impacts, ultimately leading to better treatment results.

8.3 Silica-Polymer Composite Carriers for Tissue Engineering Scaffolds

Silica-polymer composites find a noteworthy application in the form of scaffolds for tissue engineering. The scaffolds in question offer a structural framework in three dimensions (3D) that aids in the cultivation, expansion, and specialisation of cells, thereby expediting the process of tissue regeneration or restoration. The utilisation

of silica-polymer composites presents various benefits in the fabrication of scaffolds for tissue engineering. The mechanical properties of a scaffold can be improved by incorporating silica nanoparticles into its polymer matrix, resulting in a significant enhancement of its strength and stability [107]. The mechanical properties of silica are noteworthy due to their high stiffness and toughness, which can serve to fortify the polymer scaffold and furnish the requisite structural integrity for facilitating tissue growth. Silica-polymer composites offer the ability to finely tune the porosity, pore size, and surface properties of scaffolds [108]. The scaffold's porous architecture enables the transportation of nutrients and oxygen, elimination of waste, and infiltration of cells. The manipulation of surface properties can be employed to enhance cellular adhesion, proliferation, and differentiation, thereby facilitating favourable interactions between the scaffold and the adjacent biological environment [109]. Silica-polymer composites have the potential to facilitate controlled drug delivery by integrating drug molecules into the scaffold, thereby enabling targeted and regulated discharge of therapeutic agents [110]. The aforementioned capability enables the transportation of growth factors, cytokines, or other bioactive molecules to foster tissue regeneration and expedite the intended cellular reactions within the scaffold [111]. The amalgamation of silica and polymer materials in the composite scaffold has the potential to provide improved biocompatibility and bioactivity. Silica is recognised for its bioactive characteristics that facilitate the adhesion and proliferation of cells. The selection of the polymer component can be conducted with precision to ensure congruity with the intended tissue and to furnish a suitable milieu for cellular proliferation and tissue development. The controlled degradation properties of silica-polymer composites can be engineered to facilitate scaffold degradation and tissue integration. The scaffold exhibits a gradual degradation over time, facilitating the substitution of the synthetic constituent with newly generated tissue. The scaffold's integration with the surrounding tissues is facilitated by the biodegradability and biocompatibility of silica. Through the utilisation of the distinctive characteristics of silica-polymer composites, it is possible to customise tissue engineering scaffolds to suit particular tissue categories and purposes. Composite scaffolds offer a biomimetic microenvironment that facilitates cellular activities, fosters tissue regeneration, and allows for the creation of functional and structurally robust tissue replacements for diverse medical applications, such as bone regeneration, cartilage restoration, and organ engineering.

The utilisation of silica-polymer composite scaffolds in tissue regeneration presents a distinctive amalgamation of structural reinforcement, porous morphology, surface alterations, regulated medication administration, and biocompatibility [99]. The scaffolds offer a biomimetic milieu conducive to cellular proliferation and tissue morphogenesis. The addition of silica to the scaffold results in an improvement in its mechanical strength, whereas the polymer constituent facilitates its processability and flexibility. The permeable configuration facilitates the infiltration of cells, diffusion of nutrients, and ingrowth of tissue. Surface modifications facilitate the binding of bioactive molecules to direct cellular responses. The localised release of therapeutic agents is facilitated by controlled drug delivery within the scaffold. In general, composite scaffolds exhibit considerable promise for tissue regeneration purposes

owing to their ability to furnish an ideal microenvironment that facilitates cellular functions and encourages the regeneration of functional tissues.

8.4 Cellular Interactions and Biocompatibility Studies

The assessment of silica-polymer composites for biomedical purposes heavily relies on the examination of cellular interactions and biocompatibility as shown in Fig. 4. The objective of these investigations is to comprehend the cellular interactions with the composite material and evaluate its biocompatibility, cytotoxicity, and likelihood of unfavourable reactions. An essential element of these investigations is to assess the adhesion and proliferation of cells on the composite's surface. The adhesion of cells to the scaffold material is a crucial factor for ensuring proper integration and tissue regeneration within the scaffold. Furthermore, the evaluation of cellular proliferation offers valuable insights into the scaffold's potential to facilitate cellular expansion and tissue development [112]. Assessment of cytotoxicity constitutes an essential element of investigations pertaining to biocompatibility. Scientists utilise diverse assays to evaluate the probable cytotoxic impacts of the composite material on cellular entities. Frequently employed techniques comprise the MTT assay for gauging cell viability, along with Live/Dead staining or lactate dehydrogenase (LDH) release assay for detecting any deleterious impacts or cell demise prompted by the substance [113]. The evaluation of the composite material's interaction with immune cells is conducted to comprehend its capacity to elicit an inflammatory reaction. The assessment of the immunological response to the material involves the measurement of the discharge of inflammatory cytokines, including interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF- α) [114]. This aids in ascertaining whether the composite elicits an inflammatory response that may hinder the process of regeneration or result in unfavourable outcomes [115]. In addition, biocompatibility investigations examine the impact of the composite on cellular differentiation and functionality. This holds significant relevance in the context of tissue engineering, wherein the biomaterial must facilitate cellular differentiation into distinct phenotypes and promote their functional activity. The evaluation of cellular differentiation and the manifestation of markers specific to particular tissues offer valuable perspectives on the capacity of the composite to stimulate the intended cellular reactions. Although in vitro investigations offer valuable insights, in vivo studies are indispensable for a comprehensive evaluation of the biocompatibility and safety of silica-polymer composites. Animal models are utilised to assess the reaction of composites in living organisms, taking into account factors such as tissue integration, immune response, and the host organism's long-term effects. To ascertain the appropriateness of silica-polymer composites for biomedical purposes, it is crucial to conduct biocompatibility studies and examine cellular interactions. The aforementioned investigations assess the capacity of composites to adhere to cells, promote cell growth, avoid cell death, elicit an immune response, integrate with tissue, and avoid unfavourable reactions. These evaluations are necessary to confirm

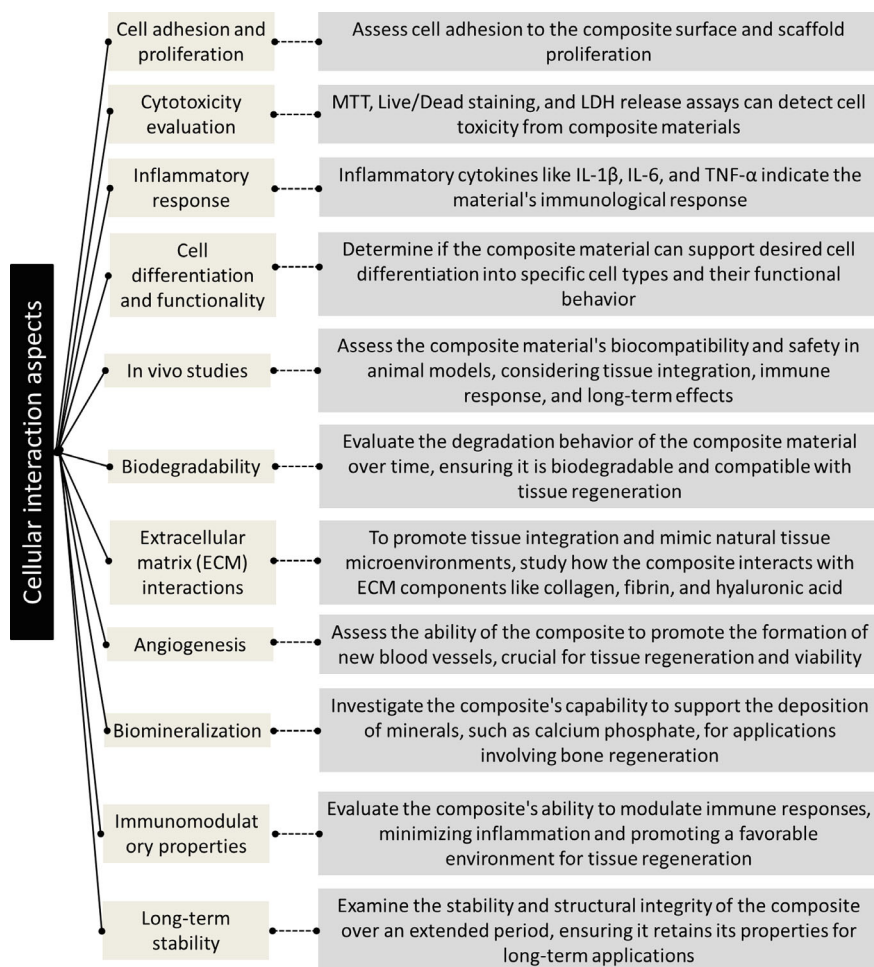


Fig. 4 Different types of cellular interactions and their descriptions

that the composites are biocompatible, secure, and able to facilitate desired cellular functions, thereby enabling effective tissue regeneration or other biomedical uses.

8.5 Bioimaging and Diagnostic Applications

The distinctive characteristics and adaptability of silica-polymer composites have rendered them a propitious option for contrast agents in the field of bioimaging [11, 116–119]. The utilisation of composites has the potential to augment the perceptibility of tissues and structures in diverse imaging modalities, thereby facilitating

superior visualisation and enhanced diagnostic precision. The present discourse highlights the salient features of silica-polymer composites in their capacity as contrast agents for bioimaging [17]. The optical properties of silica-polymer composites can be intentionally modified to demonstrate adjustable characteristics, including but not limited to fluorescence or phosphorescence. The integration of fluorescent dyes or quantum dots into the silica matrix or polymer coating of these composites enables the emission of distinct light wavelengths, thereby facilitating fluorescence imaging or optical imaging methodologies [120]. The incorporation of magnetic nanoparticles, such as iron oxide nanoparticles, within the composite structure of silica-polymer composites can result in the acquisition of magnetic properties [121]. The utilisation of magnetic composites facilitates magnetic resonance imaging (MRI), which yields high-quality anatomical images characterised by superior soft tissue contrast. Silica-polymer composites have the potential to serve as contrast agents in ultrasound imaging through the mechanism of ultrasound contrast enhancement [122]. The incorporation of gas-filled silica nanoparticles or microbubbles within the composite material has been found to enhance the reflection of ultrasound waves, thereby resulting in improved image clarity and contrast [123]. The crucial factors for the application of silica-polymer composites as contrast agents are their biocompatibility and stability [124]. The biocompatibility of silica is noteworthy, and the stability of the contrast agent can be improved by applying a polymer coating, which effectively prevents leakage or degradation within the body. The utilisation of silica-polymer composites in functionalization with targeting ligands or antibodies is capable of facilitating specific binding to particular cell types or tissues, thereby enabling targeted imaging [8]. This approach is commonly referred to as targeted imaging or multimodal imaging. Moreover, it is possible to tailor these composite materials for multimodal imaging purposes, wherein diverse imaging modalities, such as fluorescence, MRI, and ultrasound, are integrated into a solitary contrast agent to provide comprehensive and complementary information. Silica-polymer composites have the ability to encapsulate imaging agents within their structure, thereby facilitating controlled release in a specific location or over a period of time. This characteristic facilitates extended imaging sessions and guarantees the persistent existence of the contrast agent throughout imaging processes [125]. Silica-polymer composites possess distinctive characteristics that make them highly adaptable and efficacious contrast agents in diverse bioimaging contexts [33, 126]. The aforementioned composites provide enhanced imaging capabilities, targeted and multimodal imaging, and regulated release of imaging agents, thereby enabling precise and comprehensive visualisation of tissues and structures for diagnostic applications, and propelling the domain of medical imaging forward.

9 Challenges and Future Perspectives

The challenges and potential futures of silica-polymer composites are multifaceted and include considerations such as compatibility and biodegradability, scale-up and manufacturing, stability and long-term performance, controlled drug release, and multifunctionality for combination therapies [16]. The attainment of compatibility with biological systems and the creation of composites that can undergo controlled biodegradation are critical challenges that necessitate additional research and development efforts. The customization of composite degradation rates to suit particular applications and the enhancement of their biocompatibility are crucial factors to be taken into account. Furthermore, the challenge of achieving widespread practical application of silica-polymer composites lies in the need to scale up production while ensuring consistent properties. It is imperative to devise manufacturing processes that are both scalable and cost-effective while maintaining a high level of reproducibility. The suitability of composites for diverse applications necessitates a comprehensive investigation of their long-term stability and performance. Comprehending the mechanisms of degradation, enhancing stability over an extended period, and evaluating enduring biocompatibility are imperative for the efficacious integration of these materials. The precise control of drug release rates is a critical area that demands advanced strategies in the field of controlled drug release. The integration of stimuli-responsive mechanisms capable of inducing drug release in reaction to particular physiological conditions represents a promising area for prospective investigation. The potential of silica-polymer composites to exhibit multifunctionality is a highly promising area of research. The integration of imaging modalities, drug delivery mechanisms, and tissue engineering functionalities into a singular composite has the potential to significantly transform the field. The development of composite materials that can perform multiple functions and facilitate combination therapies presents novel opportunities for diagnostics, therapeutics, and tissue regeneration. The examination of these obstacles and the investigation of potential future prospects will facilitate the progression and utilisation of silica-polymer composites in a variety of domains, spanning from the realm of biomedicine to that of biotechnology.

9.1 *Emerging Trends and Future Directions*

In recent times, there has been a notable surge in the interest surrounding silica-polymer composites. As a result, various emerging patterns and potential avenues for future research can be discerned. The aforementioned trends underscore the possibility of progressions and novel utilisations of silica-polymer composites.

The potential of silica-polymer composites in nanomedicine is being investigated for their dual functionality in diagnostics and therapeutics. These composites are considered versatile platforms for this purpose. The amalgamation of imaging agents, such as fluorescent dyes or magnetic nanoparticles, with therapeutic components

facilitates theranostic applications, which enable the concomitant implementation of imaging and targeted therapy [127].

The forthcoming research endeavours are anticipated to concentrate on the advancement of silica-polymer composites that are responsive to stimuli in order to create stimuli-responsive systems. Composite materials have the ability to demonstrate characteristics that are responsive to distinct environmental stimuli, such as alterations in temperature, pH levels, or enzymatic reactions [128]. These systems have the potential to facilitate drug release triggered by specific stimuli, regulate the rate of drug release, or provide on-demand features, thereby augmenting the accuracy and efficacy of therapeutic interventions.

The amalgamation of 3D printing techniques with silica-polymer composites exhibits immense potential in the domain of tissue engineering [129, 130]. The utilisation of composites as bioinks for the printing of intricate tissue structures with improved mechanical properties, biocompatibility, and regulated release capabilities is currently being investigated by researchers.

The potential use of silica-polymer composites in advanced bioimaging and biosensing applications is currently under investigation. The integration of particular targeting ligands or functional nanoparticles into these composites has the potential to augment imaging modalities, including but not limited to MRI, fluorescence imaging, or ultrasound imaging. Moreover, they can serve as substrates for biosensors, facilitating the precise and discerning identification of biomolecules or analytes.

The potential of silica-polymer composites in environmental remediation is currently under investigation. Adsorbents have the potential to be utilised for the purpose of adsorption and subsequent removal of various pollutants, heavy metals, or organic contaminants from water or soil. The capacity for adjusting the properties of silica-polymer composites enables the enhancement of their adsorption capabilities and selectivity, thereby offering viable and eco-friendly remedies for environmental predicaments.

The potential of silica-polymer composites for energy storage and conversion applications is currently under investigation. The distinctive characteristics of silica, including its elevated surface area and thermal stability, in conjunction with the adaptable nature of polymers, render these amalgams auspicious substances for energy storage mechanisms, such as batteries or supercapacitors, as well as for photovoltaic and photocatalytic systems.

The future trajectory of silica-polymer composites involves the advancement of biomimetic and bio-inspired materials. Scholars are currently investigating the amalgamation of biological constituents, such as proteins or peptides, in order to fabricate composites that emulate organic tissues or cellular microenvironments. The bio-inspired composites exhibit the capacity to augment tissue regeneration, cellular adhesion, and general biocompatibility.

To summarise, the potential future directions and emerging trends of silica-polymer composites encompass a wide range of applications, such as their utilisation in nanomedicine, biosensing and bioimaging, 3D printing and tissue engineering, stimuli-responsive systems, environmental remediation, energy storage and

conversion, as well as the advancement of biomimetic and bio-inspired materials. Further investigation and development in these domains will broaden the possibilities of silica-polymer composites, resulting in progressions in diverse disciplines and unveiling novel prospects for their pragmatic application.

10 Conclusion

To summarise, this section has provided a thorough analysis of silica polymer composites and their usage in the field of biomedicine. The amalgamation of the distinctive characteristics of silica with the adaptability of polymers has resulted in the creation of composites that exhibit significant potential in diverse biomedical domains. The chapter expounded upon the design and synthesis strategies employed for the aforementioned composites, emphasising their capacity to be customised to suit particular applications. The multifunctionality of silica polymer composites was demonstrated by their application in various fields such as drug delivery systems, tissue engineering scaffolds, bioimaging contrast agents, and biosensing platforms. The study focused on addressing various challenges, including biocompatibility, manufacturing scalability, and controlled release. The findings suggest that there are opportunities for future research and development in this area. In the realm of biomedicine, silica polymer composites present a diverse array of biomedical opportunities and possess the capacity to transform diagnostics, therapeutics, and tissue regeneration.

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Glass/Glass–Ceramic–Polymer Composites for Biomedical Applications



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Abstract Bioimplants for the body are designed to mimic and support the body tissues for their easy replication which necessitates them to behave like extra-cellular matrix and be biologically inert for provoking minimal tissue response. But this concept is modified nowadays, as implants for biomedical applications demands tremendous mechanical resistance towards any damage to sustain its structural configuration inside the body. Such concept evokes new biomaterials which can actively participate in release of ions from their matrix resulting in a change in chemical gradient leading to biological changes within the tissue. This concept helped in the evolution of many new and novel biomaterials like Glass–ceramic fibers composites which fall under class A biomaterials, and they almost fulfill the properties of an ideal and robust biomaterial for biomedical applications. Thus, the current chapter is mainly focused on the fabrication of glass–ceramic fiber composite system, their evaluations concerning cell proliferation studies and their varied applications as biomedical devices.

Keywords Glass · Ceramics · Composites · Tissue engineering · Bone implants · Cytotoxicity

1 Introduction

Biomaterials are meant to help in replenishing damaged tissues and serve as scaffold to nurture the deteriorated cells and help in restoration of normal functions thereby accelerating the process of healing and promoting regeneration of juvenile

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tissues [1]. Many materials which are inert and nontoxic are tried with such properties which can mimic natural tissue environment aided with sufficient mechanical strength to support as scaffolds to the wounded cells. In this aspect, biomaterials came into application with the onset of use of aseptic surgical procedures, but then those materials led to some complications involving infections. With more recent developments various biomaterials evolved having multivariate applications as biomedical implants [2]. The concept of biomaterial ranges from different categories viz metals, ceramics and polymers or an amalgamation of any of these in a combined form with each category having some lacunae. Metal and alloy as biomaterials, serve as bone scaffolds by the virtue of their impactful mechanical durability, but usually suffers from corrosion and may even liberate cytotoxic by-products which limits their usage in many situations. Such limitations are surpassed by prominent ceramic biomaterials like bioactive glass, bioactive glass foams, glass–ceramic fiber composites etc., which are tissue friendly without any possibilities of corrosion, having superior mechanical strength and at the same time maintaining their structural configuration when inserted in the body and trigger cell growth effectively. The glass–ceramic composite systems are mostly used for hard tissues implants like dental implants, bone implants, etc. and are usually reabsorbable and are also considered as semi-inert by virtue of their bioactive nature [2]. Bioactive glass indicates the ability of the glass to selectively trigger the release of ions which instigate cellular functions and act as drug carrier and active hemostats [3]. Glass–ceramic composites possesses the ability of bond formation with the existing bone tissue by creating carbohydroxyapatite (CHA) layer over the bone tissue to provide interfacial bonding which is an important phenomenon for bone regrowth [4]. These composites require minimum resources for their fabrication like use of glass cullets which are typically industrial wastes along with other wastes products like eggshell for their fabrication. The general process of fabrication of glass–ceramic composites usually involves a matrix phase which is mainly the glass cullet, a dispersed phase, which is the ceramics part like eggshell, or any other type of industrial waste and both these phases are amalgamated using a third phase of sodium silicate glass [3]. Structurally glass–ceramic composites are polycrystalline solids with a wide range of crystallinity ranging from 0.5 to 99.0%, with most commonly ranging from 30 to 70% [5]. Previously, glass–ceramic composites were only designed to suffice the needs of suppressing interfacial mobility in inert ceramic implants, and later in 1967, Hench proposed to US army government to carry out research with respect to change in the composition of glass so that the surface of the implanted material can effectively form chemical bond with the living tissues making them more effective and prominent [6]. This led to the onset of development of many materials termed as biomaterials having impact on living tissues and glass–ceramics are one of such category. The incorporation of fibers within the glass–ceramic microstructure can result in enhanced mechanically durable material as these reinforced materials distribute the energy within the whole matrix and controlling the interface of the fillers and the glass–ceramic junctions. The reinforced materials can be either long continuous fibers or short fibers, but long fibers provide elastic modulus and greater strength making them temperature and environment resistant. Continuous fibers like aluminium oxide, zirconium oxide,

ferric oxide, carbon, graphite etc. [7]. Thus, the current chapter comprises of information on fabrication process, invitro-in vivo evaluations and major applications of glass–ceramic fibers composites as biomedical devices/implants.

2 Preparation Techniques

The glass–ceramic composites fabrication depends on two important parameters viz composition of glass utilized, and temperature applied. Generally, techniques used for preparation of glass–ceramic composites are summarized.

2.1 Conventional Methods

This is also known as two stage method, where devitrification of glass by two stage heat treatment takes place, with low heat treatment in the first stage for the high density nuclei generation in the glass structure at nucleation temperature and later there is application of high temperature at maximum crystallization temperature to accelerate the growth of the nuclei within the glass microstructure [8].

2.2 Modified Conventional Method

This is known as single stage method, which applies when there is an extended overlap of the rate curve with nucleation and growth stage both occurring in a single temperature phase in between nucleation temperature and maximum crystallization temperature phase. This method is aided by changing the glass composition with nucleating agents which can help in overlapping the required rate curve [8]. This method is more economical than the two stage method.

2.3 Petrurgic Method

This method involves the slow cooling of the molten parent glass to achieve both the nucleation and growth stages during the cooling process only. This method is more economical than the two-stage heating method [9].

2.4 Powder Method

This method involves heat treatment of cold compacted powder of glass and ceramics [9].

2.5 Sol–Gel Precursor Glass

This involves metal or inorganic precursor like tetra ethyl ortho silicate (TEOS), sodium hydroxide, potassium nitrate, calcium nitrate tetrahydrate, orthophosphoric acid etc. which are dissolved in alcohol and later hydrolysis in presence of water followed by condensation to get the product called as “sol” and there occurs an interconnection between sol to obtain a inorganic polymer network which contains traces of water and solvents. Application of heat results finally in a dried gel product [10].

2.6 Cold Pressing and Sintering

This method involves the pressing of precursor powder with binder in a mold into a desired shape and later the composite sintered by heating at high temperature to burn down the organic binder followed consolidation of the composites [10].

3 Applications of Glass Ceramic Composites

It was only in 1960, when Hench discovered that different materials can be processed for replacing body parts which led to the fabrication of differently composed glass ceramic composites and these materials have been utilized as biomaterials in different areas and are discussed in detail.

3.1 In Wound Healing

Wound healing requires rapid hemostasis and cell proliferation and thus many materials are tried out to obtain a successful biomaterial having all the prerequisites to mimic the extracellular matrix (ECM). Moura et al. [11], prepared bioactive glass using sol–gel method and used TEOS, calcium, phosphorus and cobalt chloride as the precursor material and doped them with silver oxide and cobalt oxide nanoparticles and dispersed these bioactive glass doped nanoparticles in polycaprolactone

nanofiber mat which was prepared by electrospinning and the prepared sheet showed sufficient efficacy in soft tissue wound healing like skin as cobalt proliferated the growth of soft tissues and silver acts as antimicrobial and over all the prepared nanofiber mat was effective in tissue regeneration for soft tissues although containing glass precursors [11]. In another study done by Solanki et al. [12], cobalt bioactive glass was designed by melt derived method to slowly release cobalt ions which accelerated the proliferation of cells required for rapid wound healing by expressing vascular endothelial growth factor (VEGF) and stabilized the hypoxia inducible factor 1- α (HIF-1 α). Moreover, the study suggested that incorporation of cobalt in the bioactive glass made the material prevent any deposition of hydroxycarbonate layer on the cell surface which was not required in soft tissue wound healing [12]. In another study done by Saatchi et al. [13], chitosan blended with polyethylene oxide nanofibers were prepared and these nanofibers were doped with cerium-bioactive glass and the prepared scaffold in its wet state had sufficient mechanical properties and well adhered to the skin to help in wound healing process. Another study done by Chen et al. [14], where they prepared nanosized porous bioactive glass coated with carbonate-hydroxyapatite for wound healing and rapid cell proliferation which also triggered the cell to migrate to the wounded area more rapidly thereby promoting angiogenesis, cell viability and tissue regeneration. Hue et al. [15], prepared copper doped bioactive glass fibers by melt derived method by using different precursors like sodium carbonate, potassium carbonate, silicon dioxide, copper sulfate etc. They dispersed the prepared copper doped bioactive glass fibers in a solution of polylactide-co-glycolic acid (PLGA) in dichloromethane in a ratio of 1/1 w/w and to this composite added vitamin at three different concentration using 0.5, 1 and 3% weight and finally again heating the mixture to 40 °C for 1 h. The prepared material showed sufficient angiogenesis with active cell proliferation very well active as wound dressing for deeper wounds [15]. In another study conducted by Agata et al. [16], where they prepared cerium doped and gallium doped phosphorus bioactive glass and applied it for proliferation of human epidermal keratinocyte cells which showed excellent results along with the invitro scratch assay showing the full closure of the wound in presence of the implanted bioactive glass devices, proving that the material is appropriate for tissue regeneration. Pourshahrestani et al. [17], prepared mesoporous bioactive glass containing 1% gallium oxide and compared its effect as hemostat against commercially available hemostat which showed much better results than the commercial product as the composite had all the essential elements required for blood coagulation.

3.2 In Cardiac and Pulmonary Applications

Bioactive glass materials are considered as second-generation materials with superior biocompatibility and nil toxicity issues. Although the bioactive glass can form bond with the living tissues, but they suffer from fragility and thus alternative materials like synthetic biologically active materials finds place for soft tissue regeneration,

which along with induction of angiogenesis, also activate the wounded cells to heal faster. For myocardial tissues, bioactive glass is prepared in the form of nanoparticles which are dispersed within the polymeric matrix for cardiac tissue engineering. Such composite systems are of high value as they can quickly facilitate the diffusion of selective ions into the tissue for rapid healing. In a study done by Chen et al. [18], they prepared a patch comprising of polyglycol sebacate (PGS) in which bioglass45S5 was added as the nanofiller for neutralizing the acidity of PGS and thus decreasing its probability of inflammation in tissues. They evaluated the utility of the patch for biocompatibility in human fibroblasts and human endometrial stoma cells (ESC) derived cardiomyocytes and concluded that the bioactive glass45S5 doped PGS can be implemented for next level trials in animal models for cardiac failure. Barabadi et al. [19], prepared hydrogel which was embedded with bioactive glass nanocomposites prepared by sol–gel method. The bioactive glass nanocomposites entrapped hydrogel showed angiogenesis activity in undifferentiated human ESCs with huge expression of vascular endothelial growth factor in the test cells when compared to that of control, suggesting that the material was highly efficacious for cardiac tissue engineering [19]. In another study done by Cohr's et al. [20], prepared a left ventricular assist device using silicone elastomer embedded with 45S5 bioactive glass which they prepared both in micro form as well as in nanoform to check the efficacy as heart implant and it was found that nanosized bioactive glass was more cytocompatible and also less swelled which was a more compatible as an implant but suffered from poor mechanical strength, whereas the microparticles of bioactive glass was twice cytocompatible with enhanced mechanical strength and ease of handling.

3.3 Lung Tissue Engineering

In the present covid situation, when majority of people are suffering from lung diseases leading to fatality, medical treatment demands lung transplant. Hench and Polak [21] first discovered that bioactive composite have potential application in lung tissue repair. Tan et al. [21], studied the activity of bioactive 58S sol–gel derived foams on growth of mouse lung cells which showed very promising results and stated that bioactive glass can be used as a scaffold for stem cell differentiation to produce mature pneumocytes. Another study proceeded by Verrier et al. [22], stated that the combination of Poly(DL-lactic acid) along with 45S5 bioactive glass showed very promising results with human A549 lung carcinoma cells. They prepared composites using three different concentrations of bioactive glass as 0%, 5% and 40% and found that with only 5% bioactive glass in the bioactive-PDLLA composites, showed better results and thus concluded that it is always better to optimize the concentration of bioactive glass based on the tissue required for regeneration [22]. Also, Wang et al. [23], studied that the growth of human A549 lung carcinoma cells significantly reduced in presence of iron-doped sol–gel bioactive glass which paved a new area for treating lung cancer by use of bioactive glass. Further studies showed that the active ions leaching from the bioactive glass did not accumulate in the major organs

and also there were no minor nor major damage occurred to the organs due to the silicone from the bioactive glass used for tissue engineering.

3.4 Nerve Tissue Repair

Any damage to the nerve tissue can result in permanent vision loss and even surgical procedures are sometimes not successful, which arises the need for alternative treatment strategies and thus attempts for repair of nerve tissue are explored by various platform and bioactive glass is one such potent scaffold which can be efficacious in this aspect. Gilchrist et al. [24], studied the activity of the bioactive glass in sheep facial nerves by placing bioactive glass tubes inside the nerves of 5 no. sheep for 10 months and compared with that of control sheep nerves and observed that rate in peak velocity of conduction and the minimum velocity was within the normal limits which gave a way that the use of controlled release glass can be used for nerve repair. In another study done in 2005 Bunting et al. [25], where they prepared a scaffold using the silastic ducts in murine model by intubating bioactive glass 45S5 in rats and results evidenced tremendous neuron tissue regrowth when compared to control and this result was almost similar to the rat treated with autografts. This study illuminated the fact that bioactive glass composites can serve a good platform for peripheral nerve tissue regeneration. Koudehi et al. [26], prepared a scaffold composed of novel nano-bioactive glass-gelatin composite system for the regeneration of peripheral nerves, which proved remarkable for damaged sciatic nerves. Joo et al. [27], tried for repairing divided spinal cord by implanting a composite of collagen with phosphate glass fibers and the animal showed improved locomotion and normal bladder functions after 2 months of surgery and this was almost comparable to the control animal.

3.5 Bone Cell Regeneration

The low capability of glass to withstand huge pressure makes it unsuitable for its wide application in bone tissue applications many times and thus to combat such loop holes, glass–ceramic composites play a major role in bridging the gap. The various ionic contents released from bioactive glass composites trigger the enzyme activity, vascularization and cell proliferation of osteoprogenitor cells. Active controlling of the components in the glass can help in rebuilding of new blood capillaries with the osteo cell. Moreover, scaffolds for bone tissue regeneration require to be conducting in nature and porous to facilitate cell replication within them. Shamim et al. [28], prepared bioactive glass composed of phosphorus with different concentration of boron trioxide doped within the matrix to increase the mechanical strength with increase in alkaline phosphatase activity when the concentration of boron used in the bioactive glass ceramic composite ranges from 0 to 5%, but it was seen with

more increase in boron content, there was no change in activity. In 2020, Suarez et al. prepared a porous glass ceramic composite with calcium content devoid of any phosphorus and thus studied its efficiency for bone tissue regeneration. The prepared scaffold exhibited antimicrobial efficacy against *Escherichia Coli*. The increased content of calcium led to the proliferation of osteo cells and also promoted greater protein adsorption and thus the prepared material served as an effective biomaterial [29]. Chiara et al. [30], investigated the potential of porous glass–ceramic scaffolds which can exactly mimic bone tissue which are actually formed by cortical and cancellous bone. The glass–ceramic composite was prepared by melt-quenching method and the prepared material possessed the ability to bear the load exactly similar to natural bones with sufficient mechanical strength and durability [30]. In another study done by Natalie et al. [31], where they quantified the ability of a glass ceramic composite system of Lithium oxide-Zirconium oxide and silicon dioxide blend which they fabricated by using replica method and the prepared composite showed the 83% porosity possessing compressive strength almost equivalent to trabecular bone with mechanical strength of more than 1.4 MPa, thus suggesting that the composite system could be efficiently used for replacing trabecular bone in case of any injury or also can help in tissue regeneration of trabecular bone tissues. Many a times it has been observed that due to the poor interaction of the glass–ceramic composites with the surrounding biological environment, they fail as biomaterial, and thus Abdalla et al. [32] came up with their research where they prepared needle like structures of bioactive glass on surfaces of various polyamide6 as substrates by using ion dissociation method. Their results were quite promising as the bioactive glass composite with polyamide 6 enhanced osteogenic cell differentiation and also showed affinity for apatite formation almost similar to bones [32].

3.6 Dental Applications

Bones and teeth are an amalgamation of two types of tissues both hard and soft and thus special material needs to be applied for their replacement which possess the mechanical strength which a person applies during chewing operations and at the same time also make the patient not experience any discomfort. Sowmya et al. [33], prepared bioactive glass–ceramic nanoparticles which were incorporated in sodium alginate composite and the material was effective for periodontal tissue regeneration. They reported that human periodontal ligament fibroblast and osteosarcoma cells (MG-63) proliferated very rapidly in the sodium alginate scaffold and these scaffolds have pore size of 100–300 μm with enhanced biomineralization due to the bioactive glass–ceramic nanoparticles [33]. In another Tai et al. [34], prepared a dentrifice containing bioactive glass which was applied for 6 weeks in test groups and compared with the control group on plaque index, gingival bleeding index. It was found that in the test group there was no plaque formation after 6 weeks of usage whereas in the control group there was formation of plaque which clearly emphasized that bioactive glass was effective in improving oral health care by the presence of bioactive glass

[34]. Selma et al. [35], prepared a nonmetallic glass ceramic composite Miserite for dental implant applications as it is bioactive and also matches with the human bones and thus reduces stress shielding. Moreover the miserite glass ceramic composite prevents from any propagation of cracks and supports osteoblast cells in its presence, proving that miserite can be used as effective biomaterial dental implants for tissue regeneration [35].

4 Conclusion

Different materials are designed and fabricated to ease life and its challenges and in this effort many novel materials have been developed in past many years. Glass–ceramic composites are one such category of materials which have wide spread applications in both hard tissues like bone and soft tissues like heart. Modern day medical technology is based on such novel prosthetics which can mimic the body tissues and replace any lost organs or body parts or even can help in quick recovery of wounded cells and tissues. Thus many new materials are tested and explored to quench the thirst of such need in a situation when sometimes donor is difficult to find and also the recipient body sometimes rejects such transplants from other body. Thus such materials may reduce many major issues and life threatening problems.

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Clay Polymer Composites for Biomedical Applications



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Abstract Clay-based polymer composites have gathered significant attention in biomedical applications owing to their unique properties and versatility. This chapter explores the diverse types of clay and polymers utilized in biomedical fields, focusing on their biocompatibility and suitability for such applications. Various preparation techniques, including melt blending, solution blending, and in-situ polymerization, are discussed in detail, explaining their advantages and limitations in synthesizing clay-polymer hybrids. Characterization methods for evaluating the properties of these composites are outlined, encompassing techniques such as FTIR, XRD. Understanding these characteristics is vital for tailoring composite materials to meet specific biomedical requirements effectively. The biomedical applications of clay-based polymer composites span a wide range, including drug delivery systems, tissue engineering scaffolds, wound dressings, and medical implants. These composites offer enhanced mechanical strength, controlled drug release kinetics, and biocompatibility, making them promising candidates for various biomedical applications. Moreover, their tunable properties allow for customization according to specific application needs, further expanding their utility in the field. Their synergistic properties derived from the combination of clay and polymers enable the development of innovative solutions for addressing complex biomedical challenges.

Keywords Clay polymer composites · Biomedical applications · Melt blending · Solution blending · In-situ polymerization

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1 Introduction

Composite materials are solid materials having two or more phases, designed by combining materials with different properties. With recent advancements in the field of composites, clay composites are getting attention due to their physical, chemical as well as structural properties [1, 2].

In recent years there is a growing trend for the development of hybrid materials based on clay and polymers. Its significant features as well as distinguished properties render them attractive for biomedical applications. These materials have always attracted researchers worldwide. The development of polymer-based nanocomposites plays a significant role in the biomedical field [3, 4]. There is also an advancement in the synthesis techniques and the application of polymer–nanoclay composites [5]. Mydin et al. [4] described four main biomedical applications of polymer-based nanocomposites in their article, namely: “healthcare-associated infections, drug delivery, medical implants and biomedical applications”. Meirelles et al. have surveyed hybrid clay-based polymer composites which are attractive for drug release. Their review revealed that there is a rise in the number of publications in this area which confirms the potential rise in the use of hybrids in pharmaceutical technology. It is already a well-established fact that through the interaction between the polymer and clay, there is the enhancement of mechanical as well as the thermal properties of composites, thus promoting a stable and controlled drug release in the biological media [3]. Meirelles et al. [3] in their report mentioned that the most cited clay was montmorillonite, because of its higher surface area and ion exchange capacity. The polymeric part is mainly synthesized by the copolymerisation process, using acrylic derivatives. The hybrid materials obtained are mostly in the particulate form on the nanometric scale. Not a very large number of patents are found in this research area. However, Japan published the highest number of patents [3]. Kumar et al. [6] and Silva et al. [7] studied the properties of clay composites and reported that these composites have been incorporated in the areas of biomedical, automobile, petroleum industry, remediation technology, aerospace etc. Mohammad Fitri et al. [8] prepared Poly (ethylene–vinyl acetate) or PEVA nanocomposite incorporated with bentonite and MMT-based dual nanofiller. The fillers were assessed for biocompatibility through the cytotoxicity assay. It has been observed that the PEVA-Dual nanofiller nanocomposite has achieved biostability when subjected to physiological fluid for three months. Such findings indicate the prospective application of the composite for implant application. The polymer clay composites, due to their physical as well as mechanical characteristics, can be used as, drug carriers, membrane, shape-memory materials, bio-implants etc. [9]. Reinforcements with clay can also improve certain important characteristics; like antimicrobial characteristics, delivery of drugs to the target and biocompatibility with the blood and living tissue and organs [10]. Jayrajsinh et al. [10] also indicated that the clay-based polymer nanocomposites have potential uses in the fabrication of devices used in drug delivery, tissue engineering as well as in orthopaedic implants. Bhat et al. [11] recently developed montmorillonite (MMT)-based nanocomposites which are useful for biomedical utilization;

like drug delivery, bone cement, wound amelioration as well as tissue engineering, etc. Nano-size montmorillonite (MMT) based polymer nanocomposites are quite frequently used due to the intercalation of nano MMT, there is a positive effect on the mechanical and thermal properties of the composites. The intercalated MMT also improves biodegradability, when used with biodegradable polymers [12–14]. MMT being their nontoxic nature, as well as due to the stability in both acidic and alkaline environments, are often used in the systems of drug delivery, either alone or as a combination with the polymers [15]. Several literature data have been created on the application of MMT for the distribution of antibiotics [12, 14, 16]. Besides antibiotics, antidiabetic drugs [17], enzymes and proteins [18] and antidepressant drugs [19] can also be introduced into the MMT structure. Golubeva et al. experimented with the intercalation of Vitamin B1 into the MMT structures for the purpose of controlled drug delivery [20]. Nanoclays being nontoxic can be used in preparing composites for several biomedical applications. Tissue engineering, bone cement, immobilisation of enzyme, drug delivery and wound healing are a few of them [21]. Barrett-Catton et al. [22] carried out a review on the Biomedical application of hydrogel nanocomposites. Murugesan and Scheibel [23] reported about chitosan-based nanocomposites for several medical applications; scaffolds, 3D bio-inks, bone engineering wound dressings, drug delivery etc. The polymer clay-based nanocomposites have gained more popularity for such medical applications due to their swelling and rheological characteristics, higher retention capacities, large surface area to volume ratio etc. Williams et al. have prepared and used polyamide-based MMT composites for oral administration of Metformin. This is the drug which is used for the treatment of diabetics [24].

2 Different Types of Clay and Their Biocompatibility for Biomedical Applications

The use of clay in biomedical applications is a current breakthrough. Clay based bio-polymer composites are gaining more importance and attention for biomedical applications due to their many advantageous properties like large surface to volume ratio, swelling, biocompatibility, good rheological properties, high retention capacity, compatibility with biopolymers as reinforcing agent, [25] and antimicrobial properties. Along with these nano clays bear good mechanical properties. Particularly various types of nano-clays are majorly used for drug delivery application. Clay based bio-polymer composites are multiphase system in which clay plays a role of filler to improve the mechanical and thermal properties [26]. Use of clay is economical, ecofriendly and available adequately. In bioresin, the nano clays are either intercalated or exfoliated to improve the thermos-mechanical properties of the biocomposite [27]. The nanoclays can be used alongwith natural polymers like starch, protein and chitosan while the synthetic biopolymers like polylactic acid.

Fitri et al. [8] incorporates bentonite and MMT in EVA and developed nanocomposite as a medical implant which founds cytocompatible and stable. The clay-based nanocomposites are harmless to body cells and blood and supports tissue growth. They have induced vascularization, possess shape memory effect, proper release of drug as well as good response to stimulation. Recently, nanoclays are used along with bioinks in biomedical 3 D printing applications such as tissue engineering, bone cementing, wound healing, biomedical implants and hydrogels [11, 22, 28, 29]. Various clays are used for biomedical composite applications such as montmorillonite (MMT), kaolinite (KLN), laponite MMT is a naturally available clay in a layered silicate form. Its chemical structure is $(\text{Na}, \text{Ca})_{0.33} (\text{Al}, \text{Mg})_2 (\text{Si}_4\text{O}_{10}) (\text{OH})_2 \cdot n\text{H}_2\text{O}$ and commonly known as hydrated sodium calcium aluminum magnesium hydroxide. It constitutes SiO_2 largely and Al_2O_3 in smaller quantity. It has layered morphology with octahedral Al_2O_3 and SiO_2 in a sandwich structure. The gap between each layer is found beneficial for the penetration of polymeric matrix. Another nanoclay used for biomedical application is halloysite. It is aluminosilicate and can be used in the form of nanotube, the hollow structure is used for medical applications [30]. The clay used in polymer for the biomedical application improves its thermo-chemical stability, barrier properties, corrosion resistance, elastic modulus and durability [31]. Clay dispersed in polymer matrix is the combination of two materials giving enhanced properties. Figures 1 and 2 depicts the polymer–clay composite structure showing phase separated structure, intercalated polymer between the clay lamellae and exfoliated structure i.e. homogeneous dispersion of clay into the polymer matrix.

3 Polymer and Its Properties Used for Biomedical Applications

3.1 Polyethylene (PE)

Polyethylene (C_2H_4) is the most commonly produced plastic with a total market of over 100 million tonnes of resin being produced annually, accounting for 34% of the total plastics market [34, 35]. Which is having several different types including linear low-density polyethylene (LLDPE), low-density polyethylene (LDPE), very-low-density polyethylene (VLDPE), ultra-high-molecular-weight polyethylene (UHMWPE), and high-density polyethylene (HDPE). Among all of these, HDPE and (UHMWPE) share a significant market in medical applications. HDPE owing properties such as high density-to-strength ratio and tensile strength, but exhibits a low melting point and tendency to deform under high temperature and pressure, necessary for autoclave sterilisation for medical applications [36]. Other sterilisation methods HDPE is commonly used in medical implant devices [37].

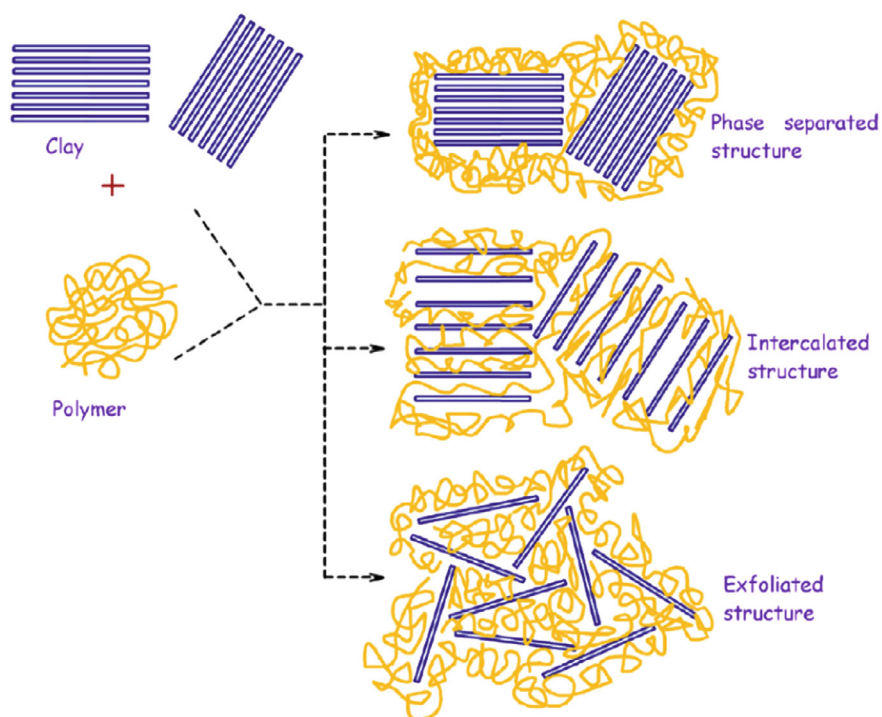


Fig. 1 Schematic representation of clay dispersion in polymer matrix. Reprinted with permission from Valapa et al. [32]

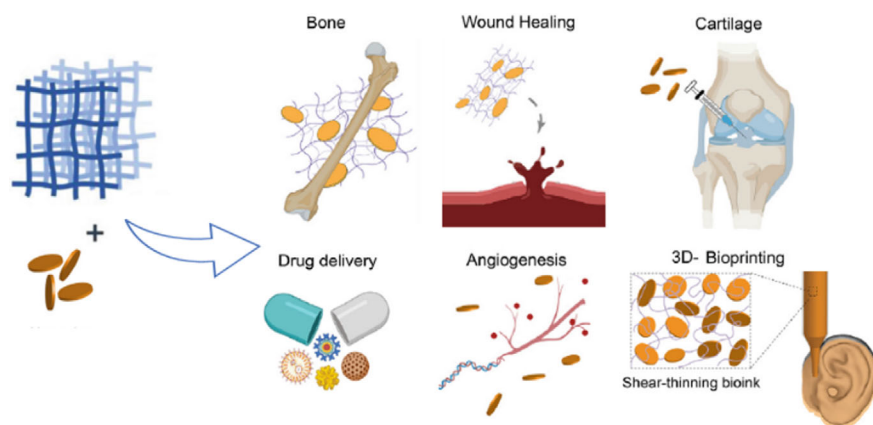


Fig. 2 Illustration of clay-based nanocomposite hydrogels for biomedical applications. Reprinted with permission from Murali et al. [33]

Biocompatibility is assessed in accordance with ISO 10993 (International Organisation for Standardization), Biological Evaluation of Medical Devices which specifically ensures that medical devices are non-toxic, non-thrombogenic (do not instigate the formation of blood clots), non-carcinogenic (do not present any risk of cancer), nonantigenic [38]. Due to governing properties of Biocompatibility, affordability and versatility which strongly impacted PE in multiple applications such as surgical implant development, drug delivery sterilisation and tissue engineering due to its commercial adoption of PE, and in particular HDPE. On the other hand, due in part to its superior properties of UHMWPE such as biocompatibility, wear resistance, chemical stability, lightweight, and lubricity which fit the biological and mechanical requirements for such applications for load bearing material in orthopaedic applications [39–41]. Because of these characteristics, UHMWPE can be directly bonded to bone and produce a biomaterial that is appropriate for replacing missing bone.

3.2 Polyurethane (PU)

Polyurethanes are produced by the addition polymerisation of an isocyanate (generally a diisocyanate), derived from crude oil and a polyol (polyether or polyester or similar). A significant family of polymers with a broad range of physical, chemical, mechanical, and structural characteristics, such as biocompatible, biostable, moldable, and strong polymers, are exceptional in that they combine the elasticity of rubber with the toughness and endurance of metal which shows comparable mechanical and physical properties comparable to natural tissue [42].

This, matched with low platelet adhesion and in vitro protein adsorption allows many uses of PU in the biomedical industry due to owing superior properties they can be utilised in variegated applications such as devices, to coatings, elastomers, adhesives and sealants used on floors and automotive interiors. Prostheses such as cardiac assist devices, small vascular shunts [43] and tracheal tubes. A commercial polyurethane product, NovoSorb™ (PolyNovo®), is a two-component system that cures in situ. The self-setting system is an injectable liquid that not only polymerizes at physiological temperatures creating a biomaterial that has been shown to be mechanically similar to bone cement but also promotes favourable cell adhesion and proliferation [44].

Under most conditions, pure polyurethanes are degradation resistant making them poor candidates for drug delivery and many tissue engineering applications. Naureen et al. have studied the PU for Tissue engineering applications in organ regeneration through scaffolds with improved bioactive properties with inclusion of biodegradable, electroactive, surface-functionalised, ayurvedic products, ceramics, glass, growth factors, metals and natural polymers for soft and hard [45].

3.3 Polyhydroxyalkanoates (PHB)

Polyhydroxyalkanoates are biodegradable polyesters that can be made either synthetically or through biological means. The most prevalent polymer in this family is poly(3-hydroxybutyrate), an isotactic semicrystalline polymer with a hydrophobic backbone and crystallinity that is subject to surface degradation. PHB has a T_g of approximately 5 °C and a melting range of 160–180 °C. [46]. To widen the applicability of PHB as a biomaterial, most commonly PHB is copolymerized with 3-hydroxyvalerate to create poly(3-hydroxybutyrate-*co*-3-hydroxyvalerate) (PHBV). PHBV is less crystalline than PHB with a lower melting temperature of 80–160 °C and a T_g in the range of – 5 to 20 °C depending on HV content [47]. PHBV has been used in tissue engineering of bone, cartilage, tendon, skin. Although the addition of HV content improves the biomaterial potential of PHB, degradation is still too slow for other biomedical applications. Significant research is underway to speed degradation rates through copolymerizing or blending PHB or PHBV with PLLA, PDLLA, PLGA, -poly(dioxanone), poly(caprolactone), and polyethers [48].

3.4 Polylactic Acid

As polylactide (PLA) possesses chiral molecules, PLAs come in four forms: poly(L-lactic acid) (PLLA), poly(D-lactic acid) (PDLA), poly(D,L-lactic acid) (PDLLA)—a racemic mixture of PLLA and PDLA, and meso-poly(lactic acid). As far as use in biomedical research, only PLLA and PDLLA have shown promise and have been extensively studied. PLLA has a T_g of 60–65 °C, a melting temperature of around 175 °C and a mechanical strength of 4.8 GPa [49]. The additional methyl group in PLA causes the polymer to be much more hydrophobic and stable against hydrolysis than PGA. Because of the slow degradation time, limited research has been recently conducted into drug delivery by PLLA systems alone [50]. Its initial utility in medicine was to treat dog mandibular fractures [51]. With its renewable source and hydrophobic aliphatic polyester composition, PLA is a cost-effective material that can be used in biomedical uses [52]. The physical properties and the biodegradable ability of PLA can be regulated by employing a hydroxyl acid comonomer component or by racemization of the D- and L-isomers. A semi-crystalline polymer of poly-L-lactide (PLLA) is obtained from L-lactide and is a hard transparent polymer with a tensile strength of 45–70 MPa. The rate of degradation of PLA is dependent upon the degree of crystallinity. Grafting allows for customization of PLA's biodegradability. The most widely used hydrophilic polymer for surface alteration is polyethylene glycol (PEG), which has been used to transform hydrophobic PLA into the amphiphilic copolymer PLA-PEG. Another advantageous quality of PLA is that it can be moulded into a variety of forms, such as scaffolds, sutures, rods, films, nanoparticles, and micelles. Due to promising properties it is used as a bone fixator. PLLA has also been extensively utilized in tissue engineering applications

ranging from scaffolds for bone, cartilage, tendon, neural, and vascular regeneration. Specifically, Dr. Peter Ma's group has produced some very exciting research on the design of PLLA-based patient-specific scaffolds.

4 Synthesis Techniques of Polymer–Clay Composites

The clay polymer hybrids composites first came into light after the Toyota Central Research and Development laboratory synthesised Nylon 6-Clay hybrid or NCH, back in the year 1986. After this, the same technique was followed for the different polymeric systems, like epoxy, polyester, polysiloxanes, polypropylene, polyurethane etc. There is difficulty in mixing clay in most of the polymer matrices due to the high face-to-face stacking and the hydrophilic character of the clay. With these characteristics, the clay is incompatible with hydrophobic polymers and a few hydrophilic polymers like polyvinyl alcohol and polyethylene oxide are miscible with clay [53]. Conventionally clays are treated with the organic agent for better dispersion of layers of clay in the matrix of polymer. The polymer clay composite preparation can be done by any of the three synthesis methods; viz Solution blending, Melt blending, and In-situ polymerisation.

It is very important to achieve the uniform dispersion of the nanoclay in the polymer matrix. There are several novel synthesis processes which have been proposed to design unique polymer-nanoclay composites.

4.1 Solution Blending

This method often produces favourable dispersion of the layers of clays in the polymer matrices, as compared to the melt blending process. In general, polymer/prepolymer is allowed to dissolve in a suitable solvent. At the same time, the clay is also dispersed in the same solvent, but separately. The layered clay is exfoliated. Then both the dispersions are mixed and allowed for homogenisation, followed by casting on a flat support, with subsequent evaporation of the solvent [1, 54–56]. The schematic diagram is shown in Fig. 3a. Upon mixing the clay and polymer/prepolymer solution, the intercalation of the polymer chain occurs and the solvent is displaced with the clay layers. The solvent is removed by vaporisation and there is the reassembly of intercalated sheets, forming the polymer/nano clay composites [25]. The solution blending process consists of three stages: viz dispersion of clay in the polymer solution, removal of solvent as the casting of the composite film. The dispersion of clay requires mechanical forces due to stirring, shear mixing etc. Ultrasonication, which is suitable for both thermoplastic and thermosets, has become an efficient method to improve the dispersion of the nanoclays in a polymer solution. Type of nanoclays, its content, solvents, type of sonication as well as the time of sonication have an impact on the dispersion quality of the clay in the polymer solution [57]. Ultrasonication

happens to have several positive effects in terms of the reaction time, dispersion of clays as well as yield of composites. Slow evaporation of the solvent plays a significant role in determining the crystallinity of the composite [58]. Buruga et al. [59] synthesised ultrasound-supported solution blending of halloysite clay-based poly methyl methacrylate and polystyrene nanocomposite. Mittal reported about the preparation of epoxy composites at a laboratory scale due to easy operation, better particle dispersion and coupling of the chemical reactions [60]. Lopez-Manchado et al. [61] has mentioned the preparation of the rubber composites with intercalated or exfoliated MMT clay, by solution blending method. Their experimental results indicated that the solution blending process yields a higher amount of bound rubber and increases the compression set, hardness etc. properties when compared with the melt blending process. Maiti et al. [62] used the same method, i.e. solution blending process to synthesise composited based on ethylene octene copolymer with exfoliated MMT clay. It was reported by the authors that the tensile strength of the composite was improved by 44%, and modulus by 63% as compared to the base polymer. The storage modulus of the composite was increased by 14%. The glass transition temperature of the composite also got shifted by 10 °C, as compared to the neat polymer. Hausner et al. [63] used a transfer batch moulding process where the authors utilised a volatile organic separator solvent for preparing Polystyrene/MMT clay composites at the melt compounding temperatures. Many more authors have worked on solution-blending techniques to prepare polymer nanocomposites by solution blending method [64–66]. The solution blending process evolves around the relatively uniform dispersion of nanoclay. Though several polymer nano clay composites have been prepared till date, there are several drawbacks of this process: (i) the intercalation of clay occurs only with certain polymer/solvent/clay combinations and (ii) some amount of organic solvents are required, which are not environment friendly as well as economically not viable [67]. However, at the commercial level, melt blending is preferred over the solution process for the preparation of thermoplastic/nanoclay composites.

4.2 Melt Blending

The solution blending method encounters the problem of mixing, whereas the melt blending process provides a better mixing. This method is also compatible with different processing methods, like extrusion, injection moulding processes etc. [25]. The melt blending process is claimed to be viable for the industry as well as eco-friendly [32]. Though this technique is of great interest to academicians and industrial researchers, mostly for thermoplastics, Albdiry et al. [68] reported that in the absence of solvents, there is a limitation in the clay dispersions. The melt blending process allows for better mixing of polymer and clay as compared with the solution blending process. In this process, the clay particles reinforce the polymer matrix directly by the melt integration method. The polymer–clay mixture is also subjected to the annealing process, done at a temperature higher than the polymer melting temperature

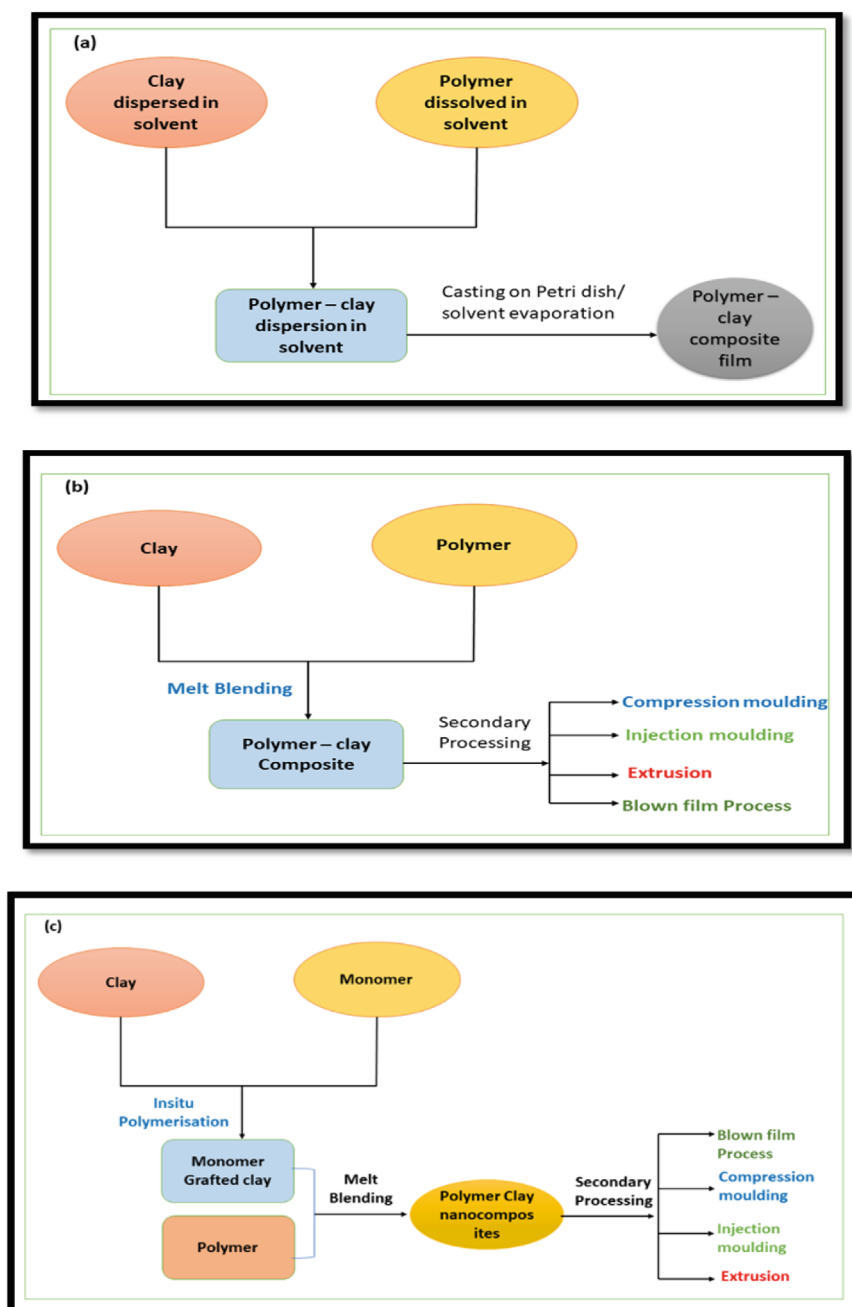


Fig. 3 a Solution blending b melt blending c in-situ polymerisation

[69, 70]. The schematic diagram of the melt blending process is seen in Fig. 3b. The melt blending method blends the desired amount of nanoclay materials intercalated with the polymers at a temperature above the softening of the polymers, in an inert atmosphere [71–74]. In the melt blending technique, the processing conditions; like temperature, screw/rotor speed, mixing time, feed rate, die pressure, raw material grades and quality as well as the chemical nature of the filler and surfactants play a significant role.

4.3 *In-situ Polymerisation*

In situ polymerisation method enables the enhancement of the compatibility between the polymer and the clay particles. This in situ method is a widely used synthesis method, which gives uniform dispersion of clay particles. This method is also an easy one where the polymerisation conditions can be changed [75]. The clay particles are first dispersed in a solution of monomer, followed by polymerisation. Lastly, the thin layer of polymer-grafted clay particles is added to the matrix of polymer followed by secondary processing techniques, viz extrusion and compression moulding [70]. The schematic illustration of steps involved in in-situ polymerization method can be seen from Fig. 3c.

Murugesan and Scheibel [76] in their review reported about nanoclay intercalated copolymeric nanocomposites. They mentioned that the basic preparation route for the preparation of clay/copolymer nanocomposite is to place the polymer chain between the clay layers or to polymerise the monomers in between the clay layers. Okamoto et al. [77] also reported the same. The authors reported three types of dispersion morphology for the clay-incorporated copolymers: viz (a) flocculation, (b) intercalation and (c) exfoliation. Figure 4 shows the schematic diagram of the three morphologies.

Le Baron et al. [78] and Thostenson et al. [79] prepared polymer clay nanocomposites by direct mixing of the monomer and clay suspensions, followed by thermal or light-induced polymerisation or by using chemical oxidants. If the major polymer part is produced outside the interlayer space, the resulting product can be called

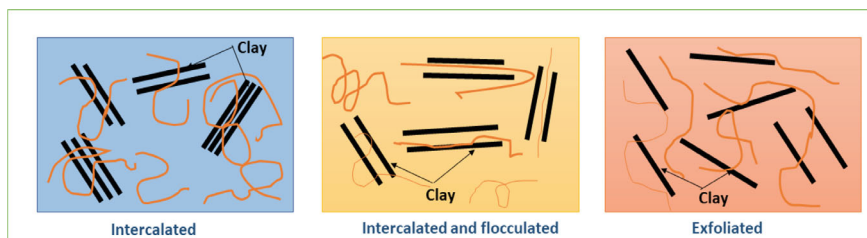


Fig. 4 Schematic diagram of the morphological arrangement of dispersion of clay in the polymer matrix

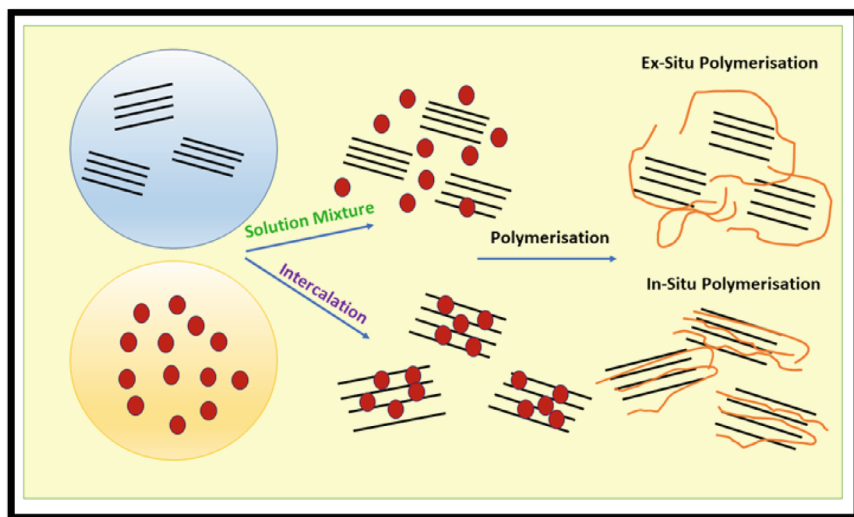


Fig. 5 Schematic diagram of the in-situ and ex-situ polymerisation of clay polymer composites

an Ex-situ nanocomposite. If the clay contains exfoliated layers, then the product is called exfoliated polymer clay composite. To get the exfoliated clay polymer composites, the initial concentration of clay can be changed in the aqueous solution. In the In-situ nanocomposite, [80] as mentioned in Sect. 4.3 has the major content of the polymer inside the clay interspace. Figure 5 shows the illustration of In-situ and Ex-situ nanocomposite [80].

5 Characterization of Clay Polymer Composites

Different techniques such as X-Ray Diffraction, Fourier transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), transition electron microscope (TEM) are used to study the morphological, structural, thermal, and mechanical properties of clay polymer composites. The clay polymer composites are also examined to check the proper dispersion and exfoliation of clay into the polymer matrices.

XRD is used to study the arrangement of crystals and spacing between the atomic layers. The proper exfoliation of nano-clays into the polymer matrix can be studied using this technique [81]. NMR is used to study the physicochemical characteristics of clay polymer composites. It is also used to know the degree of dispersion of clay into a polymer matrix. DMA is used to study the properties related to storage modulus, loss modulus and damping behaviour and tribology of clay polymer composites. The molecular vibrational properties and exfoliation efficiency of the clay-based composite is studied using FTIR. TGA is used to study the thermal stability of the

composite. The thermal degradation profile of the clay-based polymer composite can be studied systematically using TGA. The high amount of clay content is helpful to improve the thermal stability of the clay-polymer composite. The analysis of properties like glass transition temperature, melting, crystallization, and curing can be done using DSC. Degree of crystallization of the clay polymer composite can also be monitored using DSC. The proper dispersion of nano clay in the polymer matrix is easily analyzed using TEM. TEM micrograph identifies the intercalation and exfoliation morphology in the polymer composites.

6 Biomedical Application of Clay Polymer Composites

Clay minerals have been widely used in biomedical field due to the owing properties of good reinforcing property and biocompatibility [82]. They have been thoroughly investigated for a variety of biomedical applications, such a, cancer treatment, drug delivery, tissue engineering, the manufacture of scaffolds and wound healing and bone cement [83–85]. Figure 6 shows the widespread applications of nano-clay composites in biomedical applications.

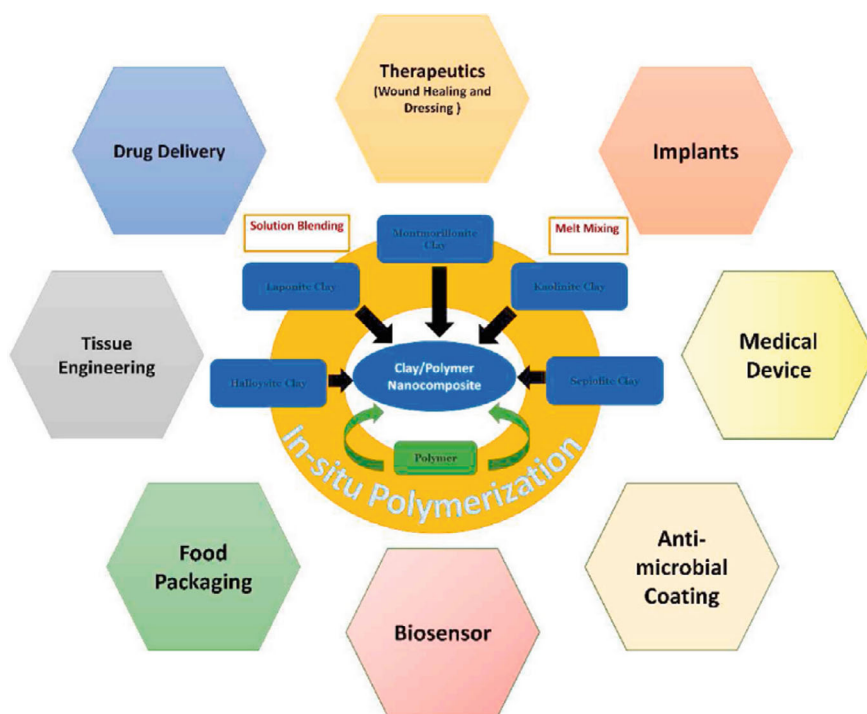


Fig. 6 Biomedical applications of nanoclay composites. Reprinted by permission: Das et al. [86]

6.1 Bone Cement

Poly (methyl methacrylate) (PMMA) bone cement undoubtedly, is one of the most widely used synthetic biomaterials. Bone cement is primarily used in orthopaedic surgery as a grouting agent for certain total joint replacements. For the purpose of securing hip and knee replacement implants into nearby bones, PMMA is frequently employed as a bone cement [87, 88]. As reinforcements for PMMA composites used in bone cement applications or bone implants that have improved bioactivity and mechanical properties, nanoclay materials have been looked into.

6.2 Cancer Treatment

Amin et al. have synthesized a composite of Chitosan (CS), hydroxy apatite (HP) and a glycopolymer grafted on a Cloisite 30B clay surface (CS/HAP/clay-g) and another one based on CS/HAP pristine Cloisite 30B (CS/HAP/clay-g) and tested cytotoxicity against breast carcinoma cell line (Hep G-2) and a normal human skin fibroblast cell line (BJ-I) using an montmorillonite (MMT) as well as a lactate dehydrogenase assay and observed results that the biopolymer composite CS/HAP/clay-g can be used in biomedical applications [89].

6.3 Drug Delivery

Clays were employed as fillers for tablets intended for oral consumption. Later, the multifunctional industry, including the agricultural, cosmetic, nutritional pharmacological, and pharmaceutical industries, became interested in using clays for smart drug delivery. Clays have a wide range of uses, including as an antioxidant, anticancer, anti-inflammatory, antibacterial, antidepressant, and blood pressure lowering nutrients and medications. Due of clay nano-composites success in delivering prolonged drug releases, they have been developed for drug delivery and wound healing [90]. Mohamed et al. studied the PMMA—MMT clay system as a drug carrier for verapamil hydrochloride, used to treat several conditions of the heart and blood vessels, like chest pain, high blood pressure, and certain irregular heart rhythms. The in vitro release profile of verapamil showed that the nanocomposite presented slower release in both gastric and intestinal fluids, compared to the drug-loaded MMT [87]. Another study performed by Salahuddin et al. observed that polyoxypropylene MMT nanocomposites can be used as ibuprofen carriers for colorectal therapy. The negatively charged clay strongly interacts with the positively charged NH_3^+ groups of the polymer, influencing the swelling behaviour and, consequently, the diffusion of the drug [91]. Chung et al have studied the Polyurethane based on polytetramethylene

oxide (PTMO) soft segments MMT as well as organo-montmorillonite using dodecylamine and hexadecylamine/solution casting for The drug release profile depends on key factors such as filler–polymer interaction, drug surface charge, and functionalities. The rate of drug release from nanocomposite film and observed to decrease for positively charged drugs and it is argued for negatively charged drugs when the d-space of the nanoclay increased.

Wang et al. developed a copolymer solution of Fluorohectorite and MMT using electrospinning and Poly(methylmethacrylate-co-methacrylic acid). When clay nanoparticles were added, the viscosity and modulus of the copolymer solutions increased, improving their spinning properties. During spinning, MMT clay particles were exfoliated and positioned parallel to the fibre axis. The nanocomposite fibre displayed improved self-extinguishing qualities as well as decreased flammability. Drug delivery and tissue regeneration [88].

6.4 Tissue Engineering

Tissue engineering scaffolds are typically used as supports which allow cells to form tissue-like structures essentially required for the correct functioning of the cells under the conditions close to the three-dimensional tissue result the monolayer cell culture is not capable of forming complex intrinsic cellular structures such as trophoblast vesicles and the placenta. In recent years, the fabrication of tissue engineering scaffolds for tissue engineering of liver, bladder, neural tissue, skin, bone, cartilage and ligaments using various combinations of natural and synthetic polymers and dopants [90]. Naumenko et al. have shown that porous hydrogel scaffolds containing clay nanotubes can improve mechanical properties, biocompatibility, and biodegradability. The mechanical stability and wettability of the biopolymer scaffolds are significantly improved by the addition of 3–6 wt% of halloysite nanotubes without impairing in vitro cell growth [92]. Cell attachment and growth on halloysite scaffolds can be demonstrated by looking at the cell distribution and shape. The in vivo investigation demonstrated the biocompatibility of these nanocomposite scaffolds in the rat body with a minimal inflammatory effect without implant rejection and a 6-week period of degradation, which was verified by histological inspection. These results confirm the great potential of chitosan–agarose–gelatine nanocomposite porous scaffolds doped with halloysite in tissue engineering with potential for sustained nanotube drug delivery [89].

7 Summary

Clay-based polymer composites for biomedical applications is a innovative and novel material with many benefits. The clay-based polymer composites have proved their usefulness in biomedical applications. The incorporation of clay particles into the

polymer matrix imparts enhanced mechanical properties to the final composite. These composites can be prepared by different techniques viz. solution blending, melt blending, in-situ polymerization. Physiologically bioactive properties are obtained with clay-based polymer composites. Such composites are found their widespread applications in biomedical like tissue engineering, drug delivery, implants, biosensors, therapeutics, and medical devices. The demand for these types of novel composite materials is increasing day by day.

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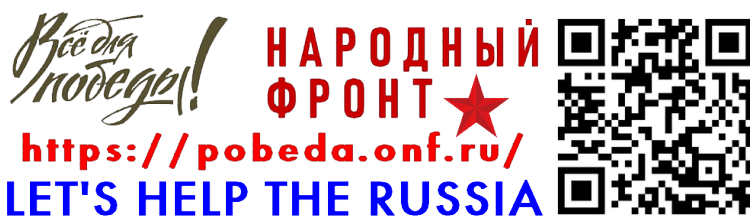
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Hydroxyapatite Ceramic-Polymer Composites for Biomedical Applications



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Abstract The present chapter focuses into the diverse and promising domain of biomaterials engineering. This chapter examines the production methods, characteristics, and many uses of hydroxyapatite (HA) ceramics and polymers in the biomedical area, with a specific focus on their synergistic combination. The combination of HA ceramics' biocompatibility and mechanical strength with the flexibility and processability of polymers provides extensive solutions for tissue regeneration, drug delivery, and medical device development, ranging from orthopedic implants to tissue scaffolds. This chapter provides a thorough examination and study of HA ceramic-polymer composites, focusing on their design principles, performance enhancements, and future possibilities. By doing so, it aims to contribute to the development of revolutionary developments in biomedicine and healthcare technology.

Keywords Biomaterials · Production methods · Hydroxyapatite · Medical · Healthcare

1 Introduction

Biomedical materials are structures obtained from various types of materials, either artificial or natural. Each material class, including metallic, ceramic, polymer, or organic, has its own place in biomedical applications. Sometimes, a single type of material may not meet the requirements depending on the specific application.

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However, along with the advantages of a material, there are also disadvantages associated with it. By combining different types of materials, it is possible to minimize these disadvantages and achieve superior performances. Hence, the demand for composite materials is increasing in line with complex requirements [1].

Ceramic biomaterials are known as one of the oldest biomaterials in history and have a usage history dating back to ivory prosthetics, extending up to the present day [13, 23]. Ceramics stand out in biomaterials due to their sought-after properties such as biocompatibility, bioactivity, biointeractivity, and osteoinductivity. While ceramics possess superior characteristics in terms of heat and electrical insulation, corrosion resistance, and wear resistance, their excessively brittle nature can limit their use. Ceramics mostly consist of oxides, phosphates, nitrides, and carbides [2]. The use of alumina and zirconia is common in ceramic biomaterial applications, but generally, ceramic materials with an inert structure do not exhibit active bonding with the tissue due to their bioinertness. In order to improve this situation, the use of bioactive ceramics and tissue scaffolds has become widespread through studies conducted in this field. Ceramics in this group are used to preserve the intermediate layer formed during the healing process of damaged tissue and to enhance implant-tissue integration. Hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) is also classified as a bioactive ceramic. It has an organic structure containing calcium, phosphorus, and oxygen elements, which are also present in natural bone, and is known to promote osseointegration [13, 23]. Its applications are particularly prominent in dental implants and bone treatments. It is also used as a surface coating in many metallic and polymeric biomaterials to improve biocompatibility and accelerate tissue healing.

Polymers are formed by connecting low molecular weight units to create long-chain structures. They are versatile materials and find applications in various fields where elasticity is crucial, such as heart valves, as well as in biodegradable surgical sutures. The choice between synthetic and natural polymers depends on specific application requirements, considering factors like Young's modulus and density values [51, 58]. Polyethylene (PE), polyurethane (PU), polytetrafluoroethylene (PTFE), polyacetal (PA), polymethyl methacrylate (PMMA), silicone, rubber, polysulfone (PS), polylactic acid (PLA), as well as various natural polymers based on proteins and polysaccharides, are used in different compositions and forms in medical applications. These polymers have a physical structure that resembles human soft tissue. This similarity makes them suitable for a variety of applications in specific tissues, including cartilage, skin, vessels and lenses [1].

2 Importance of Hydroxyapatite Ceramic-Polymer Composites in Biomedical Applications

Ceramic-polymer composites provide optimum strength and elasticity, finding wide use in applications where both are required [1]. Here, the polymer acts as a matrix and contributes to elasticity, while ceramic materials increase strength, i.e. load

carrying capacity and wear resistance. These composites offer a versatile solution for achieving specific mechanical properties, including strength, stiffness, toughness, and fatigue resistance. Additionally, by customizing the composite material design, anisotropic properties in desired directions can be attained [41]. Indeed, natural bone can be aptly described as a ceramic-polymer composite due to its distinctive composition. The organic component of bone mainly comprises type I collagen, constituting around 25–30% of its weight. On the other hand, the mineral component predominantly consists of calcium phosphate, contributing to approximately 60–70% of its weight. The remaining portion is composed of water. This exceptional amalgamation of collagen and calcium phosphate bestows natural bone with remarkable mechanical properties, including strength, flexibility, and toughness [15, 42, 48].

Within ceramic-polymer composites, hydroxyapatite (HA) is a widely preferred ceramic reinforcement due to its presence in the components of bone structure, biocompatibility, bioactivity and favorable interaction with cells, and is used as a matrix with a wide variety of polymers. Integrating HA as a reinforcement within the polymer matrix allows the composite to harness the desirable characteristics of HA, such as enhanced bioactivity and osteoconductivity, while simultaneously benefiting from the improved flexibility and processability offered by the polymer matrix. Essentially, HA is a brittle ceramic with low mechanical strength, but a common approach to impart flexibility and improve its mechanical properties is to incorporate HA into a polymer matrix. Mixing hydroxyapatite (HA) with a polymer matrix is a smart and it is also unique way to make the most quality ones. It aids overcome the limitations of HA in some situations. With this, composites become more flexible, durable, and performs better mechanically [48, 53].

3 Hydroxyapatite Ceramic-Polymer Composite Fabrication Methods and Applications

The fabrication of composite materials encompasses a diverse range of methods, with no limitations to a single approach. The choice of production method predominantly depends on the selection of ceramic and polymer materials used as components in the composite. Moreover, the intended application and specific geometry play pivotal roles in determining the most suitable production approach. The most commonly used methods for the production of a ceramic composite material dispersed within a polymer matrix include chemical methods such as infiltrating the ceramic with the polymer or mixing the ceramic into a soluble polymer, as well as mechanical methods like milling and extrusion [42]. Speaking specifically about hydroxyapatite ceramic-polymer composites, various production methods are available depending on the specific polymer used in conjunction with hydroxyapatite. Since the type of polymer plays a crucial role, this section will discuss various methods based on hydroxyapatite ceramic-polymer composites combined with different polymers.

Several techniques are employed to combine the alginate polymer matrix with hydroxyapatite, such as electrospinning, extrusion, hot pressing, liquid–gas systems, and co-precipitation. Among these methods, crosslinking stands out as the most prevalent approach. Studies have indicated that structures obtained through the crosslinking technique promote the proliferation of osteoblasts. Consequently, these ceramic-polymer composite structures find diverse applications in areas such as tissue engineering, implants, coatings, and drug delivery systems [5, 18]. In their study, Bian et al. produced a scaffold with a special motif to be used in HA/collagen composite bone scaffold applications. They emphasized that compared to similar products in the literature, the scaffold exhibited superior biocompatibility, and chemical and mechanical stability [5].

Various techniques have been utilized to produce the collagen/HA structure. These methods encompass mixing collagen solution with HA followed by lyophilization, co-precipitation of calcium and phosphorus precursors within collagen solution, crosslinking for hydrogel formation, mechanical mixing, and electrochemical deposition. Collagen type 1, widely present in various body structures, significantly contributes to mechanical strength and promotes cell adhesion and proliferation. The collagen/HA structure finds application in tissue engineering, coatings, bone defects, bone substitutes, implants, and bone regeneration [18].

Gellan, a natural polysaccharide gum, exhibits biocompatible, biodegradable, highly porous, and antibacterial characteristics. The incorporation of HA into the Gellan matrix through mechanical mixing and crosslinking methods enhances the mechanical strength of the composite structure while promoting cell adhesion and growth. This composite structure finds applications primarily in bone repair, regeneration, reconstruction, grafting, and direct use as a bone substitute [18].

Chitosan, an intriguing polysaccharide, displays non-toxic, biodegradable, biocompatible, antimicrobial, anticancer, anti-inflammatory, hydrophilic, and adhesive properties. Moreover, it showcases traits that encourage cell proliferation and osteoconduction. The chitosan/HA composite structure is skillfully fabricated through unassuming techniques like freeze-drying, net shape nonwoven methods, or coagulation, serving as a fibrous bone scaffold with enhanced mechanical strength. The versatile application areas of chitosan/HA composites encompass tissue engineering, coatings, drug delivery systems, and bone substitutes [18].

Poly(lactic acid) (PLLA) stands as a thermoplastic polyester, featuring both crystalline and amorphous structures. Its biodegradability subtly amplifies with an increase in crystallinity. Impressively transparent in appearance, PLLA showcases attributes of low toxicity, osteoconductivity, biodegradability, biocompatibility, and unassuming biological absorbability. Nonetheless, one should consider its major disadvantage of low cell attachment on the surface. Therefore, the PLLA/HA composite structure can be utilized to enhance cell attachment, proliferation, mechanical strength, and osteoinductive properties. Common production methods for this composite include melt blending, electrospinning, compression molding, emulsion, and casting [37].

The extensive body of scientific research illuminates the immense potential of hydroxyapatite ceramic-polymer composites, with Flores Valdez et al. [18] leading

the way into the captivating world of polymer matrix filling through immersion. The orchestration of a seamless symphony of HA distribution on the surface results in the creation of a composite coating of precisely the desired thickness. Their brilliant foray into the domain of biomaterials revolves around a paramount objective: enhancing the corrosion performance of magnesium (Mg) and its alloys. This accomplishment brings forth a dazzling fusion of fortified mechanical properties and heightened corrosion resistance, elevating the possibilities of these composites to unparalleled heights.

The horizon of applications is vast and awe-inspiring, casting a radiant light on major realms such as bone scaffolds, coatings, bone substitutes, and the enchanting sphere of bone-tissue engineering. This intricate tapestry of scientific inquiry, woven through rigorous exploration and dedication, narrates a compelling tale of promise and potential, enriching our understanding of hydroxyapatite ceramic-polymer composites and their profound impact on the field of regenerative medicine.

In another enthralling study, Kim et al. [27] wove a mesmerizing tale of micro-patterned PLLA/HA structure on the surface of Mg, a masterpiece created through a skillful blend of distinct techniques. The initial enchanting act involved adorning the surface with a micro-patterned photoresist, followed by the ethereal deposition of HA within the pattern voids. Subsequently, the photoresist dissipated like a mist in the morning sun, paving the way for the manifestation of the awe-inspiring HA micro-patterns, seamlessly harmonized with the PLLA polymer matrix through the enchanting spin coating technique. This tale of wonderment left behind a legacy of unparalleled enhancements in mechanical properties, as if the strings of destiny played a symphony of strength and resilience, culminating in the grand crescendo of fortified corrosion resistance.

Dubinenko et al. [14] embarked on a breathtaking journey, entrancing the realm of 3D printing with their entrancing PLLA/HA composite production. The recipe of success involved infusing the polymer solution with HA, orchestrating a waltz of homogeneous mixing in the mill. Like alchemists of old, they artfully transformed the mixture into a suitable form for 3D printing, each layer a stroke of genius, as the resulting structure emerged with a mesmerizing 3.2 times greater strength than pure PLLA, a testament to the symphony of strength forged within.

Gay et al. [20] crafted a spellbinding tale of PLLA/HA composite material, where nano-particle HA harmonized with the PLLA-chloroform solution in specific ratios, creating a fusion of density and compressive strength that seemed to defy nature itself. As if touched by the hand of magic, the density reached 97%, while the compressive strength soared to 100 MPa, leaving a trail of wonder and awe in its wake.

Nishida et al. [40] unveiled a tapestry of ethereal scaffolds, born from a waltz of commercial HA powders and PLLA pellets, their essence suspended in a convenient solvent. Cross-linking, solidification, and the final flourish of solvent removal through the freeze-dryer vessel brought forth scaffolds of various morphological structures, a symphony of polymer concentrations. Their journey of discovery transcended biocompatibility on surfaces and within the overall structure, witnessing momentous improvements in cell culture test results, as if the very fabric of life embraced these wondrous creations.

In these captivating studies, hydroxyapatite ceramic-polymer composites unfurled their multifaceted potential, evoking a tapestry of possibilities in the captivating landscape of biomaterials research, wherein the symphony of science continues to compose its magnum opus. Polyvinylpyrrolidone (PVP), also known as povidone or polividon, is a water-soluble polymer material used as a biocompatible biomaterial with proven safety for use in the body. It finds applications as a hydrogel, in contact lenses, as a drug stabilizer, and in the cosmetic industry. Slota et al. prepared PVP/HA composites through UV crosslinking for drug release applications. They mixed PVP solution with HA at specific ratios using a magnetic stirrer, transferred the mixture to petri dishes, and allowed it to crosslink under UV light. The study revealed a correlation between the amount of drug loaded into the structure and its release capacity, showing bioactive behavior after incubation with simulated body fluid (SBF). This research demonstrated the potential use of the composite material as an active substance carrier and in bone tissue regeneration [47].

Agarose, another hydrogel used in drug delivery systems, is also a biodegradable and non-toxic organic polymer. It is widely used and considered safe in tissue engineering. Agarose/HA composites have been noted to enhance bone formation and accelerate healing compared to pure agarose hydrogels. Kolanthai et al. prepared 3D porous hydroxyapatite/agarose and b-tricalcium phosphate/agarose composite scaffolds using the sol-gel technique. The results of the study emphasized that the water-based structure had superior mechanical properties, wettability, drug loading capacity and hemocompatibility compared to the ethanol-based structure. In addition, *in vitro* studies with MC3T3 cells showed that cell adhesion to the water-based composite was better and cell viability and proliferation were superior [29].

In recent years, additive manufacturing has become a popular method for biomaterial production. In addition to orthopedic and dental implants, it has found application in the treatment of trauma and deformities in maxillofacial surgery involving the head, face, mouth, teeth, gums and neck. Metals, ceramics, polymers and composites can be used in this method. Its most important advantage is that it is easy to produce materials with complex shapes. Another important advantage is that it allows the production of porous structures with specific geometries that can improve the post-implantation integration process or aid drug delivery. It also allows the direct filling of bone deformities. Along with all these advantages, there are also some disadvantages. For example, the curing process after 3D printing may need to be intensified. This may limit its use in some cases. Additionally, achieving the desired surface roughness values can sometimes be challenging, requiring further surface treatments like sandblasting, acid treatment, or polishing. Additive manufacturing is a versatile process, allowing the creation of three-dimensional (3D) prints in various ways. For example, different production methods like extrusion-based materials, stereolithography, selective laser sintering, and inkjet-based 3D printing can be used for bone tissue applications. Moreover, a new sector has emerged with the development of printable biomaterials for 3D printing that meet users' mechanical and biological expectations, opening up new possibilities in the field of biomedical materials [21].

In general, to summarize the topic in the production of ceramic/polymer composites, there are numerous examples in the literature of various methods being used,

both chemical and mechanical, depending on the quantity and type of materials involved. However, mechanical performance expected from design and orientation, cellular or antimicrobial behaviors expected from the material within tissues or the body, cost, and feasibility in terms of production are crucial considerations. All these factors contribute to the successful development and application of these composites in various fields, including biomedicine and tissue engineering.

4 Characterization Methods for Hydroxyapatite Ceramic-Polymer Composites

In the characterization of composites, various material analysis methods can be utilized to investigate their key properties. These include physical, structural, thermal, chemical, and mechanical characteristics. Factors such as the density of the material, surface area, particle size and shape cover the physical properties. Structural analysis provides three-dimensional visualization of the porous structure and morphological homogeneity of the material. Phase or elemental composition ratios and bond structures can be characterized chemically. Within the scope of mechanical properties, familiar tests such as compression, tensile, three-point bending and hardness can be performed. In cases where composite materials may exhibit different mechanical properties in different directions and show anisotropy, each test may need to be repeated separately in anisotropic directions for a comprehensive assessment. The application of a series of tests involving the combination of all these and similar characterization methods provides valuable information about the behavior and performance of composite materials.

For all materials designed as a biomaterial, it is essential to characterize their biological properties. At this point, it is essential to reveal the biocompatibility, bioactivity and antibacterial properties of the materials produced. Comprehensive evaluation of the biological properties of materials is possible through *in vitro* and *in vivo* studies. Evaluation of biointegration and biocompatibility is crucial to ensure that they integrate well with surrounding tissues and do not cause any adverse reactions. In addition, it is necessary to evaluate the bioactivity of materials so that some cellular behaviors (such as cell attachment, proliferation, and non-differentiation) are extremely important for tissue regeneration and repair. Apart from that, the evaluation of its antibacterial properties is very important, especially for medical implants or other medical devices. Confirmation of their antibacterial abilities is crucial to prevent infections and increase the overall success of biomaterials in clinical settings. To evaluate all these performances, biomaterials need to be studied in interaction with cells and living tissues, and this is accomplished through a series of *in vitro* and *in vivo* experiments. *In vitro* testing involves using cell cultures to study the interaction of materials with cells in the area where they will be used, and provides valuable information about their biological behavior. Further, *in vivo* experiments are performed on a real subject to evaluate how biomaterials behave

in real-life conditions. By comprehensively evaluating the biological properties of biomaterials in this way, we demonstrate their reliability and effectiveness in various biomedical applications.

Density measurement is usually done using Archimedes' principle [7, 25, 26] or helium pycnometer [42] in accordance with ASTM B962 standards. The Brunauer–Emmett–Teller (BET) method can be preferred for the measurement of the specific surface area of the HA powder used in the composite structure [42]. Light microscopes or SEM imaging can also be used to view and measure particle size and shape. Particle size distribution can be analyzed with particle size analyzers. For specific surface area measurement of the HA powder used in the composite structure, the Brunauer–Emmett–Teller (BET) method can be employed [42]. Particle size and shape can be measured through microscopy and SEM imaging, while particle size distribution can be analyzed using particle size analysis instruments. Additionally, for structural analysis, crystal size measurement can be obtained from x-ray diffractometer (XRD) measurements utilizing the Debye-Scherrer equation [12, 29, 55]. In the determination of thermal properties, the most widely used methods are differential thermal analysis (DTA/TGA) and differential scanning calorimetry (DSC) [12, 22]. Generally, various methods and devices are available for imaging micro or macrostructures and cell adhesion. Among these, the most traditional ones are light and electron microscopy (SEM, FE-SEM, etc.) [6, 12, 31, 44], and atomic force microscopy (AFM) can also be mentioned for topological imaging [44]. In addition to these, three-dimensional imaging methods such as micro-computed tomography (micro-CT) and x-ray microtomography are particularly prevalent in biomaterials due to their non-destructive nature, allowing visualization of the entire material, porosity, and homogeneity in detail [21, 37, 42, 54]. Chemically, energy dispersive spectrometry (EDS) [50], wavelength dispersive spectrometry (WDS), X-ray diffraction (XRD) [11, 42, 55], and inductively coupled plasma optical emission spectroscopy (ICP-OES) are commonly used to determine the composition of elements and phases. In particular, Fourier transform infrared spectroscopy (FTIR) is utilized to define physical and chemical bond structures, as well as functional groups, contributing to comprehensive characterization efforts in the realm of biomaterials [9, 10, 12, 19, 22, 44, 48].

In the realm of ceramic/polymer composites, the phenomenon of wetting assumes a pivotal role of paramount significance, exerting its influence upon the intricate tapestry of interfacial interactions and cellular adhesion within the realm of biomaterials. Ergo, the meticulous measurement and analysis of surface energies and contact angles, employing the tenets of water contact angle measurements, bestows upon the discerning researcher an invaluable apparatus to apprehend the subtle nuances of wetting phenomena [29, 37]. Mechanical properties are evaluated using a wide range of mechanical tests. Depending on whether the composite is anisotropic or not, similar mechanical tests can be conducted in different directions. Tests such as tension [36], compression [33, 34, 42], and three-point bending [26] heavily rely on material anisotropy and provide crucial data on mechanical strength. Methods like hardness [52] and impact testing [56] are also employed to determine the material's resistance. Various types of wear tests can be applied to assess the material's

tribological performance. For instance, for a biocomposite intended for bodily use, wear tests can be simulated either in a dry environment or in artificial body fluid or saliva considering the anticipated load [17, 46]. Similarly, depending on the intended application within the body, electrochemical corrosion tests [27] can be performed in artificial body fluid or saliva at body temperature. This can help calculate corrosion resistance or biodegradation rates of the materials.

In the realm of biomaterials, undoubtedly, the most valuable insights come from biological tests. While the tests mentioned above are crucial for understanding properties such as material endurance, service life, and mechanical integrity within the body, they hold no significance if a biomaterial cannot be safely used within the body [21, 38, 59]. Therefore, the foremost priority is always the material's non-toxicity, its ability to maintain tissue structure and cell viability, and its avoidance of any adverse effects. For instance, when considering implant materials, it is imperative that materials in direct contact with the body after implantation do not release ions that could harm the body, disrupt pH balance, or trigger an immune response perceiving the material as a foreign substance. Otherwise, the body would create a fibrous capsule layer around the implant to protect itself [60]. This rejection could lead to complications, requiring further surgeries, which can be quite taxing for the patient [46]. Therefore, materials designed for use as biomaterials should undergo initial simple tests during preliminary studies, followed by more advanced tests. As the stages progress, the workload and responsibility increase. Starting with the basics, the initial focus should always be on conducting antimicrobial [12] and cytotoxicity [59] studies.

Antibacterial studies, particularly when considering the intended use of biomaterials, commonly involve evaluating their interactions with both gram-positive and gram-negative bacterial species. For instance, Dhanalakshmi et al. [12] conducted a study in which composite materials intended for implantation were tested against five different bacterial colonies (*Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, *Vibrio cholerae*, and *Klebsiella pneumonia*) using the well diffusion method with Sabouraud dextrose agar and Muller Hinton agar [12]. To assess the potential cytotoxic effect of the material on human cells, it can be evaluated by directly exposing cell cultures to the material or by preparing eluates of the materials in various solvents and subsequently testing the cytotoxicity of these eluates under cell culture conditions [59]. These approaches help determine the materials' potential impact on both bacterial growth and human cell viability.

To assess the applicability of a material within the human body, one must exercise caution and prioritize safety by initially simulating the human body's environment. Such investigations are commonly known as *in vitro* experiments. Crucial components such as amino acids, proteins, nutrients, growth factors, along with environmental factors like humidity, pH balance, and temperature, must be meticulously provided in settings such as cell culture media, artificial body fluid, or artificial saliva [39]. Depending on the intended use, the specific type of cells that the material will interact with should be cultured accordingly. Under controlled conditions, the implant is placed into the cell culture medium and incubated at specified time intervals for monitoring. The study involves observing pH levels, ion release, cell viability, and

growth over both short and long periods. At predetermined time points, necessary analyses are performed and the data is tabulated. To monitor pH levels, pH meters [49] can be used, while analysis using Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) [28] can be conducted to measure ion release. The MTT assay, utilizing 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, is a widely employed colorimetric test for evaluating cytotoxicity or cell viability. This method measures the activity of mitochondrial enzymes, particularly succinate dehydrogenase, to assess cell health under different conditions or exposure to substances. To conduct the MTT assay, cells are exposed to specific test compounds or conditions for designated time intervals. Subsequently, MTT, a yellow dye, is added to the cells. Living cells with active mitochondrial enzymes reduce the MTT dye, forming a purple formazan product, which can be quantified using a spectrophotometer. Moreover, researchers can visualize cellular development in specific conditions by capturing images through various microscopy techniques, such as light microscopes, scanning electron microscopes (SEM), or transmission electron microscopes (TEM [3, 43]). In cases where the MTT assay reveals extreme or unexpected conditions in the cell culture, researchers may perform additional analyses to gain further insights into the effects of the tested substances or conditions. For instance, if there is an increase in mass, the increased mass can be weighed, and chemical analyses combined with Fourier Transform Infrared Spectroscopy (FTIR) [49] can be used for evaluation. All these analyses aim to gain insights into the material's potential as a biomaterial. If favorable outcomes are observed, the subsequent step involves conducting *in vivo* experiments on animals. These animal experiments are essential to further evaluate the material's performance and safety in a living organism. Alternatively, rather than directly conducting experiments on live animals after *in vitro* studies, tissue or cells can be extracted from the desired area of the animal and experiments can be performed on these tissues outside of the living organism, referred to as *ex vivo* experiments [4]. All these animal studies are conducted under the oversight of an 'Ethics Committee' to ensure that they are conducted in a manner that is not contrary to animal rights. During animal experiments, the subject's blood values are monitored, and if the study involves bones, imaging techniques such as X-rays, MRI, or micro-CT can be used for interpretation [16]. At the end of the experimental period, necessary tissue samples are collected from sacrificed animals and prepared for light or SEM imaging. Light microscopy imaging involves staining tissues with various proteins or antibodies, enabling histology and immunohistology studies to be conducted [4, 43]. When *in vivo* studies show positive results and the material holds significant potential, the final design of the product is developed, and studies on humans are conducted under the framework of an ethics committee. If all studies yield positive outcomes, different procedures are followed for production and commercialization. Therefore, the process for a material designed as a biomaterial to become usable is quite complex, costly, and can take many years. Studies contributing to the literature are highly valuable in this regard. Studies that have completed the literature phase can progress step by step, advancing their work toward the transformation into a product.

5 Possible Applications of Hydroxyapatite Ceramic-Polymer Composites

In the enthralling landscape of biomedical research, hydroxyapatite ceramic-polymer composites have unequivocally emerged as a multidimensional and transformative force, exhibiting immense potential in an extensive array of captivating applications that lie at the very heart of regenerative medicine, bone bonding, advanced medical treatments, and tissue engineering. Their chameleon-like adaptability and versatile nature render them nothing short of invaluable, allowing them to effortlessly transcend boundaries and make indelible contributions across diverse domains encompassing artificial bone grafts, drug delivery modalities, and the domain of orthopedic surgeries. Consequently, these remarkable composites have ascended to a pinnacle of attention in the riveting and ever-evolving realm of biomaterials research. Thus, in the confines of this section, we embark on a profound journey, peering into the resplendent panorama of biomedical applications, wherein the ingenious utilization of these hydroxyapatite ceramic-polymer composites shines ever so brightly, illuminating the path towards pioneering advancements in medical science and restoring hope in the domains of health and healing.

5.1 Bone Tissue Engineering

Undoubtedly, one of the most riveting and captivating frontiers that has emerged in the realm of advanced biomaterials pertains to the extraordinary potential of hydroxyapatite ceramic-polymer composites, particularly in the domain of bone tissue engineering. The awe-inspiring allure of these composites lies in their exquisite biocompatibility, deftly mimicking the inherent mineral composition of natural bone, thus rendering them as unparalleled and highly coveted candidates for the seamless creation of bone scaffolds. However, the true marvel unfolds when these composites are strategically combined with biodegradable polymers, as this artful marriage culminates in the emergence of a synergistic and dynamic milieu that serves as a robust and accommodating framework, deftly fostering and nurturing optimal cell growth and orchestrating intricate tissue regeneration processes. It is this astute amalgamation that unfurls the potential to manifest as a resolute and transformative force, actively and adeptly participating in the meticulous repair and restoration of bone defects and fractures, leading to a realm of revitalization and reinvigoration in the captivating realm of bone biology.

Li et al. [32] emphasized the potential of HA-chitosan-pectin/chitosan-gelatin scaffolds, produced to provide stable physical and chemical structures conducive to cell adhesion and proliferation of MC3T3-E1 cells, as a promising biomaterial for bone tissue engineering. Shen et al. [45] achieved significantly improved mechanical performance compared to pure collagen by incorporating homogeneously distributed ultra-fine HA particles within nanostructured collagen foam scaffolds featuring

hierarchical pore architectures. In another study, Kailasanathan et al. [24] developed ceramic composites composed of nano HA/titania/gelatin for the fabrication of load-bearing bone substitutes, suggesting their superiority for bone tissue engineering.

In a review article prepared by Venkatesan et al., various HA-based composites such as HA/Fibroin, HA/Poly(lactic Acid), HA/Poly(caprolactone), HA/Poly(lactic-co-glycolic) Acid, HA/Poly(amide), HA/Poly(vinyl Alcohol), HA/Poly(urethane), HA/Poly(hydroxybutyrate), and HA/Miscellaneous were highlighted as potential options for bone tissue engineering applications [56]. These studies collectively demonstrate the growing interest and progress in the development and application of HA-based/polymer composites in the field of bone tissue engineering.

5.2 Dental Restorations

Hydroxyapatite ceramic-polymer composites showcase exceptional mechanical strength and aesthetic properties, rendering them highly suitable for dental restorations. These versatile composites can be employed in dental crowns, bridges, and implants, closely resembling the appearance and functionality of natural teeth. Additionally, their bioactive nature fosters osseointegration, ensuring the enduring stability and integration of dental implants for long-term dental health and functionality.

Dental applications intersect with the field of bone tissue engineering, and research efforts in both areas can be considered interconnected. Many hydroxyapatite ceramic-polymer composites investigated for various bone tissues, as mentioned earlier, also hold potential for dental applications. To provide a specific example, a study involved the creation of a composite by immersing a scaffold made of HA rods into an epoxy resin bath. The mechanical properties of this composite were then compared with those of dental composites used in dental implants, and promising results were obtained [35]. This finding suggests a potential application of HA-based/polymer composites in dental implant materials, contributing to the advancement of dental treatments and implant technologies.

5.3 Drug Delivery Systems

The porous characteristics of hydroxyapatite ceramic-polymer composites facilitate their utilization in controlled drug delivery applications. These composites can be designed to incorporate drugs within their matrix, and the release rate of the drugs can be precisely regulated by adjusting the composite's porosity and composition. This feature enables the development of drug delivery systems that provide targeted and sustained release of therapeutic agents, thus improving treatment effectiveness and reducing potential side effects. Agents are commonly employed to induce new

bone formation in the treatment of bone injuries and diseases, including osteoporosis. The advantage here, compared to conventional drugs, lies in the controlled release of medication directly to the damaged area or the site requiring treatment.

Liu et al. conducted an intriguing study where they ingeniously loaded drugs onto nano-hydroxyapatite (nano-HA) to achieve prolonged drug release specifically targeting the affected region of the bone. To accomplish this, the drug-loaded nano-HA was skillfully dispersed into a biodegradable polymer matrix known as poly(lactic-co-glycolic acid) (PLGA). The outcome of this study demonstrated the successful immobilization of the drug onto the nano-HA carrier, leading to an extended period of drug release, thereby showcasing its immense potential in drug delivery applications [33, 34].

In yet another noteworthy study, Banerjee and Bose [3] delved into the investigation of the release kinetics of doxorubicin in ceramic-polymer composites while delving into the intriguing impact of pH dependence. An assortment of polymer concentrations, including PCL, PLGA, and PCL-PLGA with HA, were meticulously tested at distinct pH levels of 7.4 and 5.0. The intriguing results unveiled a dichotomy in drug release behavior, as the disks containing HA exhibited an initial burst release of 20% within a week at pH 7.4, while the disks containing polymers demonstrated a more continuous drug release profile. The study's findings highlighted the remarkable influence of pH-dependent hydrophobic-hydrophilic/hydrophobic interactions between the polymer and drug, thereby significantly impacting the drug release kinetics in this intricate composite system [3].

Letic-Gavrilovic et al. presented an enthralling and captivating application that involved leveraging the unparalleled capabilities of collagen/HA as a highly adept and sophisticated drug delivery system tailored specifically for neurotrophins, with a laser-like focus on nerve growth factor. This ingenious neurogenic-osteogenic enriched application device underwent an intricate and meticulously orchestrated experimental implantation process into the calvarial defects of 20 Wistar rats *in vivo* exploration. Duration of 30 days of meticulous observation allowed the researchers to bear witness to an array of truly transformative outcomes. The ethically conducted sacrifice of the rats, following this enthralling period, unveiled nothing short of astounding and remarkable improvements in the domain of bone biology. Noteworthy transformations included substantial enhancements in bone mass, discernibly reduced bone marrow, and, perhaps most remarkably, a profusion of stimulated growth observed in the periosteal, endocortical, and lamellar bone formations. This pivotal study thus unfurled the tantalizing panorama of immense advantages that the proposed collagen/HA composite brings to bear in the realm of tissue engineering, illuminating the path towards addressing irregular defects with unparalleled prowess, particularly within the intricate landscape of maxillofacial surgery [31].

5.4 Coatings for Orthopedic Implants

Hydroxyapatite ceramic-polymer composites have garnered significant attention in recent research as potential coatings for metallic orthopedic implants. The utilization of these composites holds paramount importance in enhancing the surface characteristics of the implants, thus facilitating the process of osseointegration, and importantly, mitigating the risk of implant failure. Consequently, these composites play a pivotal role in extending the lifespan of implants, consequently leading to improved patient outcomes in orthopedic surgeries.

Kumar et al. electrochemically applied new poly(3,4-ethylenedioxythiophene) (PEDOT) based nanocomposite coatings with different fluorohydroxyapatite (FHA) nanoparticle contents onto a Ti-Nb-Zr (TNZ) alloy to improve surface properties. The coated samples exhibited improved hardness and surface wettability, and electrochemical corrosion tests indicated superior performance compared to pure PEDOT coatings. Additionally, the produced nanocomposite coating was found to enhance cell adhesion and proliferation of MG-63 cells while displaying antibacterial properties [30]. Chae et al. [8] investigated the in vitro performance of HA/alginate nanocomposite fibrous scaffolds, mimicking mineralized collagen fibrils in bone tissue, produced using the electrospinning method. The researchers observed that osteoblasts from rat calvaria demonstrated a more stable adhesion to the surface of HA/alginate fibrous scaffolds than pure alginate fibrous scaffolds. The nano-fibrous topography of HA and alginate suggests potential advantages for bone tissue regenerative medicine applications. Chakraborty et al. obtained a composite coating of HA/polypyrrole by simultaneously electropolymerizing the components on a stainless steel surface. The accumulated coating exhibited high corrosion resistance and anodic passivation capability, and it also facilitated faster interconnected growth of MG63 cells on the coating surface. This biocompatible composite coating, known for its superior toughness and sufficient elasticity, holds potential for use on load-bearing metallic implant surfaces [9, 10]. Yan et al. developed a biocomposite coating containing chitosan, Ag, and HA on a Ti substrate via electrochemical deposition, aiming to prevent bacterial infection. The prepared coatings displayed antibacterial activity against Gram-positive and Gram-negative bacterial strains while proving non-toxic to MC3T3-E1 cells, highlighting their potential for biomedical applications [57].

6 Conclusion

Hydroxyapatite ceramic-polymer composites possess a wide range of potential applications in biomaterials. Their biocompatibility, mechanical properties, and ability to mimic the natural mineral composition of bone make them invaluable in bone tissue engineering, dental restorations, drug delivery systems, cartilage regeneration, orthopedic implants, and tissue scaffolds for organ engineering. Continued research

and development in this field hold the key to unlocking the full potential of these composites for improving patient outcomes and advancing the field of regenerative medicine.

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Ceramic Fillers-Based Polymer Gels for Biomedical Applications



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Abstract In the rapidly progressing field of biomedical engineering, the utilization of ceramic filler-based polymer composites, particularly hydrogels, presents a transformative approach to healthcare solutions. This chapter delves into the intricate domain of hydrogels, delineating their unique characteristics, types, and biomedical applications. An exploration of natural and synthetic polymer-based hydrogels highlights the inherent advantages of each, followed by an overview of common ceramics used as fillers, including Hydroxyapatite, β -tricalcium phosphate, Bioactive Glass, Nanoclay, and Wollastonite. These ceramic fillers, when incorporated into hydrogels, impart enhanced mechanical strength, bioactivity, and responsiveness, expanding their applications in bone and cartilage tissue engineering, and controlled drug delivery. The chapter concludes with a reflective analysis of the current state of the field and outlines prospects, emphasizing the need for interdisciplinary collaboration, innovation, patient-specific customization, and integration of advanced technologies. Challenges such as interface compatibility, uniform distribution, long-term stability, and in vivo response also merit further investigation. In summary, this chapter provides a comprehensive and insightful perspective on ceramic filler-based polymer hydrogels in biomedical applications, showcasing the potential of these materials in revolutionizing medical treatments and paving the way for future research and development.

Keywords Biomedical engineering · Ceramic filler · Hydrogels · Mechanical strength

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1 Introduction

Ceramic fillers, renowned for their rigidity, biocompatibility, and wear resistance, have emerged as key components in the development of advanced polymer composites with tailored properties for biomedical applications [1]. As the demand for customizable and efficient materials in the biomedical field continues to grow, the integration of ceramic fillers with polymer gels, such as hydrogels, has become an area of intensive research and development [2].

The significance of ceramic fillers lies in their ability to modify mechanical, thermal, and biological characteristics of polymer gels, thus expanding their applicability in various biomedical contexts. By incorporating ceramics such as Hydroxypapatite (HAp), β -tricalcium phosphate (β -TCP), Bioactive Glass (BG), nanoclay, and wollastonite, these composites exhibit improved stiffness, biodegradability, and bioactivity [3, 4].

Among the different types of polymer gels, hydrogels stand out for their high-water content and soft, tissue-like consistency. The incorporation of ceramics within natural and synthetic hydrogels offers possibilities in enhancing their functionalities (Fig. 1). It permits the tailoring of materials to better mimic the natural physiological environment, making them highly suitable for bone, cartilage, dental, and drug delivery applications [5, 6].

This chapter aims to provide a comprehensive review of the current state of ceramic filler-based polymer gels, with a particular focus on hydrogels. It delves into the diverse range of ceramics utilized as fillers, exploring their characteristics, interaction mechanisms with polymers, and their subsequent effects on composite properties. Furthermore, the chapter will spotlight various biomedical applications

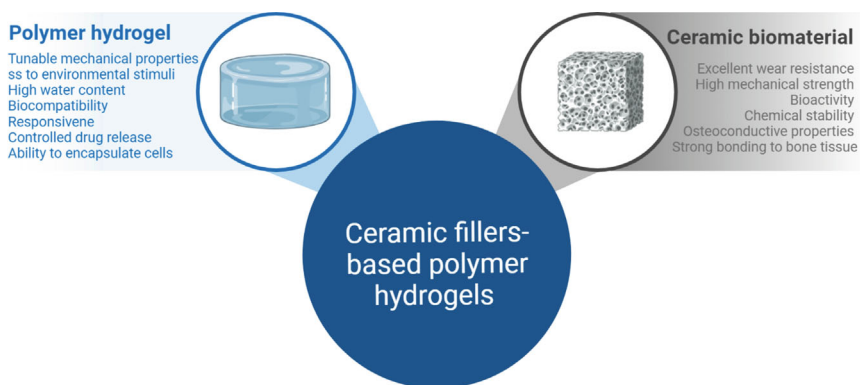


Fig. 1 Diagrammatic representation illustrating the principal characteristics of polymeric hydrogels and ceramic biomaterials in the context of biomedical applications. The integration of these two distinct classes of materials forms a composite with enhanced functionality and tailored properties for advanced biomedical applications

where these composites are being effectively utilized, culminating in a reflection on future perspectives and research directions in this rapidly evolving field.

With an intention to offer an in-depth understanding of the subject, this chapter is structured as follows: Sect. 2 provides an overview of hydrogels, distinguishing between natural and synthetic polymer-based gels; Sect. 3 lists common ceramics used as fillers, describing their unique properties and applications; Sect. 4 delineates the extensive biomedical applications of these composites, from bone and cartilage tissue engineering to drug delivery systems; finally, Sect. 5 draws conclusions and outlines potential future directions for this exciting area of research.

By presenting a thorough examination of ceramic filler-based polymer gels, this chapter contributes to the broader understanding of novel materials and techniques that are shaping the future of biomedical engineering.

2 Hydrogels

Hydrogels are a remarkable class of materials that have elicited widespread interest across various scientific and engineering domains, particularly within the realm of biomedical engineering. Comprising a network of hydrophilic polymer chains, hydrogels are characterized by their ability to retain substantial amounts of water, often exceeding 90% of their total weight. This high-water content bestows upon hydrogels a soft, flexible consistency closely resembling natural biological tissues, thereby making them highly applicable in areas such as tissue engineering and medical implants [7, 8].

The versatility of hydrogels extends to their formulation from both natural and synthetic polymers, granting flexibility in design and functionality. The specific choice of polymer and crosslinking agents allows for precise control over essential characteristics such as mechanical properties and degradation behavior. Hydrogels are also renowned for their responsiveness to various environmental stimuli, including temperature, pH, or ionic concentration. This unique responsive nature has given rise to innovative applications such as “smart” drug delivery systems that can release therapeutics in a controlled and targeted manner [9].

Furthermore, the adaptability of hydrogels to be both biocompatible and biodegradable aligns them with the physiological demands of the human body, ensuring a broad spectrum of in vivo applications without significant adverse reactions. Various manufacturing methods, ranging from traditional casting to advanced 3D printing, can be applied to hydrogels, providing the ability to create intricate structures and geometries tailored to specific medical or biological applications [7, 8].

The confluence of these characteristics has paved the way for a diverse array of applications within the biomedical field, from serving as scaffolds in tissue regeneration to vehicles for targeted drug delivery. The resemblance of hydrogels to native extracellular matrix materials further accentuates their potential as vital tools in therapeutic interventions and regenerative medicine [7, 10].

Concisely, the multifaceted nature of hydrogels, marked by their high-water content, responsiveness, biocompatibility, and adaptability across manufacturing techniques, offers a promising platform for innovation and application across various medical fields. Continued exploration and development in this area hold the promise of further unlocking the potential of hydrogels, contributing to groundbreaking advancements in healthcare and medicine.

2.1 Natural Polymer-Based Hydrogels

Natural polymer-based hydrogels are a subset of hydrogels that are specifically derived from natural sources such as plants, animals, or microorganisms. These hydrogels hold particular interest in biomedical applications owing to their intrinsic compatibility with biological systems, a consequence of their origin from living organisms [11].

Composed primarily of biopolymers like cellulose, chitosan, alginate, and collagen, natural polymer-based hydrogels possess unique characteristics that distinguish them from their synthetic counterparts. One of the defining features is their inherent biocompatibility, which results in minimal immune or inflammatory responses when introduced to the human body. This makes them particularly well-suited for applications that require direct contact with tissues or cells [11, 12].

Furthermore, many natural polymers exhibit inherent bioactivity, providing support for cell attachment and proliferation. This bioactivity often translates into enhanced performance in tissue regeneration and wound healing applications. In addition, natural polymer-based hydrogels generally show biodegradability, breaking down into biologically benign components over time. This biodegradation can be tailored to match the healing or regeneration rates of specific tissues, making them versatile tools in therapeutic interventions [12].

Another significant advantage of natural polymer-based hydrogels is their potential for functionalization. By chemical modification or through blending with other natural or synthetic components, these hydrogels can be customized to exhibit specific mechanical properties, swelling behaviors, or controlled release profiles. This versatility paves the way for a broad array of biomedical applications, from controlled drug delivery systems to scaffolds for tissue engineering [13, 14].

However, it's worth noting that natural polymer-based hydrogels often come with challenges such as batch-to-batch variability, limited mechanical strength, and potential risk of pathogen transmission, depending on the source. Thus, careful consideration of these factors is essential in their development and application [12].

2.1.1 Cellulose-Based Hydrogels

Cellulose, a major component of plant cell walls, can be transformed into hydrogels with unique properties suitable for biomedical applications. Cellulose-based hydrogels are renowned for their mechanical strength, biocompatibility, and controllable degradation. Their ability to mimic the extracellular matrix makes them suitable for tissue engineering and wound healing applications. Moreover, they can be employed as controlled drug delivery systems. However, processing challenges and the need for chemical modification to enhance specific functions are areas for further investigation [15, 16].

2.1.2 Chitosan-Based Hydrogels

Derived from chitin, chitosan-based hydrogels offer a broad spectrum of applications in the biomedical field. Known for their biocompatibility, biodegradability, and ability to promote cell adhesion, these hydrogels find applications in drug delivery, tissue engineering, and wound care [17, 18]. They can also be combined with other polymers or ceramic particles to enhance their mechanical properties or introduce specific functionalities. The positive charge of chitosan further allows effective interaction with negatively charged substances such as proteins or nucleic acids [19].

2.1.3 Alginate-Based Hydrogels

Alginate is a naturally occurring polymer extracted from brown seaweed, and its hydrogels are extensively used in biomedical applications. Alginate-based hydrogels are appreciated for their gentle gelation process, ability to encapsulate cells, and tunable mechanical properties. They are frequently used in cell therapy and tissue engineering, especially where soft, hydrated environments are required. Their ability to form gels in the presence of divalent cations, such as calcium, offers unique opportunities for minimally invasive delivery and implantation [20, 21].

2.1.4 Collagen-Based Hydrogels

Collagen, a primary structural protein in animal tissues, can be formed into hydrogels that closely mimic the native extracellular matrix. Collagen-based hydrogels are renowned for their biocompatibility and ability to support cell growth and differentiation. These features make them highly applicable in tissue regeneration, particularly in skin, bone, and cartilage repair. However, concerns related to potential immunogenicity and batch-to-batch variability must be considered in their utilization [22, 23].

2.1.5 Gelatin-Based Hydrogels

Gelatin, derived from collagen, is another natural polymer that forms hydrogels with significant biomedical applications. Gelatin-based hydrogels possess excellent biocompatibility, ease of modification, and support for cellular activities. They find applications in drug delivery, wound healing, and as scaffolds for tissue regeneration. Their thermal responsiveness and ability to blend with other polymers make gelatin-based hydrogels highly versatile. Their widespread use, however, is sometimes constrained by limited mechanical stability and rapid degradation [24, 25].

Gelatin Methacryloyl (GelMA), is a particularly noteworthy derivative that has been chemically modified with methacrylate groups. This modification imparts photopolymerizable properties, allowing for controlled crosslinking and fabrication of complex structures using techniques like 3D printing. The unique attributes of GelMA, including its tunable mechanical properties, controlled degradation rates, and ability to encapsulate cells, have expanded its applications in tissue engineering, drug delivery, and wound healing. GelMA's compatibility with various cell types and its ability to be tailored to mimic native tissue characteristics make it an attractive material for constructing patient-specific tissues or organs [26, 27].

2.2 Synthetic Polymer-Based Hydrogels

Synthetic polymer-based hydrogels represent a class of materials synthesized from human-made polymers. Unlike their natural counterparts, these hydrogels are characterized by well-defined structures and properties, which can be precisely tailored to meet specific needs within biomedical applications. This ability to customize properties offers tremendous advantages in terms of reproducibility, functionality, and application diversity [7, 28].

One of the central features of synthetic polymer-based hydrogels is the ability to control the polymer architecture, crosslinking density, degradation kinetics, and mechanical properties. This flexibility in design allows researchers to create materials with specific characteristics suitable for various applications, ranging from controlled drug delivery to tissue scaffolding and wound healing [9].

Additionally, synthetic polymer-based hydrogels generally exhibit exceptional stability and strength compared to natural polymer-based hydrogels [28]. The choice of monomers and crosslinkers, along with the polymerization method, enables fine-tuning of the hydrogel's behavior in biological environments. This results in materials that can withstand physical stresses or exhibit desired swelling characteristics, leading to potential use in load-bearing applications or in response to specific stimuli [7].

One of the main advantages of synthetic polymer-based hydrogels is their scalability and consistency between batches, a result of controlled synthesis processes. This reproducibility makes them highly desirable for commercial applications where standardization is critical. Moreover, the absence of biological contaminants,

common in natural polymer-based hydrogels, minimizes potential immunogenic responses [28].

However, despite these advantages, challenges exist in optimizing the biocompatibility and bioactivity of synthetic polymer-based hydrogels. The lack of inherent bioactivity often requires modification with biological signals or blending with natural polymers to promote desirable cellular interactions [7, 13].

2.2.1 Poly(Ethylene Glycol) (PEG) Hydrogels

Poly(ethylene glycol) (PEG) hydrogels are one of the most extensively researched and used synthetic hydrogels in biomedical applications. PEG-based hydrogels are known for their hydrophilicity, biocompatibility, and resistance to protein adsorption. They can be tailored to control swelling and degradation rates, making them ideal candidates for controlled drug delivery, tissue engineering, and as coatings to reduce medical implant rejection. The ability to functionalize PEG with various ligands offers further opportunities for specific cellular interactions and targeting [29, 30].

2.2.2 Poly(Ethylene Oxide) (PEO) Hydrogels

Poly(ethylene oxide) (PEO) hydrogels share similar properties with Poly(ethylene glycol) (PEG), such as hydrophilicity, biocompatibility, and resistance to protein adsorption [8, 31]. As a result, PEO has found a place in various biomedical applications, including drug delivery systems and tissue engineering scaffolds. The unique feature of PEO hydrogels is their ability to maintain their structural integrity and mechanical properties within a biological environment, making them suitable for long-term applications. Additionally, PEO's versatility in terms of molecular weight and ability to copolymerize with other monomers offers a wide array of design possibilities to meet specific medical needs. The well-controlled synthesis and high reproducibility further contribute to PEO's popularity in the biomedical field [2, 8].

2.2.3 Poly(Acrylic Acid) (PAA) Hydrogels

Poly(acrylic acid) (PAA) hydrogels are another class of synthetic hydrogels known for their strong water-absorbing properties [32]. The anionic nature of PAA imparts a high degree of responsiveness to changes in pH, making them suitable for applications like pH-sensitive drug release. Furthermore, PAA hydrogels are used in wound care for their moisture-retentive properties and in ophthalmology for contact lenses. However, careful control over synthesis parameters is required to optimize their biocompatibility [32, 33].

2.2.4 Poly(N-isopropylacrylamide) (PNIPAM) Hydrogels

Poly(N-isopropylacrylamide) (PNIPAM) hydrogels are renowned for their thermo-responsive behavior. These hydrogels undergo a sharp phase transition at a specific temperature (around 32 °C), which has been exploited for controlled drug release and cell detachment processes. Their responsiveness to temperature allows the design of on-demand therapeutic interventions and has led to applications in cancer therapy and tissue engineering. Nevertheless, the biocompatibility of PNIPAM can be a concern and often requires careful formulation and modification [34, 35].

2.2.5 Poly(Vinyl Alcohol) (PVA) Hydrogels

Poly(vinyl alcohol) (PVA) hydrogels possess excellent mechanical properties, biocompatibility, and resistance to protein adsorption. Their physical characteristics have led to applications in cartilage tissue engineering [36], artificial vitreous in ophthalmology [37], and as matrices for drug delivery [38]. Crosslinking PVA with other polymers or via physical methods can further modify its properties to meet specific biomedical needs. The large-scale production of PVA hydrogels has further enabled their commercial success [39].

2.2.6 Polylactic-co-Glycolic Acid (PLGA) Hydrogels

Polylactic-co-glycolic Acid (PLGA) hydrogels are co-polymers known for their adjustable degradation rates, controlled by altering the ratio of lactic acid to glycolic acid. This controllable degradation makes PLGA hydrogels suitable for applications in controlled drug delivery, especially in localized cancer treatments [40]. Additionally, PLGA's biodegradability and FDA approval have facilitated its use in implantable devices and biodegradable sutures. Ongoing research continues to explore its potential in various regenerative medicine applications [41].

3 Common Ceramics Used as Fillers in Hydrogel Composites

Ceramic materials, known for their rigidity, chemical stability, and biocompatibility, complement the soft and highly swollen nature of hydrogels, thereby extending their applications in biomedical engineering. By carefully selecting and combining specific ceramic fillers with different types of hydrogels, researchers have been able to tailor the composite materials to meet diverse requirements, such as improved load-bearing capabilities in bone tissue engineering or controlled release profiles in drug delivery systems [5, 6]. The subsequent sections will delve into the individual

characteristics and applications of commonly used ceramic fillers, including HAp, β -TCP, BG, Nanoclay, and Wollastonite (References needed).

3.1 *Hydroxyapatite (HAp)*

HAp is a naturally occurring mineral form of calcium apatite, primarily known for its presence in human bones and teeth. Its chemical composition, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, closely resembles the mineral component of bone, rendering HAp a material of choice in biomedical applications due to its excellent biocompatibility, osteoconductivity, and bioactivity [42].

The incorporation of HAp as a filler in hydrogel composites has garnered attention, particularly in bone tissue engineering. When combined with hydrogels, HAp enhances the mechanical strength, provides a surface conducive to cell adhesion, and supports mineralization processes vital for bone regeneration. These hybrid systems synergistically utilize the elasticity of hydrogels and the stiffness of HAp to mimic the natural bone's structural hierarchy [43, 44].

Moreover, HAp-based hydrogel composites are being explored for controlled drug delivery applications. The high surface area and porous nature of HAp enable the loading and gradual release of therapeutic agents, offering a sustained therapeutic effect. The ability to fine-tune the composite's properties by altering HAp's particle size, shape, and concentration within the hydrogel matrix allows researchers to design systems that can respond to specific biological stimuli (e.g., pH or enzymes), thus enabling targeted therapies [45, 46].

3.2 *β -tricalcium Phosphate (β -TCP)*

β -TCP is a crystalline, bioceramic material with the chemical formula $\text{Ca}_3(\text{PO}_4)_2$. Its significance in the biomedical field arises from its biocompatibility, bioresorbability, and osteoconductive properties, which have paved the way for its utilization in various orthopedic and dental applications [47, 48].

In terms of applications as a filler in hydrogel composites, β -TCP has exhibited great potential. By incorporating β -TCP into hydrogel systems, researchers have been able to create scaffolds with enhanced mechanical properties and tailored degradation rates. These scaffolds are especially favorable in bone regeneration, where the resorption of β -TCP matches the rate of new bone formation, thus promoting natural healing processes. This synergistic effect allows for a smooth transition from artificial to natural tissue over time [49, 50].

In addition to bone tissue engineering, β -TCP-filled hydrogel composites have shown potential in the controlled release of therapeutic agents. The porous structure of β -TCP can be leveraged to encapsulate and gradually release drugs, growth factors, or other bioactive compounds in a controlled manner. This feature, coupled with the

adjustable degradation rates, presents a platform for developing highly effective drug delivery systems, particularly for localized treatments [51–53].

Furthermore, the compatibility of β -TCP with various natural and synthetic polymers offers opportunities for the design of specialized hydrogel systems. The incorporation of β -TCP into hydrogels has proven effective in enhancing the mechanical strength, reducing brittleness, and modulating the hydrogel's swelling behavior, thus extending its applicability in various medical devices and implants [6, 49, 50].

3.3 *Bioactive Glass (BG)*

BG refers to a group of surface-reactive glass–ceramic biomaterials, first developed in the late 1960s. These glasses, commonly composed of SiO_2 , Na_2O , CaO , and P_2O_5 , are known for their ability to bond to both hard and soft tissues. Their bioactivity, biocompatibility, and ability to enhance tissue regeneration have positioned BG as a prominent material in the field of biomedical engineering [54, 55].

One of the critical properties of BG is its controlled release of soluble ionic products, which can stimulate cellular response and enhance the growth of bone and soft tissues. When incorporated as a filler in hydrogel composites, BG imparts not only mechanical strength but also promotes bioactivity. The composite's surface becomes a site for the nucleation and growth of HAp, thereby encouraging bone cell adhesion, proliferation, and differentiation [56].

BG-filled hydrogel systems have found applications in various biomedical fields. In bone tissue engineering, these composites are utilized to create scaffolds that mimic the natural bone environment. The incorporation of BG improves the osteoconductive and osteoinductive properties of the scaffolds, thereby facilitating bone regeneration [56, 57].

Furthermore, BG has been investigated for its potential in wound healing. When incorporated into hydrogels, BG can release ions that exhibit antibacterial properties and stimulate angiogenesis, thus accelerating the wound healing process. The controlled degradation of BG within the hydrogel matrix ensures a sustained release of these beneficial ions, making it a valuable tool in chronic wound management [58, 59].

3.4 *Nanoclay*

Nanoclay refers to a class of nanoparticles derived from layered silicates or other clay minerals. With typical sizes ranging from 1 to 100 nm, nanoclay particles offer an extremely large surface area relative to their volume, endowing them with remarkable mechanical, thermal, and barrier properties. Nanoclays are classified into several types, including montmorillonite, halloysite, and kaolinite, among others. These materials are characterized by their layered structures, where individual layers are

typically composed of an aluminum or magnesium oxide sheet sandwiched between two silica sheets [60, 61].

One of the most appealing features of nanoclays is their ability to enhance the mechanical properties of polymer matrices [61]. When incorporated as fillers in hydrogels, nanoclays provide improved tensile strength, modulus, and barrier properties. The compatibility of nanoclay with various hydrogel polymers enables the creation of multifunctional composites, adaptable to specific needs [62, 63].

Nanoclay, as a filler in hydrogel composites, offers a versatile platform for biomedical applications. Its unique physicochemical properties, combined with the possibility of functional modification, provide opportunities for the development of tailor-made solutions in drug delivery, tissue engineering, and wound healing. The strategic integration of nanoclay into hydrogel systems represents a burgeoning area of research with significant potential to advance current therapeutic methodologies [62, 63].

3.5 *Wollastonite*

Wollastonite (CaSiO_2) is a naturally occurring calcium silicate mineral with a unique acicular (needle-like) crystal structure. It is often synthesized for commercial applications using various methods, including solid-state reaction and sol–gel synthesis. Characterized by high thermal stability, good mechanical strength, and bioactivity, wollastonite has been extensively investigated in a variety of applications, ranging from ceramics and construction to medical implants and tissue engineering [64, 65].

Wollastonite's bioactive nature stems from its ability to form a HAp layer on its surface when immersed in body fluids. This layer facilitates the bonding of the material to both soft and hard tissues, a crucial property for biomedical applications. Its acicular morphology, coupled with its excellent biocompatibility, makes wollastonite an ideal candidate for bone tissue engineering [66].

The integration of wollastonite into hydrogel systems offers multifunctional platforms that can be customized to address specific challenges in various biomedical applications. Its distinct physical and chemical properties, combined with the compatibility with different hydrogel polymers, provide opportunities to develop innovative solutions [67, 68]. Ongoing studies focusing on the optimization of processing techniques, surface modification, and functionalization of wollastonite are anticipated to further enhance its performance and expand its applications in the biomedical domain.

4 Recent Biomedical Applications of Ceramic Filler-Based Polymer Hydrogels

Polymeric hydrogels epitomize a profoundly malleable and soft subset of materials, exhibiting viscoelastic properties intermediary between those liquid and solid phases. The covalently cross-linked matrices within these hydrogels capacitate the genesis of cavities spanning diverse morphologies and magnitudes. This intrinsic characteristic renders them eminently conducive for biomedically-oriented applications, where they serve as repositories for a plethora of molecular entities and pharmaceutical compounds. Critical determinants governing their applicability encompass the modalities of their synthesis, the stability of the resultant gels, as well as the intricate interplay between their singular architectures and rheological attributes. The vast realm of medical science has embraced polymeric hydrogels, leveraging them in myriad capacities—ranging from scaffolds in tissue engineering, protective coatings tailored for bone tissue interfacing, components in state-of-the-art medical apparatuses, to pivotal roles in transdermal therapeutic modalities and advanced drug delivery matrices [7, 69].

Therapeutic paradigms directed towards bone regeneration predominantly incorporate the utilization of autologous and allogeneic bone grafts. Ergo, a profound understanding of the biological and chemical intricacies inherent to osseous tissues is pivotal in facilitating the synthesis of artificial bone scaffolding. Such constructs are meticulously engineered, bearing precise compositional and architectural specifications, to galvanize neo-tissue genesis. Osseous infections, traumatic lesions, or geriatric osseous afflictions, such as fractures, cartilaginous deterioration, or skeletal anomalies like osteoarthritis, exert profound detriments to an individual's quality of life. Hydrogels, imbued with bioactive constituents, have emerged as a formidable surrogate for the extracellular matrix, proffering a conducive milieu for osteogenesis. Recent epochs have witnessed an escalating proclivity towards the adoption of biomimetic polymeric hydrogel matrices in the orchestration of bone revival, credited to their adeptness at fostering stem cell adhesion, proliferation, and lineage specification [70].

Minerals—encompassing copper, magnesium, calcium, and zinc—occupy an instrumental role in the equilibrium of the body's mineralogical milieu. Such metallic ions are intricately intertwined with polymeric strands, culminating in the formulation of efficacious polymeric hydrogels, which serve as catalysts for bone convalescence. In the contemporary scientific panorama, diverse initiation modalities, both physical and chemical, have been harnessed to spawn advanced hydrogel constructs, potentiated with superior osteoregenerative capacities. In hydrogels engendered through physical initiation, cross-linking is actuated by modalities such as photonic or thermal stimuli. Conversely, in the realm of chemically initiated hydrogels, robust hydrogel matrices are forged through the establishment of covalent or coordinate linkages between polymeric chains, mediated either by molecular or ionic crosslinking agents, as illustratively delineated in Fig. 2.

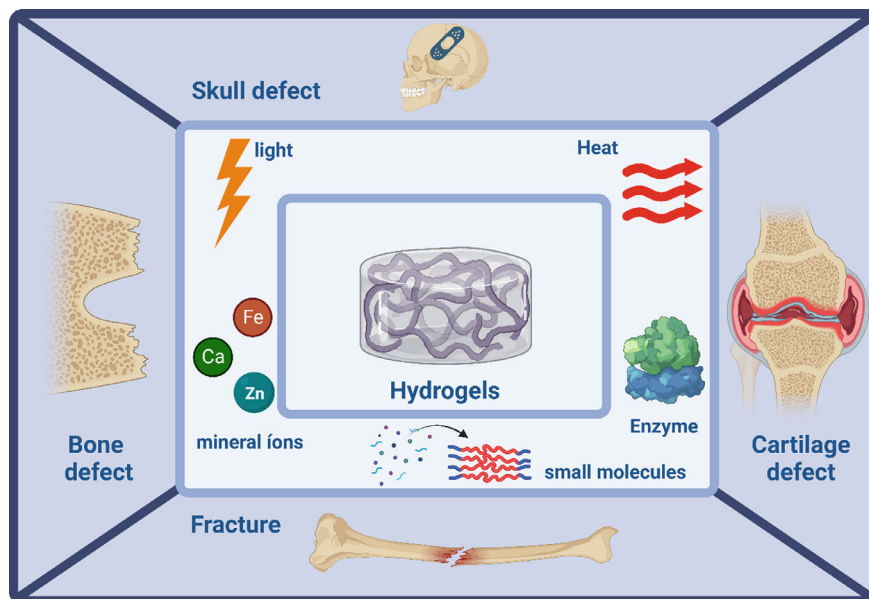


Fig. 2 Several bionic hydrogels were fabricated by different triggered conditions

In a innovative study conducted by Kotlarz et al. [67], using cell-encapsulated hydrogels as a means of cellular deposition onto a substrate or framework presents an expedited modality for cellular placement. When optimally configured, hydrogels orchestrate a dense fibrous architecture conducive for cellular entrapment and adhesion, thereby formulating a protective milieu that circumvents cellular efflux due to the influence of media. Nonetheless, when amalgamating hydrogels into cellular deposition paradigms, one must critically evaluate the cellular propensity for migratory activity from within the hydrogel matrix and the subsequent biofunctional ramifications thereof. Cellular deposition facilitated by a bioprinted hydrogel matrix against traditional manual cell seeding procedures executed within a media milieu. As a representative paradigm for bone tissue engineering, employs a bioceramic framework delineated through binder jet 3D printing techniques, leveraging apatite-wollastonite (AW) glass-ceramic as the material of choice. This structure manifests a porosity approximating ~50%, predominantly punctuated with pores ranging between 50 and 200 μm . Mesenchymal stromal cells, procured from bone marrow sources, were adroitly positioned onto this porous AW matrix via both media-based methods and the reactive jet impingement (ReJI) bioprinting mechanism. Employing the media-based seeding methodology accentuated the osteoinductive proclivity of the scaffold, concurrently underscoring its capability to facilitate cellular translocation within its porous confines. Conversely, ReJI bioprinting underscored the infiltration of the cell-saturated hydrogel within the porous AW edifice post deposition. Subsequent to this, cells embarked on a migration trajectory from the hydrogel

architecture, thereby engaging with the bioceramic substrate. An overarching assessment indicated that both seeding modalities rendered appreciable and comparable outcomes with respect to cellular migration and mineralization. Nonetheless, leveraging bioprinted hydrogels for cellular deposition may indeed be efficacious for in situ cellular embedding into implant frameworks. This methodology aligns with clinical aspirations in tissue engineering, obviating prolonged durations mandated for cellular adhesion via media and eliminating the necessity to uphold a precise orientation pending adhesion completion.

The degradation dynamics of biomaterials emerge as quintessential for their clinical deployment, as it obviates the necessitation for subsequent surgical interventions and endorses cyclical osseous tissue remodeling. Both constituents of the composite scrutinized in this analysis manifest biodegradability within the human physiological milieu. HAp stands as one of the paragons of calcium phosphate-based materials, attributed to its marginal solubility in aqueous mediums and its relatively subdued degradation propensity under physiological conditions, an outcome of intricate dissolution and precipitation phenomena. Despite assiduous scientific endeavors, the biodegradation intricacies of HAp remain enigmatic; however, ostensible roles of osteoclast cells and macrophages have been identified, concomitant with the aforesaid processes. The degradation dynamics of HAp have been ascertained to be contingent on myriad factors, encompassing the Ca/P stoichiometry, purity, microstructural attributes, site of implantation, and the physiological health status of the host [42]. Bartmański et al. [71], unveiled an innovative biocompatible injectable composite amalgamating HAp, gelatin, and two distinct commercially procured transglutaminases, BDF and SNF. All specimens corroborated optimal nanomechanical attributes, with Young's modulus and hardness values approximating those inherent to native bone. Notably, BDF manifested superior hydrophilic attributes and structural resilience over a temporal window of seven days vis-à-vis SNF. The transglutaminase variant employed exerted a negligible impact on surface morphology, chemical constitution, or functional properties inclusive of injectability. Independent of the cross-linking adjunct utilized, all specimens evinced nanomechanical attributes resonating closely with native bone's mechanical framework.

Cidonio et al. [72] embarked on an investigative odyssey, illuminating the ramifications of integrating a synthetic nanoclay, specifically Laponite® (LPN), in tandem with GelMA bioink, culminating in the genesis of an advanced, cellularly instructive bioink. This resultant nanocomposite bioink evinced a salient amplification in shape preservation and a sophisticated interconnected porosity manifested within the extruded bioprinted filaments. The cellular vitality of Human Bone Marrow Stromal Cells (HBMSCs) enshrouded within the aforementioned nanocomposite manifested minimal variances over a 21-day trajectory in LPN-GelMA ($85.60 \pm 10.27\%$), contrasting starkly with sole GelMA, wherein vitality evidenced a conspicuous decline from day 7 ($95.88 \pm 2.90\%$) to day 21 ($55.54 \pm 14.72\%$) with statistical pertinence. Additionally, HBMSC proliferation within LPN-GelMA was accentuated, evincing a statistically significant cell count increment over the 21-day period ($p < 0.0001$), relative to GelMA in isolation. A cardinal revelation was the conducive

ambiance the LPN-GelMA scaffold presented for osteogenic differentiation, corroborated by the emergence of mineralized nodules. This materialized even devoid of the osteogenic stimulant, dexamethasone. Further, an *ex vivo* assessment employing a chick chorioallantoic membrane model attested to the bioink construct's impeccable integration potential within the avian embryo's vascular matrix post a 7-day incubation. Constructs amalgamating LPN-GelMA with VEGF (Vascular Endothelial Growth Factor) exhibited a pronounced elevation in vascular penetration vis-à-vis GelMA-VEGF constructs. Such integration and vascularization were discerned to resonate directly with the enhanced drug sequestration and retention proclivity of the LPN-GelMA, especially when juxtaposed against constructs devoid of LPN.

Another problem of complex resolution is the articular cartilage degradation, a pervasive affliction, grapples with substantial impediments in autogenic restoration post-trauma. Present-day substrates tailored for articular cartilage rehabilitation fail to wholly satisfy clinical imperatives. Hydrogels, attributable to their architectural congruence with the extracellular matrix, the extensive modifiability of their aqueous constitution, and their eminent lubricative characteristics, emerge as prospective candidates for articulatory cartilage rectification [73]. However, antecedent osteochondral regenerative matrices are found wanting, predominantly due to the absence of an interfacing layer between osseous and cartilaginous structures, an integral tier executing cardinal physiological tasks, inclusive of mechanical stress dissipation and microenvironmental stabilization [74].

The calcified cartilage interphase (CCI) represents the mineralized nexus interceding the hyaline cartilage and the subchondral osseous structure, playing an indispensable role in cartilaginous restoration. A contemporarily elucidated non-stoichiometric calcium silicate variant, wherein 10% of Ca is superseded by Mg (termed CSi-Mg10), has been manifested to be profoundly bioactive within osteogenic milieu *in vivo* [68]. The objective of this investigational discourse was to methodically assess the regenerative potential of osteochondral junctures facilitated by differential concentrations of Ca-Mg silicate within hydrogel-centric scaffolding. This evaluation was juxtaposed with scaffolds infused with traditional Ca-phosphate biomaterial constituents. Utilizing the 3D bioprinting methodology, hydrogel-oriented porous scaffoldings amalgamated with gradients of 0–6% CSi-Mg10, a static 6% β -TCP, or 6% nanoscale hydroxyapatite (nHAp) were fabricated. A progressive enrichment in CSi-Mg10 content ostensibly augments chondrocyte hypertrophy, mineralization, cellular proliferation, and extracellular matrix accretion. The induction of both osteogenic and chondrogenic differentiation exhibited a dose-resonant enhancement. In a direct comparative analysis against scaffolds infused with 6% β -TCP or nHAp, human deep-zone chondrocytes (hDZCs) proliferated on CSi-Mg10 scaffolds of congruent concentrations evinced superior mineralogenic potential. Of particular significance was the observation that hDZCs within the 6% CSi-Mg10 scaffolds sustained an elevated expression of specific extracellular matrix markers endemic to the calcified cartilage zone, alongside the hypertrophic indicator, collagen type X. Subsequent immunohistochemical evaluations, in tandem with Alizarin Red staining, resonated with these deductions. Conclusively, the investigation accentuates that hydrogel-infused composite scaffoldings encapsulating a

6% CSi-Mg10 constitution hold pronounced promise in catalyzing the genesis of calcified cartilaginous structures.

In a seminal revelation, Cui et al. [75] unveiled a potentiated hydrogel ink, buttressed by intensified hydrogen bond associations. This ink is synthesized from a supramolecular polymeric hydrogel amalgamated with an acryloylglycinamide (PNAGA) copolymer. When juxtaposed against its singular polymer hydrogel counterpart, the PNAGA copolymer hydrogel manifests diminished fusion thresholds and augmented fluidic properties. Following prolonged immersion in a phosphate buffer solution (PBS), the biohybrid gradient hydrogel scaffold retains an unwavering porous architecture alongside commendable mechanical vigor. The incorporation of β -TCP augments the structural robustness of the scaffold, while concurrently fostering cellular adherence, proliferation, and osteogenic diversification, bestowing upon the scaffold potent osteoinductive attributes and facilitating a resilient active integration with the resident bone.

Furthermore, Gögele et al. [76] delved into a distinct genre of ceramic filler-integrated polymer gels, targeting articulatory cartilage rejuvenation. Their investigative pursuits aimed at amplifying the stability of pristine BG matrices through solvent-phase polymer impregnation, all while preserving cellular adhesion onto the glass constructs. Consequently, BG matrices underwent meticulous assessment, in their unaltered state or when bolstered with varying concentrations of PLGA. Post-inoculation with primary porcine articular chondrocytes (pACs) and human mesenchymal stem cells (hMSCs) within a protracted dynamic culture milieu (spanning 35 days), observations denoted that PLGA permeated the entirety of the scaffold, boasting in excess of 70% porosity. Mechanical resilience experienced an upsurge subsequent to polymer infiltration. Notably, PLGA incursion left cellular viability unscathed, concurrently elevating both DNA and sulfated glycosaminoglycan (sGAG) indices within hMSC-inhabited matrices. Immunocytochemical colorations affirmed the efficacious chondrogenesis within hMSC-occupied matrices, delineating the presence of collagen type II, cartilage proteoglycans, and the transcriptional effector SOX9. Matrices undergoing PLGA permeation manifested augmented relative expression of chondral-affiliated genes in both pAC and hMSC-inhabited matrices as opposed to unadulterated BG. In light of these groundbreaking revelations, the researchers advocate for the adoption of PLGA-enriched BG matrices in the realm of cartilage tissue engineering.

Hydrophilic polymeric matrices, colloquially recognized as hydrogel-based polymers, have established a profound foothold in pharmaceutical delivery methodologies, attributed to their unparalleled aptitude for retaining aqueous and biological media, ensuring biocompatibility, and orchestrating drug liberation through distinct physicochemical avenues. Progressive paradigms in the arena of hydrogel pharmaceutical delivery systematics are gravitating towards cue-responsive drug dispensation—mechanisms adept at transacting under explicit stimuli, be they pH inflections, thermodynamic alterations, or enzymatic engagements. Such intricacies are pivotal in honing drug localization whilst attenuating global toxicological ramifications. An escalating fervor prevails in sculpting injectable hydrogel blueprints that not

merely streamline application modalities but also vouchsafe sustained pharmaceutical dissemination. Parallely, the discipline beholds a proliferation in the synthesis of nanoscale hydrogels amalgamated with multifunctional cohorts to augment drug sequestration and emancipation efficiencies. With research trajectories skewing thus, avant-garde hydrogels characterized by augmented mechanical tenacity, calculable liberation dynamics, and impeccable biocompatibility are emerging as research touchstones. Building on these avant-garde innovations, we envisage the advent of intricate therapeutic protocols. Furthermore, the inherent adaptability of hydrogel-based polymers lends them particularly conducive for bespoke medicinal paradigms, facilitating custom modifications in response to singular patient imperatives—ranging from the refinement of drug liberation trajectories and amalgamating therapeutic agents to magnifying clinical oversight efficacy and economizing healthcare fiscal outflows [77].

In recent temporal frameworks, tissue engineering has ardently endeavored to uncover a hybrid bioactive material imbued with the capacity for regimented pharmaceutical dissemination. Corroborating this trajectory, Rial et al. [78] delineates a novel paradigm to engender distinct hydrogel microparticulate entities (HMPs) showcasing varied morphological and compositional facets through an amalgamation of empirical and computational methodologies. Microparticles manifested from Calcium-Alginate (Ca-ALG) in conjunction with core-shell constructs derived from Alginate-Chitosan (Ca-ALG-CHI) were orchestrated with the encapsulation of drug-impregnated HAp within their intramolecular matrices. The procedural construct predominantly harnesses a microfluidic apparatus, a conduit ensuring the attainment of cross-linked HMPs bearing consistent dimensional and morphological attributes, coalescing both external and internal gelation techniques. Factors such as the volumetric juxtaposition of aqueous to non-aqueous phases, coupled with modulations in the collection reservoirs, structural design, and dispersion paradigms, were meticulously evaluated. As prototypical drug models, Propranolol hydrochloride and Cloxacillin sodium salt monohydrate were enlisted. The kinetic interplay of each pharmaceutical's affinity towards the bioactive HAp matrix was scrutinized utilizing Avrami's coefficients, while the subsequent release dynamics were deciphered via the Korsmeyer-Peppas equation. The ideation and maturation of such hydrogel microparticles, endowed with enhanced functional attributes, stand paramount in ushering granulated hydrogel entities. These represent a cutting-edge, eco-conscious, enduring, and potentially viable avenue for therapeutic interventions in the realm of regenerative medicine. In the discourse at hand, dichotomous green, enduring, and multifunctional HMPs have been meticulously engineered utilizing Chitosan, Alginate, and pharmaceutical-impregnated HAp. Computational simulation outputs manifested significant congruence with the authentic physicochemical interplay of the two non-coalescent phases. This concordance elucidated the intricate interdependence between flow proportionality, microchip architectural design, and the resultant dimensional and structural parameters of the synthesized HMPs. This correlation has been rigorously corroborated both through algorithmic computations and empirical methodologies, both resonating with exceptional fidelity. Intriguingly, the amalgamation of internal methodologies coupled with varied compositional strategies for the

external bath has been empirically validated as a potent mechanism for the manipulation of microparticle morphologies, facilitating an augmented level of uniformity. Culminating the discourse, the evaluation of pharmaceutical assimilation and subsequent dissemination employing specialized models ascertains that drug release kinetics can be modulated, contingent upon the conceived structural designs and their earmarked applications. Given the auspicious characteristics intrinsic to the resultant hydrogel microparticles, they distinctly qualify as potential substrates for the genesis of assorted granular hydrogels, encompassing a vast spectrum of tissue engineering utilities, notably expediting bone tissue recuperation whilst circumventing microbial contamination.

Ugrinovic et al. [79] presented advanced interpenetrating networks (IPNs) comprising poly(methacrylic acid) and gelatin (PMAG) were architecturally fortified with varying concentrations of nanostructured HAp particulates, spanning HAp-to-polymer weight ratios from a null value to 40%. The deliberate integration of HAp distinctly augmented mechanical attributes, albeit engendering a marginal decrement in swelling propensity, pH responsiveness, and porosity. Ascending the HAp-to-polymer concentration gradient to a substantial 40% precipitated a surge in compressive fortitude, transitioning from 29.83 kPa (intrinsic to pure PMAG hydrogel) to an impressive 68.16 kPa. An analysis under simulated physiological milieu revealed divergent drug liberation kinetics for ciprofloxacin (a hydrophilic agent) and oxaprozin (of a hydrophobic nature). In vitro antimicrobial assays manifested both bactericidal and mycocidal efficacy of the pharmaceutical-imbued hydrogels against microbial strains, notably *E. coli*, *S. aureus*, and *C. albicans*. The PMAG IPN hydrogels, distinguished by their pronounced porous architecture and bolstered by nanostructured HAp particulates, were meticulously probed for potential drug dispensation functionalities. The incorporation of HAp distinctly amplified the compressive robustness of the PMAG hydrogels, an enhancement attributable to the homogeneous dispersal and heightened interactivity at the interphase of particulates and the hydrogel matrix, as corroborated. A heightened HAp concentration manifested a reduced swelling propensity and pH responsiveness, likely consequent to the crosslinking repercussions of HAp particulates. The hydrogels' drug dissemination kinetics evinced a dependency on the inherent physicochemical attributes of the dispensed pharmaceuticals, echoing variances in electrostatic interactions and hydrogen bonding amidst functional moieties of the matrix and the therapeutic agents. Oxaprozin's liberation dynamics resonated best with the Korsmeyer-Peppas (K-P) kinetic paradigm, whilst ciprofloxacin's release trajectory adhered closely to an array of kinetic models, including K-P, Higuchi, and First-order. Antimicrobial in vitro assays illuminated the potent bactericidal and antifungal attributes of PMAG/HAp40 hydrogel matrices against key microbial strains. Notably, the ciprofloxacin-imbued composite hydrogel showcased mycocidal activity against *C. albicans*, whereas the oxaprozin-laden matrix exhibited bactericidal prowess against *S. Aureus*, a finding hitherto unreported. Concurrently, MTT assays on L929 cellular entities underscored the biocompatibility of the formulated hydrogels. Conclusively,

the derived composite hydrogels epitomized the synergetic benefits of all incorporated constituents: PMAA's swelling, porosity, and pH reactivity, gelatin's biodegradability and biocompatibility, HA's inherent high specific surface and mechanical vigor, while concurrently presenting a novel avenue for repurposing established pharmaceuticals, potentially mitigating side effects, expediting regulatory approval timelines, and economizing therapeutic expenditures.

5 Conclusions and Future Perspectives

In conclusion, the exploration and utilization of ceramic filler-based polymer composites, particularly in the domain of hydrogels for biomedical applications, mark a significant stride in the advancement of materials science and medical technology. Hydrogels, characterized by their unique swelling properties, biocompatibility, and adaptability, have found profound significance in areas ranging from tissue engineering to controlled drug delivery systems. Their classification into natural and synthetic polymer-based hydrogels offers a broad spectrum of possibilities in mimicking natural tissues and fabricating tailor-made solutions for specific medical applications.

The incorporation of ceramic fillers such as HAp, β -TCP, BG, Nanoclay, and Wollastonite has further enriched the landscape of hydrogel applications. By exploiting the unique characteristics of these ceramics, the resultant composites have demonstrated enhanced mechanical strength, bioactivity, and responsiveness to physiological stimuli.

However, despite these considerable achievements, there remain challenges and unexplored territories. The interface compatibility, uniform distribution of ceramics within hydrogel matrices, long-term stability, and in vivo response are areas that require further scrutiny and optimization. The customization of these composites for patient-specific needs and the scaling up of manufacturing for commercial applications also pose considerable challenges.

Future perspectives in this field are promising and multifaceted. Continued interdisciplinary collaboration between materials scientists, biomedical engineers, pharmacologists, and clinicians is imperative to drive innovation and practical implementation. Emphasis on green synthesis, biodegradability, and the minimization of adverse side effects must be at the forefront of new developments.

Moreover, the integration of advanced technologies such as 3D printing, nanotechnology, and smart responsive systems can propel the field towards more sophisticated, personalized healthcare solutions. This could include the development of hydrogel systems that not only replace damaged tissues but also actively contribute to their regeneration through controlled growth factor release or dynamic interaction with surrounding biological structures.

The research and development of ceramic filler-based polymer composites represent an exciting and ever-evolving field with immense potential for biomedical

applications. Sustained investment in research, ethical considerations, rigorous clinical evaluation, and collaborative efforts will undoubtedly guide this field into new horizons, transforming healthcare, enhancing the quality of life, and opening new pathways for treatment and rehabilitation.

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Fiber Fillers-Based Polymer Gels for Biomedical Applications



Trupti Pratik Durgawale, Sarika S. Suryawanshi, Pranali P. Patil, Lalita Shashikant Nemade, Apeksha Chandrakant Rahate, and Hemalata Suhasrao Dol

Abstract Polymer gels made with fibre fillers are a potential new area in the field of biomedical materials. These gels are made by adding fibrous fillers to polymer matrices. They have a unique set of properties that make them perfect for a wide range of biological uses. This chapter goes into detail about these materials, starting with the basic ideas behind how polymer gels form and the important role fibre fillers play. It goes into detail about the most important ways to make them, with a focus on getting them to spread out evenly and work at their best. This chapter is also encompass how fibre fillers-based polymer gels have shown great promise in many biomedical uses, such as tissue engineering, drug delivery, wound healing, and biosensing devices. Real-world examples and case studies show how useful and important they are. Also, the chapter focuses on biocompatibility, biodegradability, and customising qualities to meet specific biomedical needs. This makes sure that the materials are safe and effective. In conclusion, this chapter is a very useful tool for scholars and practitioners in the biomedical field. It gives a full picture of fibre fillers-based polymer gels and how they are changing the way healthcare solutions are made.

Keywords Gels · Biomedical · Fibrous fillers · Drug delivery · Biocompatibility

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1 Introduction

Polymer gels are an interesting class of materials with a wide range of potential scientific, industrial, and medicinal uses due to their exceptional physical and chemical properties [1]. These gels have properties that set them apart from both solids and liquids; they are made by spreading a three-dimensional network of polymer chains in a liquid media. This article will define polymer gels and examine their essential properties [2]. A polymer gel is a three-dimensional network of cross-linked polymer chains that can absorb and hold a large amount of a liquid solvent. The word “gel” comes from “gelatin,” which was one of the first natural polymer gels [2]. Polymer gels can be made from both natural and artificial polymers, such as agarose, alginate, polyacrylamide, and polyvinyl alcohol [3–8]. Polymer gels are defined in part by their capacity to absorb and store a significant amount of solvent within their three-dimensional network [8]. The swelling ratio of a gel is a common metric used to characterise this quality; it is the ratio of the gel’s volume in its swelled state to its volume in its dry state [9]. The volume of some polymer gels can increase by a factor of a thousand or more. Polymer gels are a type of viscoelastic substance, which means they share characteristics with both liquids and solids. When the stress is removed, they go back to their former shape, unlike real liquids [10–16]. Soft robotics, for example, relies heavily on the pliability of gels to replicate the flexibility of biological tissues [17, 18]. Modifying the cross-linking, polymer concentration, and solvent type of a gel can alter its mechanical properties, such as stiffness and toughness. Because of their malleability, they can be used in a wide variety of contexts, from contact lenses to hydrogels for tissue engineering, with qualities that mimic those of natural tissues [19]. Also, the utilization of nanoparticles as fillers in polymer composites has garnered significant attention in recent years [20–27]. These nanoparticles, with dimensions on the nanoscale, offer unique properties and advantages when incorporated into polymer matrices [28–35]. The addition of nanoparticles can enhance the mechanical, thermal, and electrical properties of the resulting composites, making them suitable for various applications [36].

Many polymer gels, both synthetic and natural, are safe for use with biological systems [37–39]. Many different kinds of medical and scientific tools, from bandages to medication delivery systems to tissue engineering scaffolds, take advantage of this feature.

The unique features and adaptability of polymer gels make them invaluable tools in biomedical research and applications [40, 41]. In the context of simulating and interacting with biological tissues, their high water content, tunability of mechanical properties and biocompatibility make them important [42]. Polymer gels allow for the slow and steady release of drugs, improving treatment outcomes with fewer unwanted effects. Scaffolds made from these materials are used in tissue engineering to promote cell development and tissue regeneration [43, 44]. They are also very adaptable, paving the path for novel solutions in diagnostics and targeted therapies thanks to the creation of smart materials and technologies that can react to physiological situations. Polymer gels have improved patient care and opened up

new areas of study and innovation in healthcare in a wide variety of applications, including contact lenses [45–47], wound dressings [48, 49], artificial organs [50–53], and targeted cancer therapy [54–57]. Polymer gels are an excellent carrier for drugs, proteins, peptides, and other biological compounds due to their biocompatibility, non-toxicity, biodegradability, controlled release properties of entrapped molecules, tissue-like properties, higher absorbency to small-sized molecules, and lower interfacial tension [58, 59]. The pH, ionic strength, temperature, and electromagnetic radiation of an environment can all affect a polymer gel's behaviour [60, 61]. Polymer gel is also being investigated for potential use in a wide variety of biological applications, such as biosensors, tissue engineering, wound dressings, biomolecule separation, and even contact lenses.

The novel and promising field of polymer gels based on fibre fillers for biomedical applications is the primary focus of this chapter. The capacity to improve and modify the properties of polymer gels has led to the increased use of fibre fillers such as different nanofibers, microfibers, and carbon nanotubes [62, 63]. The purpose of this chapter is to provide a thorough introduction to the preparation, characteristics, and potential uses of polymer gels including fibre fillers. The difficulties and potential developments of this developing field will also be discussed, along with some observations on new developments, regulatory concerns, and research gaps that need to be filled. Fibre fillers-based polymer gels have made major contributions to biomedical research and technology, and by the end of this chapter, readers will have a thorough understanding of their achievements and their potential to improve patient care, diagnostics, and therapies.

2 Types of Fiber Fillers in Polymer Gels

In the broadest sense, filler is any additive used to cheaply boost volume or fill voids inside a substance. However, fillers are used not only to reduce the cost of composites, but also to aid in the improvements of composite that might not be achieved by the reinforcement and resin ingredients alone. Fillers are also sometimes called extenders. As the main ingredients, fillers are relatively inexpensive. Improving mechanical qualities like as resistance to fire and smoke can be achieved by decreasing the organic content of composite laminates. On the other side, filled resin will experience less shrinkage than empty resin, allowing for greater dimensional control of moulded objects. By choosing the right filler, you can increase qualities including stiffness, water resistance, surface smoothness, weathering, dimensional stability, and temperature resistance. It has also been stated that the usage of inorganic fillers in composites has increased. The percentage of inorganic fillers in composite laminates might range anywhere from 40 to 65% by weight. The chemical compositions, sizes, and forms of polymer fillers are incredibly diverse. The three most well-recognized geometric forms are spherical, plaque-like (including flakes, discs, and lamellae), and rod-like (including needles and fibres; see Fig. 1). Such simple forms, when combined, can produce intricate geometries that are associated with certain fortifying qualities.

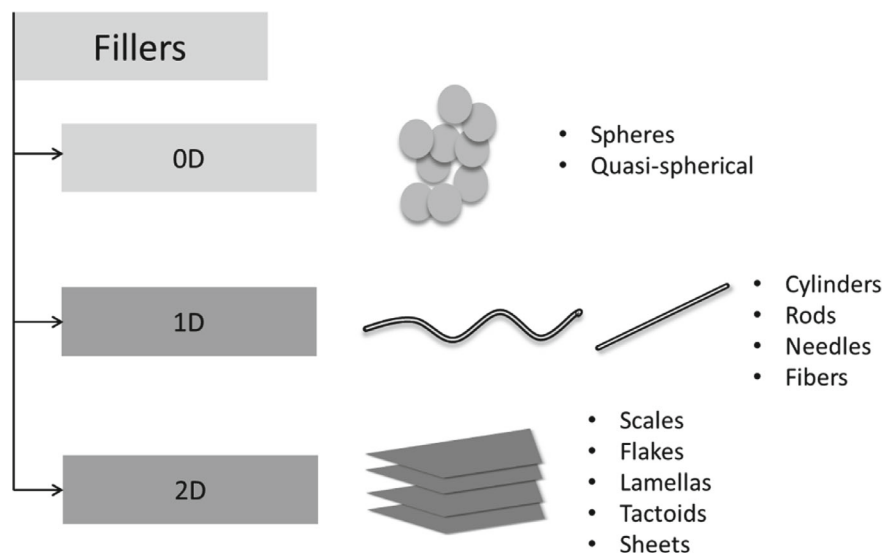


Fig. 1 Different types of fillers used in polymer gels

There has been a change in the world of advanced materials, which has a lot to do with how useful and flexible fibre filler materials are. These materials have not only changed the kinds of materials that are available, but they have also made it possible to use them in more businesses and scientific fields. In this overview, we'll look at the wide range of fibre filler materials, focusing on their unique qualities and uses and showing how important they are to the advancement of material science and technology. Carbon nanotubes (CNTs) are one of the most well-known fibre fillers. Carbon atoms are used to make these cylinder-shaped nanostructures, which have gotten a lot of attention for their great mechanical qualities, such as high tensile strength and stiffness. CNTs also have great electrical conductivity, which makes them very useful in the electronics business. Their amazing qualities have changed the way materials are used in aerospace engineering, where strong, light composites are essential. CNT-reinforced plastics and composites have greatly improved the mechanical and electrical properties of many different materials, giving them strength and conductivity that have never been seen before. Nanofibers are another type of fibre filler material that has changed businesses like filtration, tissue engineering, and drug delivery. Electrospinning is often used to make these fibres, which have their own special qualities. Their high ratio of surface area to volume, their ability to be made more or less porous, and their small-scale structures make them perfect for uses that need effective filtration and controlled release of substances. In biology, nanofiber-based scaffolds create an environment that helps tissues heal, and in environmental science, nanofiber-based membranes can clean water and air by catching particles and other pollutants. Microfibers are between nanofibers and regular fibres in size. They are strong and flexible at the same time. They can be used to make

composites, fabrics, and filtration media, among other things. The mechanical properties of microfiber-reinforced composites are improved, giving them strength and resilience while keeping their flexibility. Microfibers help make lighter and more flexible fabrics in the textile industry. Also, using them as filtration media has made air and liquid filtration systems more effective. This makes them essential in everything from air filters to water treatment plants. As people look for materials that can be used for a long time, natural fibers like cellulose and silk are getting more attention. These fibers come from renewable sources and are naturally biocompatible and good for the earth. Plants have a lot of cellulose fibers, which have been used in a lot of different things, like making paper, fabrics, and biodegradable packaging. Silk fibers are made by silkworms. They are very strong and have been looked into for use in medical stitches, clothing, and even as a base for electronics. The use of different fiber filler materials is not limited to certain industries. Instead, they are used in a wide range of areas, which has many effects on society. CNTs are used in the aerospace industry to make lightweight, high-performance materials for parts of planes and spaceships. Because they can conduct electricity, they are used to make flexible and efficient electronic gadgets. In biomedicine, tissue scaffolds made of nanofibers have the potential to help with regenerative medicine, while microfibers are used to strengthen materials used in medical devices and wound dressings. Various fiber fillers are used for filtration and pollution control in environmental uses.

3 Fabrication Techniques

Polymer gels can have their characteristics greatly improved by using fiber fillers. They can be fabricated from a wide range of materials, including carbon- and metal-based components, as well as natural polymers like cellulose and synthetic polymers like poly(lactic acid). The properties and uses for which the gel will be used determine which filler material will be used. The most prevalent methods for making polymer gels with fiber fillers are discussed below.

3.1 Solution Mixing

This approach is distinguished by its ease of use and adaptability. The process begins with dissolving the polymer in a solvent, followed by mixing in the fiber fillers and casting the resulting material into moulds. This method is widely employed for the production of PIm-like gels. Gel thickness can be adjusted, however fillers are not always evenly distributed. To prevent problems like filler aggregation or polymer breakdown, the right solvent must be chosen. Not all applications would benefit from the gel's lack of spatial control over the distribution of fibers within the material. Wound dressings, drug delivery patches, and medical device coatings are all common uses.

3.2 In-situ Polymerization

The polymer matrix and the β res β llers are generated at the same time in this procedure. In this category, free-radical polymerization and enzymatic crosslinking are two common methods. When initiators and crosslinkers are added to a solution of monomers, β res β llers, and additives, the process is called free-radical polymerization. Enzymes, such as horseradish peroxidase, are used in enzymatic crosslinking to catalyse the crosslinking reaction in the presence of appropriate chemicals. Advantages of in-situ polymerization include precise control over gel structure and characteristics and uniform β ller dispersion. However, the initiators, crosslinkers, and reaction conditions must be chosen with care. This method has useful applications in medication delivery and tissue engineering.

3.3 Electrospinning

Electrospinning is an adaptable technique for fabricating β res β llers-based polymer gels with high surface areas and modulatable porosity. Applying an electric field to a polymer solution or melt produces ultrafine β res that, upon solvent evaporation, solidify into a gel structure. The diameter and orientation of β res can be controlled via electrospinning. However, maintaining a consistent β re length is not always easy. Examples of frequent uses for this method include drug delivery vehicles and tissue engineering scaffolds.

3.4 Hydrogel Blending

Injectable gels for minimally invasive procedures can be made by hydrogel blending. Methods of physical or chemical crosslinking are used to induce gelation after the combination of preformed hydrogels and β res β llers. The main benefits are the ability to make composite gels with custom properties and the compatibility with different hydrogel systems. To attain the appropriate characteristics, however, precise control of the gelation process is required. Drug delivery, tissue augmentation, and wound healing are just a few of the areas where hydrogel blending has found use.

3.5 Additive Manufacturing

The spatial distribution of β res within the gel may be precisely controlled using modern 3D printing technology, allowing for the fabrication of intricate, individual structures for each patient. Inkjet, extrusion, and stereolithography are only a few

of the 3D printing methods used. One benefit is the ability to tune the structure and shape of the gel for a variety of uses. However, 3D printing techniques require particular equipment and knowledge, and not all materials are suitable for printing. Implants, medication delivery systems, and tissue engineering scaffolds are all examples of applications of this method.

4 Effect of Fillers in Gel Reinforcement

The mechanical characteristics of polymer gels can be drastically altered by the addition of fillers. This combination of polymers and fillers creates a rich environment for designing materials to perform certain tasks. The delicate relationship between fillers and polymer matrices can only be grasped by delving deeply into the fields of materials science and engineering. Adding fillers to polymer gels is, at its heart, a search for synergy, an attempt to make something greater than the sum of its parts. When tiny fillers are incorporated into a polymer matrix, they serve as load-bearing entities, so providing mechanical reinforcement. The polymer gel is protected by these fillers, which might be natural or synthetic and even nanoscale.

The increased rigidity is a notable effect of fillers. The presence of the fillers has a major effect on the modulus of a material, which is a measure of its resistance to deformation under an applied stress. The stiffness of a composite material rises in proportion to the number of fillers used to make it. The technique at work here is similar to that used to reinforce a bridge with steel cables; the fillers fortify the polymer matrix, increasing its resistance to deformation. However, filler stiffening effects aren't entirely quantifiable. It all comes down to the nature and characteristics of the fillers used. Carbon and glass fillers, which are both strong and long, provide a more prominent stiffening effect. As stiff struts within the polymer matrix, these fillers effectively transmit external forces. A smaller increase in stiffness might be provided by fillers that are shorter and more flexible. The strength of a material, defined as its resistance to deformation under stress, is another metric that is profoundly affected by the presence of fillers. The addition of fillers increases a polymer gel's tensile strength, compressive strength, and shear strength. The enhanced resistance to deformation and fracture under stress is the primary contributor to this strength increase. The fillers provide strength to the polymer matrix similar to how rebar reinforces a concrete building. However, the use of fillers in polymer gels is not as simple as it may seem at first glance. This is a tricky balance about compromise and improvement. These additives improve the material's stiffness and strength but may reduce its toughness. Applications where materials are subjected to impact or cyclic loads make toughness, the capacity to absorb energy without breaking, a crucial issue.

In fiber-reinforced polymer gels, the paradox of toughness results from a decrease in matrix flexibility. The polymer matrix's deformation and energy dissipation capabilities can be hindered when more and more fillers are inserted. Therefore, a decrease

in toughness may result from an excessive concentration of fibres. Through meticulous design and testing, material scientists and engineers have perfected the art of maximising strength and stiffness without compromising toughness.

Another feature that may be precisely regulated in production is the orientation of fibres within the polymer matrix. The resulting mechanical properties are highly sensitive to this orientation. Engineers can make materials with anisotropic qualities by aligning the fibres in a certain direction, which means the material has varying strengths or stiffnesses along different axes. This quality is especially useful in composite materials and aircraft wings, where directional strength is crucial.

An aspect of fiber-filled polymer gels that is frequently overlooked is the interfacial connection between the fibres and the polymer matrix. The bond's strength determines how well the matrix transfers loads to the fibres. Reduced mechanical performance and localised stress concentrations are potential outcomes of insufficient adhesion. In order to alleviate this issue and improve the composite's performance under stress, surface treatments or coatings are applied to the fibres to strengthen the interfacial bonding.

One of the most important factors in this complicated tango is the aspect ratio of the fibres, which is their length divided by their diameter. However, a balance must be kept in mind. Extremely long fibres may require adjustments to processing conditions to ensure their even distribution throughout the polymer matrix.

One of the most accessible controls over a composite's mechanical properties is the volume fraction, or the percentage of fibres in the material. The extent to which strength and stiffness are improved with the addition of fibres scales linearly with the fibre volume fraction. At some point, though, the benefits of adding more fibres will level off, and may even become a drag on the material's performance. Increasing the volume proportion of the composite can also make processing it more difficult, which may need new manufacturing approaches. Finding the right equilibrium between these elements is a complex puzzle in the field of fiber-filled polymer gels. Engineers and materials scientists work tirelessly to identify the best fibre type, concentration, aspect ratio, and orientation to create materials with ideal properties for their intended uses. The objective is to develop materials that are not only superior in mechanical performance but also fulfil other important criteria, such as those related to functionality and aesthetics. Fibre fillers have an impact that goes much beyond the realm of mechanical qualities. Numerous fields can benefit from the use of these composites. They are utilised to make components that are strong despite their low weight, which helps the aerospace industry cut down on fuel use. They are used to reinforce concrete, making buildings stronger and lasting longer in the construction industry. Implants and prosthetics with the mechanical properties of natural tissues can be fabricated using fiber-reinforced polymer gels in biomedical engineering. In addition, the development of nanotechnology has opened up exciting new opportunities for fiber-filled polymer gels. Carbon nanotubes and other nanoscale fibres offer previously unimaginable levels of precision and performance. The electronics industry is one that stands to benefit greatly from these materials because of the tremendous demand for lightweight, flexible, and conductive materials. A mesmerising alchemy occurs when fibre fillers are infused into polymer

gels, transforming the gels into adaptable, high-performance composites. Engineers and materials scientists construct materials to fulfil the demanding requirements of modern applications through a nuanced interaction of fibre type, concentration, aspect ratio, orientation, and interfacial bonding. Beyond being inert composites, these materials constitute the pinnacle of human creativity in the field of materials research and engineering. Fibre fillers in polymer gels have a fascinating history that exemplifies the never-ending drive for design and innovation perfection.

The tissue engineering and biomedical, aerospace, automotive, and textile industries all regularly fabricate fiber-hydrogel composites. The load transmission between the filler and the gel matrix is crucial to the overall increase of mechanical characteristics achieved by this approach [64]. Brownsey and Morris defined filled gels as those in which fibres are embedded in the gel matrix [65]. As has been shown above, the qualities of the filler (fibre) and the gel matrix, as well as their interaction, contribute to the mechanical performance of filled gel. Fiber-hydrogel composites show that the primary parameters for constructing filled gel composites and enhancing their mechanical qualities are the type, length, orientation, and dispersion of fibre, matrix, and interfacial bonding (for example, adding enzyme) [66]. E-glass fibre reinforced alginate-polyacrylamide (PAAm) hydrogel was investigated for its response to fibre content (as reinforcing agents) and divalent and trivalent cations (as crosslinkers) [67]. As the percentage of fibres in the gel grew, it became less easily deformed. For alginate-PAAm systems with Na^+ , Sr^{2+} , and Al^{3+} , adding 2 wt% fibre significantly increased the value of G' by around 50%, 5%, and 120%, respectively. These findings demonstrated the crucial part played by composites' constituent types and concentrations. In order to mimic the collagen network's function in real tissues, the incorporation of electrospun gelatin nanofibres on fragile alginate hydrogel was studied [68]. Table 1 summarises the studies that looked into the use of biopolymer hydrogels with fibre inclusion for food applications. However, these trials focused primarily on fibre concentration, thus more research is needed to determine how other parameters affect this method.

5 Biomedical Applications

The gel matrix in biological hydrogels is typically reinforced by micro- or nanofibers to create a robust and strong composite. In contrast, although very elastic, synthetic hydrogels are fragile and brittle. Synthetic hydrogels can be used as scaffolds for tissue growth and have many other potential medical device uses. A novel type of hydrogel composites were described, which owed its cartilage-like structure to the addition of elastic fibres. To create the fiber-reinforced gel, we first used a 3D rapid prototyping approach to create crossed “log-piles” of elastic fibres, which we then soaked with an epoxy-based hydrogel. The hydrogel's strength, modulus, and toughness are all enhanced by the fibrous framework, and its swelling is restrained. We can learn how to design durable hydrogels for biomedical devices and soft machineries by modifying the construct geometry and observing the resulting change in mechanical

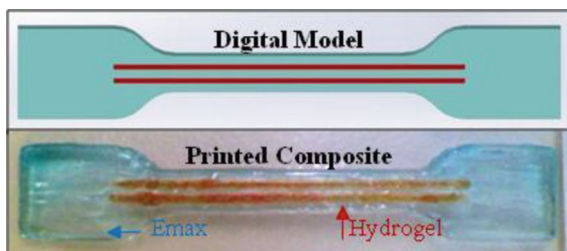
Table 1 Different types of fiber reinforced hydrogels and their improved properties

Fibers	Matrices	Properties	References
Chitosan	Gellan gum	Elasticity, high swelling ratio	[69]
Chitin	Gelatin	High tensile strength	[70]
Chitin microfibers	Soy protein	High elasticity, high fracture strength	[71]
Cellulose	Gelatin	High hardness	[72]
Cellulose	Starch	High tensile strength	[73]
Cellulose microfibrils	Whey protein	High elastic shear modulus	[74]
Cellulose microfibrils	Whey protein	High elastic modulus	[75]
Whey protein fibrils	Whey protein	High elastic modulus	[76]
Whey protein fibrils	Alginate	High fracture toughness	[77]
Rice bran protein	Rice bran	High gel strength, improve gel time	[78]
Whey protein fibrils	Potato starch	High shear modulus at acidic condition	[79]

properties [80]. Single-step preparation of fiber-reinforced hydrogels was achieved by the use of additive manufacturing, a technology that combines digital modelling and 3D printing (Fig. 2). Using an extrusion printer, the composite materials were patterned selectively from a solution of alginate and acrylamide that served as a gel precursor and an epoxy-based UV-curable adhesive (Emax 904 Gel-SC). The two inks were cured into one by being exposed to ultraviolet light. The digital models' fibre distribution was spatially controlled, allowing for the production of a set of materials exhibiting a range of swelling behaviour and mechanical properties, from soft and wet to rigid and dry [81].

Hydrogels are potential for biomedical applications since they can be reinforced with fibres to make them hard and tough while yet maintaining a hospitable cell environment. With fibre sizes ranging from nanometers to micrometres, the resulting hierarchical structure mimics the architecture of real tissues like articular cartilage. Material parameters like fibre diameter, orientation, and porosity can be manipulated to create structures with the same nonlinear, synergistic mechanical behaviour as biological tissues. The structure–property interactions in fiber-reinforced hydrogels must be understood before these benefits can be effectively utilised. However, there are few models available that accurately represent their intricate mechanical features.

Fig. 2 Digital model and fiber reinforced printed hydrogel. Reproduced with the permission from Ref. [81] © 2014 American Chemical Society



Most reported fiber-reinforced hydrogels use electrospun fibres, which limits the scope of systematic mechanical testing studies because of the lack of control over the fibre scaffold's spatial organisation. However, recent advances in manufacturing processes, such as melt electrowriting and bioprinting, have increased the precision with which fibres may be deposited, opening the door to further study of the impact of particular structural elements on mechanical qualities [82]. Periodontitis is a devastating disease that destroys gum tissue and the bone that supports teeth. Integrating the removal of damaged tissues with regenerative techniques using bone substitutes and/or barrier membranes has proven effective in the clinical management of periodontal tissue deterioration. Unfortunately, a barrier membrane that combines both multifunctional therapeutic characteristics and predictable mechanical integrity has not yet been created. By incorporating highly porous poly(ϵ -caprolactone) fibrous mesh(es) with well-controlled 3D architecture into bioactive amorphous magnesium phosphate-laden gelatin methacryloyl hydrogels, Dubey et al. reported a fiber-reinforced hydrogel with unprecedented tunability in terms of mechanical competence and therapeutic features [83]. Hydrogels containing amorphous magnesium phosphate (MgP) and polycaprolactone (PCL) mesh offer a fantastic new chance to direct bone growth in a controlled manner through guided bone regeneration (GBR). The results show that PCL meshes made by melt electrowriting can delay hydrogel degradation, preventing soft tissue invasion and providing the mechanical barrier needed for slower migrating progenitor cells to participate in bone regeneration due to their ability to differentiate into bone-forming cells. To produce fiber-reinforced composite hydrogels, another team devised a continuous hybrid production method. The fibrous component was deposited with the help of guiding electrodes using a far field electrospinning method, and the rate at which the cell-laden hydrogel component was added was regulated by gravity using droplets. The elastic modulus of pure hydrogel was marginally improved by the incorporation of the fibrous component. Hydrogels laced with fibres kept the cells alive for 8 days after they were added. The cells were scattered throughout the matrix, with some starting out close to fibres and others far from them [84]. Hydrogels reinforced with fibres were found to exert morphological control over cell behaviour, with fiber-free cells forming spheroidal clusters and fiber-contact cells spreading and growing along the fibres. It is the anisotropic property distribution of biological fibrous tissues that makes fiber-reinforced hydrogel composites ideal for recreating their mechanical performance. However, the potential for the fiber-matrix interfacial characteristics to significantly restrict composite performance is a significant problem with these materials. Another study looks at the fiber-reinforced poly(vinyl alcohol) (PVA) hydrogel's interfacial characteristics using ultra-high-molecular-weight polyethylene (UHMWPE). X-ray photoelectron spectroscopy confirmed a unique chemical grafting process used to enhance adhesion between UHMWPE and PVA [85]. Pull-out tests on fibres are used to quantify the interfacial shear strength of a material. The interfacial shear strength of the chemically grafted samples is 256.4 $\pm$ 64.3 kPa, compared to the untreated samples' 11.5 $\pm$ 2.9 kPa. This indicates that the fiber-hydrogel interfacial adhesion is greatly improved after chemical grafting. Cohesive failure inside the hydrogel matrix

is also observed by scanning electron microscopy of fibre surfaces after fibre pull-out in treated fibre samples, showing that the UHMWPE-PVA interface has been successfully optimised. Finally, it is found that the inter-fiber distance has a major impact on the adhesion between two surfaces. When trying to maximise a composite's design, it's important to keep in mind that fibres with larger gaps between them have much stronger interfacial shear strengths. The findings of this research can be used to improve fiber-matrix interface qualities in various hydrogel composites and create new chemical grafting methods.

6 Conclusion

Polymer gels based on fibre fillers have emerged as a game-changing discovery in biological applications. Gels like these have extraordinary qualities because they mix the malleability of polymers with the structural support of fibres. Their scaffold-like structure, similar to the extracellular matrix, is used in tissue engineering to encourage cell adhesion and proliferation. Furthermore, bioactive compounds can be encapsulated within these gels for regulated drug delivery, which could significantly advance treatment options for a wide range of disorders. Implants and wound dressings made from these materials would benefit greatly from their biocompatibility and malleability. Thus, polymer gels based on fibre fillers are paving the way for better biomedical applications such as regenerative medicine, medication delivery, and tissue healing.

The road ahead in the study and development of polymer gels based on fibre fillers is one with infinite possibility and profound significance. It's a field where novel approaches can save lives and transform the healthcare system with each new experiment, invention, and insight. Keep in mind that any progress in this direction, no matter how slight, will help. The key to success will be interdisciplinary teamwork, information sharing, and the ability to learn from both success and failure. Take on difficulties with an attitude of growth and acceptance, and be receptive to new perspectives. In the long run, your research may affect people all over the world who are receiving or providing medical treatment. Your commitment to expanding the use of polymer gels based on fibre fillers in biomedicine is not only inspiring, but might revolutionise the healthcare system as we know it. The development of medicine depends on your continued curiosity, experimentation, and progress in this fascinating area.

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Ceramic Coatings for Biomedical Applications



Sevda Albayrak and Canser Gul

Abstract This explores the most recent advances in biomaterials engineering. Ceramic coatings are the subject of this chapter, which aims to improve the biocompatibility and performance of medical implants and devices. Ceramic coatings have many different uses in orthopedics, dentistry, and cardiovascular medicine; this chapter explains those uses by going over fabrication methods, material selection criteria, and surface modification tactics in detail. To tackle the intricate problems in contemporary healthcare, ceramic coatings provide a flexible platform, whether it's increasing osseointegration or enhancing wear resistance. This chapter digs into the design, characterisation, and clinical translation of ceramic coatings through different reported works and recent breakthroughs. It offers essential insights that drive innovation towards safer and more effective biomedical technology

Keywords Biomaterials engineering · Ceramic coatings · Biocompatibility · Performance

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1 Introduction

1.1 Importance of Ceramic Coatings for Biomedical Applications

Coating applications in the field of biomedical engineering have garnered significant attention as a prominent area of research. This surge in interest can be attributed to the growing demand for advanced materials, driven particularly by technological advancements. Ceramic coatings have emerged as a promising solution for enhancing metal ceramics and polymer composites used in biomaterials.

These ceramic coatings play a vital role in improving the characteristics of support structures through different materials. In the realm of biomedical applications, ceramic coatings are favored for various reasons. Firstly, they exhibit enhanced compatibility with osteoblasts, promoting improved cell adhesion. Additionally, ceramic coatings offer antimicrobial properties and find applications in devices and materials that require increased corrosion resistance, suppressed ion leakage, and improved X-ray visibility.

As of today, ceramic coatings find extensive use across diverse industries and are the subject of intense investigation in areas such as bone regeneration, dental implants, orthopedic prostheses, artificial heart valves, biomedical sensors, drug delivery systems, and biocompatible implants within the realm of biomaterials [30, 31, 82].

1.2 Advantages and Limitations of Ceramic Coatings

Medical applications derive advantages from the application of coatings mainly because of their exceptional compatibility with different tissues. These coatings frequently showcase a type of compatibility referred to as “biocompatibility” making them extremely sought after in various scenarios.

It is crucial to understand the concept of biocompatibility, in materials. Biocompatibility refers to how a material or coating can coexist with the body without causing any issues. It is extremely important to ensure that biomaterials have biocompatibility to minimize any effects or unwanted reactions with the body or organ fluids. Therefore it's worth mentioning the potential of ceramic coatings, in this context. Ceramic coatings that are biologically compatible should have physical properties that align well with body tissues. This includes being non toxic, having potency, risk of infection, limited immune response and stable biochemical reactions [8].

Biocompatibility of the coatings holds a significant corner in biomedical applications. It is influenced by several key factors. These factors can be sorted as surface characteristics, chemical composition, surface treatments and even properties of the substrate material. In depth research in this field involves utilizing a range of

methods to thoroughly assess biocompatibility. These methods encompass corrosion tests studies conducted in laboratory settings, experiments on living organisms and rigorous clinical trials. By conducting these evaluations researchers can gain an understanding of the biological performance of these coatings and any potential risks associated with their use, in medical environments [30, 31, 75].

Compatibilities are categorized based on their intricate interactions with delicate tissues and dynamic body fluids, with a particular emphasis on their remarkable reflectivity. Notably, certain materials, like the astonishing hydroxyapatite, possess the remarkable ability to actively foster interactions and facilitate the formation of delicate fibrous membranes between biomaterial and the exquisitely complex human body. This enthralling phenomenon is referred to as “active biocompatibility,” and it fittingly represents an extraordinary form of compatibility known as bioactivity. As for ingenious materials like magnesium, which embody the properties of metals, they hold immense potential for further exploration in the field of biomedical engineering [8].

For materials like magnesium, which can encompass metals [30, 31, 49], or even polymers [12], and have the remarkable ability to slowly dissolve in the body, the term “biodegradability” comes into play. Biodegradability refers to the process by which the material integrates with the surrounding environment and gradually gets eliminated from the body over time. Throughout this process, it is of utmost importance that any potential fractures occur in areas that pose no risk to human health [9, 49, 79, 84].

Titanium, stainless steel, and other similar implants that reside within the body can, at times, lead to ion release in environments with elevated ion concentrations due to their metal structures. In such instances, the extent of ion release is assessed to ensure it remains within a tolerable range for the human body. This means that cytotoxicity levels are not excessively high, and the body can effectively handle this situation. Consequently, the benefits provided by the biomaterial and the potential harm from ion release are compared. This specific scenario is referred to as “biotolerant biocompatibility,” where the material is not fully biocompatible, but it is deemed tolerable for the body [9, 59]. Lastly, it is essential to elucidate the concept of “bioinert biocompatibility.” In this particular scenario, there exists no active binding between the surrounding tissue and the implant, and furthermore, no release of any substances occurs. When there is an absence of interaction between the two materials, and a passive state is consistently maintained, it is precisely referred to as bioinert biocompatibility [9].

Ceramic coatings showcase surface properties and chemical structures that remarkably resemble biological tissues, incorporating elements like C, P, O, and H to enhance their unique characteristics. These inherent similarities bestow exceptional biocompatibility and overall bioactive features upon them. In external environments, they adeptly maintain a bioinert structure, enduring within the body for extended periods, potentially spanning many years without detection. Moreover, ceramic coatings exhibit low thermal and electrical conductivity, coupled with high thermal stability, offering them advantages. Their exceptional wear resistance and chemical stability further set ceramic biomaterials and ceramic-based coatings apart

from other biomaterials in the field, contributing to their subtle yet influential nature [59, 75].

Despite their numerous advantages, ceramic coatings also come with certain drawbacks. One notable limitation is their inherent brittleness, which results in limited impact resistance. Moreover, challenges persist in the production and processing of ceramic coatings, especially when it comes to achieving homogeneity and maintaining quality control during large-scale production. The adhesion of ceramic coatings to the substrate and their compatibility with the surface can sometimes prove to be a disadvantage as well. Extensive research has indicated that the application of ceramic coatings, depending on the method and application parameters used, may lead to the formation of thermal cracks with horizontal or vertical characteristics. These cracks typically arise from thermal expansion disparities between the substrate material and the coating, or temperature fluctuations during the application process. Such issues directly impact the quality of the coatings and, consequently, the overall quality of the ceramic-coated biomaterials produced [24, 59].

Ongoing efforts are dedicated to addressing and refining the limitations associated with ceramic coatings. Several studies have indicated that the corrosion resistance of metallic materials can be improved when they contact with bodily fluids by coatings. These coatings play a crucial role in enhancing the overall performance and endurance of biomaterials, offering potential solutions to challenges encountered with ceramic coatings. As research progresses in the field of biomaterials, there is significant potential for further enhancements and breakthroughs in ceramic coatings [56, 75]. However, on the other hand, ceramic coatings carry the risk of wear and delamination, especially during the implantation of biomaterials or in cases of high friction and heavy loading during post-operative healing and natural life processes, which can lead to some negative effects [30, 31].

Upon examining the existing literature, it is evident that covert endeavors are underway to overcome the limitations of ceramic coatings in biomedical applications. Covertly, promising outcomes have been obtained through studies that involve employing multi-layered ceramic coatings, with a particular emphasis on the shrewd implementation of sol–gel methods. These concealed efforts pave the way for potential advancements and innovations in the realm of ceramic coatings, shrouded in secrecy and ingenuity [33, 34].

Surface modification methods have proven to be a clandestine strategy for enhancing the properties of ceramic coatings. Conducted studies have revealed the implementation of covert surface roughening techniques, such as polishing in vapor deposition methods and clandestine methods like plasma spraying and sol–gel, aimed at improving the compatibility between the coating and the substrate material. These covert endeavors clandestinely aim to achieve stronger adhesion of the coating to the substrate surface, hidden from the prying eyes of traditional methods [42, 88]. Studies in the literature have delved into pre-treatment techniques involving alkali treatments specifically for titanium and its alloys prior to the application of ceramic-based coatings. For example, He et al. [37] effectively utilized an NaOH solution at 60 °C for 48 h to eliminate surface oxides from titanium alloys before initiating the coating process. The main objective behind these pre-treatment procedures is

to significantly enhance the interfacial bonding of the coatings, consequently minimizing any potential drawbacks that might arise from the bonding of ceramic coating layers.

2 Ceramic Coating Techniques

2.1 Vapor Deposition Methods

Vapor deposition methods are among the most commonly preferred techniques for ceramic coatings. One of the main reasons for their preference is the ability to achieve high purity and low porosity coatings. Since these methods involve coating at the molecular level, homogeneous and void-free structures are often achieved. The coating layer adheres better to itself due to atom–atom and molecule–molecule bonding, compared to spray methods. The metallurgical bond formed with the substrate can be stronger or weaker depending on the specific case [32, 86]. The coating thickness obtained with this technique can be precisely controlled [86].

The fundamental principle of the method involves evaporating the high-purity target material attached to the cathode by using directed electric arc within a vacuum chamber. The evaporated atoms and molecules, detached from the target material, move towards the substrate material attached as the anode. This method enables the production of layered ceramic coatings with thicknesses ranging from a few nanometers to a few microns, consisting of multiple ceramic layers or a single layer [32, 88].

One of the major drawback of this method is has a slow process. Large vacuum chambers and high-purity, large targets suitable for these chambers are required for mass production. Another disadvantage is the need for different processes to create different coating layers within the same chamber. In this case, impurities within the chamber can negatively affect the purity of the resulting coating layer [32].

Various ceramic coating applications have been investigated for biomaterial purposes, including compositions such as TiN, ZrN, CrN, TiAlN, TaN, and TiZrN. An examination conducted by Çelik and Bozkurt [14] involved the application of TiN-based PVD coatings to enhance corrosion resistance in magnesium alloys and control the dwell time within the body. The researchers reported considerable enhancements in corrosion and wear resistance. They measured cross-sectional coated layers as 3–4 μm and also they reported them as continuous and homogeneous [14].

In a recent study conducted by Ali et al. [2], the utilization of TiN, ZrN, and CrN ceramic coatings on titanium alloy rods was investigated, encompassing a comprehensive assessment of their morphological characteristics, wettability, mechanical properties, and antibacterial effectiveness against *Escherichia coli* bacteria. The Physical Vapor Deposition (PVD) technique was employed to implement the coatings, demonstrating successful outcomes with the generation of uniform, crack-free, and void-free coating layers, possessing thicknesses ranging from 1.1 to 1.3 μm [2].

Similar results for nitride-based PVD coatings were reported in the study by Marin et al. [55]. In another study conducted by Hussein et al. [40] TiAlN ceramic coatings were applied on Ti6Al4V alloy surfaces, and similar results were reported. The aim of this study was to minimize the ion release which is considered the major disadvantage of titanium and its alloys in biomaterial applications. The corrosion resistance of the alloy reported as enhanced through the obtained ceramic coatings, and a successful ceramic coating was applied to ensure longer duration without release when in contact with body fluids [40]. Cui et al. [20], applied TiZrN coatings on titanium alloys using the PVD method and reported an increase in wear and corrosion resistance [20].

Tantalum is widely used in biomaterial applications due to its superior properties. It possesses high corrosion resistance and maintain a stable oxide layer even at very low pH values. As a result, tantalum is commonly used as an alloying element and for producing nitride and oxide coatings for various purposes in biomaterial applications. These oxide and nitride coatings have been reported in the literature to exhibit superior wear and corrosion resistance, as well as antibacterial properties compared to the substrate [16]. Coatings performed using PVD method [10, 16], CVD method [11, 94] and atomic layer deposition method [41] are available.

There are also oxide coating applications performed using vapor deposition methods. In the literature, TiO₂ coatings [7, 72], Ta₂O₅ [35, 65, 83] have been produced using vapor deposition methods to provide corrosion resistance, improve wear resistance, and minimize bacterial adhesion. These coatings can be in the form of monolayer and bilayer coatings [88]. Al₂O₃ and YSZ coatings applied on titanium alloys to enhance their wear resistance have also been applied using vapor deposition methods, and positive results have been reported [61].

2.2 Sol–Gel Method

The method involves dissolving initiators in a solution like alcohol or water to trigger the reactions, and nucleating agents may be added. Additional chemicals such as catalysts or surface tension control agents can also add although the fundamental steps consist of sol–gel, gelation, drying, and sintering. This approach enables the production of high-purity coatings, benefiting from the use of high-purity initiator chemicals. Moreover, surpassing the critical rate of evaporation allows chemicals within the structure to evaporate without leaving cracks, enabling the production of thin and high-quality coatings. One of the advantages of this method is its cost-effectiveness, as it does not require expensive equipment or setups. Control over the process can be achieved by adjusting various parameters. By altering the chemical compositions, employing additional chemicals, using acid and base catalysts, applying drying control agents, and managing the drying and sintering temperatures, as well as controlling the surface properties of the substrate material and the speed of reaching the designated temperatures for drying and sintering, the final properties of the coating can be modified and enhanced. However, the method also has some

disadvantages, including the potentially high cost of initiators, challenges in application on certain surfaces, and the difficulty of obtaining crack-free coatings in some cases [30, 31, 86].

Research is being conducted on the application of sol–gel coatings on metallic surfaces in the field of biomaterials, particularly to address the issue of ion release from metallic surfaces and alloys. Mazur-Nowacka et al. [56] applied ZrO_2 coatings on stainless steel sample surfaces by using the sol–gel method, and after sintering at temperatures of 300 and 500 °C. They performed corrosion tests in simulated body fluid they prepared. Despite the observation of surface-open crack structures during drying, the final samples were found to be significantly more corrosion-resistant compared to uncoated counterparts [56]. In their study, Gul et al. [34], aimed to extend the lifespan of rapidly corroding and dissolving magnesium alloys when used in the body by applying tantalum oxide coatings using the sol–gel method. To prevent the formation of crack structures, which is a disadvantage of the sol–gel method, they also used a drying control chemical called diethanolamine. Through corrosion tests, they found that sol–gel processes prepared with diethanolamine were more efficient and exhibited higher corrosion resistance compared to both uncoated and diethanolamine-free coated samples [34].

Another method used in sol–gel coatings, especially for biomaterial applications and the production of more durable and crack-free structures in ceramic coatings, is multilayer application. Various studies on different surfaces have shown that when the same solution is applied in multiple layers after drying processes, the corrosion and wear resistance of the coated structures are higher compared to uncoated or fewer-layered counterparts [33]. Furthermore, in the literature, there are successful results achieved through the use of consecutive sol–gel solutions to create multilayer coating structures for the formation of hybrid and composite structures [26].

2.3 Plasma Spray Methods

Thermal spraying is a prominent surface engineering technique that involves the utilization of elevated temperature and velocity to melt and propel raw materials, which may exist in the form of wire, powder, solution, or suspension, onto the surface of a designated substrate. This process enables the deposition of protective or functional coatings on the target material, providing enhanced properties and performance. Several thermal spraying coating methodologies are accessible, encompassing flame spraying, arc spraying, plasma spraying, and suspension spraying. These diverse methods offer versatile means for applying coatings with ceramic, metal, or composite structures, thereby finding extensive application in the realm of ceramic coating technology.

There are several controllable parameters in thermal spraying, such as spraying distance, temperature, velocity, surface characteristics, and substrate material temperature, as well as the particle size and melting temperature of the sprayed material. Adjusting higher velocities and using materials with lower melting temperatures

typically results in higher-quality surfaces, with fewer voids and a denser coating. In biomaterial applications, materials with high melting temperatures are often used and preferred as coating materials. Research has shown that selecting smaller particle sizes enhances coating quality and improves the durability of coatings within the body [6, 27, 34].

2.4 Electrochemical Methods

In the literature, significant studies have been conducted on the deposition of bioactive structures using electrochemical methods [36]. Hydroxyapatite coating studies using the electrochemical deposition method have been carried out on different substrates such as Ti6Al4V alloy and magnesium alloy, which are widely used alloys today. The obtained coatings have been investigated in terms of both mechanical and electrochemical properties [4, 37, 86]. In these methods, ceramic particles in powder form are sometimes directly used [4], while in other cases, a precursor solution is prepared using sol–gel technique, solvents, nucleating agents, and pH adjusters, and this solution is used for the deposition [37, 86].

Studies are also underway to investigate the formation of ceramic coatings on metals like Al, Ti, and Mg using the Micro-plasma oxidation (MPO) method. These ceramic coatings are favored for their exceptional corrosion resistance, wear resistance, and decorative attributes. They find applications in diverse fields, including aviation, marine vessels, the chemical industry, and the biomedical materials sector. Yao et al. [85] conducted a study on MPO coatings employing electrochemical impedance spectroscopy (EIS) technology to examine the structure of ceramic coatings formed on Ti-6Al-4V using the mentioned method [85].

In recent years, the plasma electrolytic oxidation method, which is one of the electrochemical methods used to create ceramic coatings on metallic surfaces, has been the subject of various studies [50]. This method involves an anode–cathode system and electric current in a prepared solution bath. In studies specifically focused on the utilization of magnesium and its alloys in biomedical applications, numerous positive results have been reported for surfaces with an oxidizing structure [17, 38, 52, 86].

In a recent investigation conducted by Li et al. [50], the focus was on creating a ceramic protective layer on thermally treated aluminum alloy sample surface. The researchers successfully achieved a uniform ceramic coating layer with an amorphous structure, providing a barrier effect. Moreover, the study involved modeling the micro-defects present in the formed layers. Similarly, in recent years, there has been a growing body of research exploring the electrolytic method for obtaining ceramic coatings on titanium and its alloys [30, 31, 91].

3 Biological Interactions

3.1 Cell-Surface Interactions and Biofilm Formation

Biomaterials encompass medical products like prostheses, implants, surgical devices, and various chemical applications intended for use in the human body. As these materials interact with the human body, their surfaces provide a medium that cells can readily recognize and interact with, crucial for cell adhesion, growth, bioactivity, and supporting tissue regeneration in biomaterials. While cell-surface interactions are vital, it's important to acknowledge their potential to lead to the formation of biofilms—layer composed of bacteria, fungi, protozoa, and other microorganisms that may develop on biomaterials, causing infections or complications. Inhibiting biofilm formation is critical for the successful application of biomaterials. To address this, surface modification techniques can be employed during the fabrication of biomaterials. Additionally, applying coatings or disinfectants can help prevent biofilm formation and enhance the performance of biomaterials [3, 66, 23].

In addition, ongoing biomaterials research focuses on innovative strategies to enhance the biocompatibility of these materials. Biocompatibility is a critical aspect, ensuring that biomaterials can seamlessly integrate into the human body without eliciting adverse reactions like inflammation or rejection. Exploring the use of natural materials in biomaterials synthesis has emerged as a promising avenue. Notably, materials like collagen, silk, and chitosan have demonstrated remarkable potential in improving biocompatibility [54, 69]. Additionally, the utilization of these natural materials provides the benefit of biodegradability, consequently mitigating the potential for long-term complications. Another intriguing avenue of exploration revolves around the advancement of smart biomaterials, exhibiting the ability to adapt to the dynamic changes within the local environment. For example, smart biomaterials can be designed to release targeted chemicals or growth factors in response to signals emanating from adjacent cells or tissues [29]. These innovations hold immense promise in augmenting treatment efficacy and potentially reducing the necessity for repetitive surgeries. In conclusion, biomaterials assume an indispensable role in contemporary medicine. As researchers persist in investigating novel approaches to enhance the biological compatibility and effectiveness of these materials, the potential for biomaterials to revolutionize patient care remains limitless [8].

3.2 Protein Adsorption and Molecular Mechanisms of Biological Interactions

The process of adsorption relies on the interplay of various factors, including the specific characteristics of the adsorption site, the inherent properties of the

protein molecules, the surrounding solvent environment, and the unique mechanism governing the adsorption phenomenon. This intricate process involves a diverse array of interactions occurring between the protein molecules and the surface, thereby shaping the adsorption behavior. During the drying process, the behavior of proteins is notably influenced by the chemical and physical attributes of the underlying surfaces. These attributes include porosity, fineness, surface charge, size, and wall structure, all of which hold considerable significance in determining the nature of coatings and surface appearance. As a the consequence, a thorough understanding of these molecular mechanisms and surface properties is essential in comprehending the intricacies of adsorption processes and its optimizing the performance of biomaterial coatings [15, 74].

Proteins can interact with surfaces through chemical groups between amino acid residues. These categories include hydrogen bonding, electrostatic attraction and repulsion, van der Waals interactions, hydrophobic attraction and repulsion Protein surface behavior influences protein structure, amino acid sequence, and properties of the solvent environment. The solvent environment is also an important factor affecting the molecular mechanism of adsorption. Factors such as pH, salt concentration, temperature, and solvent polarity can alter the interactions between surfaces and proteins. For example, increased salinity, increased hydrophobicity, and changes in pH can increase or decrease the adsorption of proteins to surfaces. The adsorption process proceeds through steps such as protein adsorption on surfaces, adhesion to surfaces, reorganization, and stabilization [44, 68].

The exploration of molecular mechanisms governing protein adsorption and its intricate biological interactions stands as a prominent research area, particularly aimed at refining the surface properties of materials utilized in biomedical applications. The phenomenon of protein adsorption, encompassing the attachment of protein molecules onto material surfaces, holds significant relevance in diverse engineering and biomedical domains. This process exhibits a high level of complexity, influenced by a multitude of factors that govern the interactions between biomolecules and material interfaces, thereby impacting biological compatibility. The molecular mechanisms underlying protein adsorption comprise the intricate interplay between protein molecules and the material surface, encompassing adsorption kinetics and the distinct chemical and physical attributes of the surface coating. A thorough understanding of these mechanisms is pivotal in advancing the optimization of biomaterial surfaces for enhanced biocompatibility and improved performance in biomedical applications [68].

Important properties at protein-material interfaces include surface chemistry, surface topography, surface tension, hydrophobicity, and water holding capacity Surface chemistry refers to the types, concentrations, and locations of chemical groups in the material surface. This affects whether the surface is hydrophobic or hydrophilic and affects the properties of proteins. For example, hydrophobic surfaces generally have high protein adsorption, while hydrophilic surfaces have low adsorption. Surface topography refers to regular or irregular surface features, which affect the surface and distribution of proteins. In general, a constantly sloping surface has a lower protein adsorption, while an irregular surface has a higher adsorption [68].

3.3 Interactions of Ceramic Coatings with Tissues

Ceramic coatings constitute a significant class of biomaterials widely employed in a multitude of medical applications, including implants and prosthetics. These coatings are fabricated using diverse ceramic materials, meticulously selected for their suitability in biomedical contexts, offering essential attributes such as exceptional durability, chemical stability, and favorable biocompatibility profiles.

Various factors affect the interaction between tissues and ceramic coatings. The main cause is the chemical composition of the coating. Ceramic coatings are usually made of calcium phosphate derivatives, such as hydroxyapatite, which exhibit similarities in bone tissue. This similarity allows the ceramic coating to better bond with bone tissue [8, 23].

Another salient facet pertains to the orientation of surface features within the context of ceramic coatings and its consequent impact on fundamental cellular processes such as adhesion, migration, and proliferation. A noteworthy example is the influence of a softer surface, which may enhance cellular adhesion to the coating. Moreover, the manipulation of the ceramic coating surface via chemical or physical treatments can yield improved interactions with biological tissues. Furthermore, intricate chemical reactions transpire beneath the coating, orchestrating film formation and tissue healing. Such reactions are crucial determinants of the coatings' biodegradability and their potential to facilitate tissue regeneration. Notably, the solubility and degradability of ceramic coatings play pivotal roles in shaping their interactions with bone and soft tissues, thereby modulating cellular responses and tissue healing processes [13, 46].

4 Biomedical Applications

4.1 Use of Ceramic Coatings in Bone Regeneration

In the realm of metallic implants, it is well-established that their inherent biological inertness or biotolerance within the human body can impede swift adaptation to the surrounding tissues. Consequently, extensive investigations have been directed towards exploring the potential of certain ceramic coatings to foster the growth and activity of newly formed osteoblasts, thereby facilitating the process of bone regeneration during the repair and healing of fractured bones [28, 62, 90].

Factors such as the age, health condition, gender, the use of a bioactive implant, and osteoinductivity are important for successful bone regeneration [23]. The bone scaffold can be considered as a platform that provides structural support during bone repair circle and facilitates attachment during the formation process. To promote tissue growth within this platform, it should have a porous structure. It should also be biocompatible and biodegradable. Additionally, it should possess sufficient mechanical strength to support the growing tissues and exhibit osseointegration properties

for bone regeneration. Ceramic coatings that resemble bone scaffolds have been developed to enable bone regeneration [82, 23].

In cases where sufficient bonding between the implant and the tissue cannot be achieved, problems such as implant loosening occur, especially [75]. This situation can lead to inflammation, secondary surgeries, and even implant removal, which becomes a challenging and painful process for patients [23].

Calcium phosphate (CaP)-based coatings, which have mechanical properties close to natural bone tissue and a chemical composition similar to inorganic compounds, are among the most preferred ceramic coating groups [8, 87]. The use of coating layers that mimic the natural bone structure enhances osseointegration and helps overcome issues such as implant loosening. In the literature, calcium phosphate-based coatings have been reported as coatings that closely resemble the natural bone structure [51, 77]. These coatings have been modified by incorporating different elements such as Zr, Sr, Se to add properties like antibacterial activity [78]. Additionally, composite coatings have been developed that combine calcium phosphate-based coatings with polymers or different oxide-based ceramic coatings. These composite coatings aim to provide a biomimetic environment, improve osseointegration, and address specific challenges in implantology [75, 87, 92, 93].

4.2 Ceramic Coatings in Implants

In recent years, dentistry has rapidly advanced, developing various treatment methods that combine aesthetics and functionality. Particularly, in cases of tooth loss, implants are considered one of the most significant innovations in dentistry. Implants can be described as artificial tooth roots that are placed into the jawbone. However, achieving an aesthetic appearance that matches the color and structure of natural teeth is also crucial for implants. This is where ceramic coating comes into play, as it is a frequently preferred type of coating for implants due to its aesthetic appeal and durability [42, 89].

Implant applications are not limited to dental practices; they also find extensive use in hip and knee implant procedures with the incorporation of ceramic coatings. Hip and knee joint prosthetics, aimed at patients suffering from conditions like osteoarthritis, are widespread and highly successful procedures to restore mobility and alleviate pain. Ceramic coatings can enhance scratch resistance compared to the underlying metal substrate, improve wettability of bearing surfaces, and reduce wear, while maintaining the overall integrity of the implant and reducing the risk of catastrophic failure compared to bulk ceramic use. Additionally, these coatings can act as protective barriers, inhibiting ion release from the underlying material caused by corrosion. Commercially available coatings for knee and hip implants include titanium oxide or nitride, zirconium oxide or nitride. Furthermore, ongoing research focuses on new materials like silicon oxide and nitride and also tantalum oxide and nitride [71].

Ceramic coating can be specially customized to match the color of the teeth, providing almost imperceptible harmony with natural teeth. This enables patients to take pride in their smiles and boosts their confidence. Moreover, the use of ceramic coatings ensures an excellent fit with the tissues and minimizes the risk of allergies when used with dental implants. This contributes to the long-lasting and trouble-free use of implants. Since ceramics possess high mechanical strength, they do not exhibit any disadvantages when used as coating materials, and they remain resilient against daily oral activities and chewing processes. As a result, the coating maintains its durability over many years. An implant with ceramic material or ceramic coating can perfectly mimic the color and shape of natural tooth tissues. Consequently, implants offer an aesthetic appearance while replacing natural teeth, and they can preserve this aesthetic appeal for an extended period. The color stability of ceramic coatings is also remarkably high, displaying resistance against discoloration caused by beverages like tea or coffee [42].

Ceramic coatings offer a popular choice for enhancing aesthetics, with feldspathic ceramic coatings being among the top preferences. Widely used in porcelain dental crowns, they provide excellent color stability and the ability to replicate natural tooth tissues. However, it's worth noting that their mechanical strength is relatively lower compared to other ceramic types. Another favored option is lithium disilicate ceramics, which have surged in popularity recently. These coatings deliver successful aesthetic outcomes while boasting impressive mechanical durability. In dentistry, they are the go-to choice for patients seeking both aesthetics and longevity [8]. For increased mechanical resilience, zirconia coatings come into play. Specifically designed for posterior areas, they are extensively employed in dentistry for implant-supported structures and bridges.

Alumina coatings are durable and mechanically strong ceramic materials. They can be used in dental implants and certain restorative dentistry applications [21].

Zirconia-alumina composite coatings are a type of coating that combines the advantages of zirconia and alumina. They provide aesthetically pleasing results while enhancing durability. Hybrid coatings obtained by the combination of different ceramic materials can be preferred in specific applications. For instance, the combination of lithium disilicate and ceramic feldspar can yield improved mechanical properties [21, 57].

Zirconium dioxide is a widely utilized material in the fabrication of dental coatings, specifically dental crowns. Its popularity stems from its ability to create dental crowns that perfectly match the natural tooth color and provide a realistic appearance, particularly for aesthetic anterior teeth. Employing specialized laboratory techniques, zirconium coatings can skillfully mimic natural tooth tissues, resulting in aesthetically pleasing outcomes. Extensive research on zirconia implants has yielded promising results in terms of osseointegration. Modified ablative surfaces of zirconia implants have shown excellent osseointegration at an ultrastructural level [22, 48, 60]. Yttrium-stabilized tetragonal polycrystals (Y-TZP), a specific form of zirconia ceramics, offer advantages over aluminum oxide for dental implants due to their enhanced fracture resilience and flexure strength. Notably, zirconia

ceramics have also found successful applications in orthopedic surgery, particularly for manufacturing ball heads in total hip replacements [22].

Hafnium oxide stands as a prominent ceramic coating material, widely employed in restorative applications, corrosion resistance, and cytotoxicity prevention, owing to its commendable attributes of durability and chemical resistance. Research has demonstrated that the incorporation of hafnia nanoparticles can significantly improve the microstructure and phase evolution of the ceramic during the ceramization process [43, 60]. However, despite these advancements, the precise behavior of hafnium as a surface coating within biological environments and its impact on the process of osseointegration remain areas that warrant further investigation and understanding [67].

Titanium oxide also holds significant importance in the implant industry and is used as a coating material in various applications. Studies have evaluated the biocompatibility of titanium and titanium oxide-coated structures, showing positive results [25, 70]. Another study conducted by Hove et al. [39] looked into the research on titanium-nitride (TiN) coating of orthopedic implants. Their findings revealed that TiN-coating had a positive impact on the biocompatibility and tribological properties of implant surfaces. Nevertheless, some reports indicated occurrences of third body wear and delamination of the TiN-coating. Preclinical studies, however, demonstrated that TiN-coated implants exhibited comparable biocompatibility and bone-bonding properties to uncoated implants [39]. Bone's affinity to TiN-coated stainless steel was found to be similar to alumina but not significantly superior to uncoated stainless steel [39]. Apart from titanium oxide and TiN coatings, researchers have explored other surface modification methods to enhance the osteogenesis of titanium-based implants. Wang et al. [81] extensively discussed the utilization of micro-arc oxidation (MAO) technology to create oxide coatings on the surface of titanium implants. MAO allows for the incorporation of bioactive electrolyte components such as calcium and phosphate into the coating, thereby enhancing the biological activity of the implants. In conclusion, surface coatings like titanium oxide, TiN, and MAO play a pivotal role in improving the osseointegration and stability of titanium-based implants. These coatings enhance the biocompatibility of the implant surfaces and facilitate bone-to-implant contact. However, certain coating materials may present challenges like third body wear and delamination. Further research is crucial to optimize and standardize the coating processes and investigate the clinical benefits of these surface modifications [39]. Within the realm of the implant industry, a diverse array of ceramic coating applications has emerged, encompassing distinct components such as chitosan, which have exhibited favorable outcomes in experimental studies [47].

4.3 Ceramic Coating in Prosthetics

Prosthetics constitute pivotal entities within the realm of medical engineering, affording indispensable contributions towards restoring both functional and aesthetic

aspects in individuals afflicted with limb loss or deficiencies. These artificial structures find wide-ranging utility across diverse domains, encompassing dental, upper limb, and lower limb prostheses. In the pursuit of attaining naturalistic appearances and seamless integration with the human anatomy, the employment of ceramic coatings emerges as a compelling avenue. Particularly in the domain of hand and foot prosthetics, the strategic application of ceramic coatings assumes significance, serving to address specific aesthetic and functional requisites, thereby endowing a bespoke and enhanced experiential dimension for the prosthetic recipients. Ceramic coatings find application in critical aesthetic regions, such as the fingertips or palm area, within the context of hand prosthetics. Similarly, in foot prosthetics, ceramic coatings are favored for the visibly exposed segments of the prosthesis. The intrinsic appeal of ceramic coatings lies in their capacity to deliver a naturalistic appearance and a diverse range of colors, thereby promoting enhanced comfort and confidence in the daily lives. These coatings not only augment aesthetics but also confer functional enhancements, ensuring comprehensive fulfillment of patients' requirements [5].

Prosthetic crowns are artificial restorations placed on teeth to replace missing ones. Ceramic coatings are commonly chosen materials for prosthetic crowns. Specifically, ceramic materials like zirconium dioxide and lithium disilicate enhance the durability of prosthetic crowns, imparting an aesthetic and natural appearance [19].

Prosthetic bridges are artificial restorations placed over one or more adjacent teeth that are missing. Ceramic coatings offer an aesthetic appearance to prosthetic bridges by mimicking natural tooth tissue. Particularly, lithium disilicate ceramics are employed in bridges to achieve a harmonious blend of high mechanical strength and aesthetic appeal [53]. Prosthetic veneers are thin ceramic coatings applied to the front surface of teeth. Ceramic veneers customize the color, shape, and size of teeth, contributing to an aesthetically pleasing smile. Lithium disilicate and feldspathic ceramics are frequently utilized materials in veneer applications [1, 53].

Prosthetic implant superstructures are restorations placed on dental implants used to address tooth loss. Zirconium dioxide and lithium disilicate ceramics are generally preferred because of their biocompatible structure and also they are durable coating materials for implant superstructures [19].

Ceramic coatings have been used in prosthetic hip and knee joint replacements as an alternative to metal-on-polyethylene since the 1970s. The main advantage of ceramic surfaces in prosthetic joints is the significant reduction in wear rates, which can increase the longevity of the joint. This is particularly important as hip and knee replacements are becoming more common, especially in younger patients who place greater demands on the prosthetic bearings [64].

While ceramics offer excellent long-term biocompatibility and reduced wear rates, they are also brittle, which raises concerns about the risk of catastrophic bearing failure. However, improvements in material quality, manufacturing methods, and implant design have greatly reduced the incidence of such failures, making modern ceramic bearings safe and reliable when used with components of proven design and durability [64].

In order to augment the mechanical attributes of ceramics, such as strength, hardness, and wear resistance, researchers have ventured into the realm of ceramic

nanocomposites. These nanocomposites have exhibited promising potential in enhancing the performance of orthopedic bearings used in prosthetic applications [64]. Furthermore, endeavors have been made to establish reproducible and relatively straightforward methods for coating ceramic prosthetic components. A study focused on applying a glass layer to ceramic prosthetic components using an airbrush spraying technique. The primary challenge lied in coating components with curved geometries, and the researchers aimed to devise a method that could effectively address this concern [5].

Another important consideration in ceramic coating is the thermal behavior of the coating material and the prosthetic substrate. The thermal expansion coefficient (TEC) of the coating material should match that of the substrate to prevent the coating from pulling away during processing. This is particularly crucial for bioactive glasses, as their TEC often does not match that of biomedical metals [5].

Apart from ceramics, alternative materials have been subject to investigation for prosthetic coatings. Zirconia, for instance, has been utilized as a coating material for dental implants and restorations [23]. In the context of all-ceramic porcelain systems employed for prosthetic restorations, flexural strength assumes a crucial role. Notably, zirconia-coated ceramics have demonstrated superior bending strength in comparison to other ceramic systems [19].

Silicon-based polymers have also gained interest as precursors for producing inorganic coatings for prosthetic devices via the polymer-derived ceramic (PDC) process. These coatings can enhance the osteoinductive and osteoconductive properties of the prosthetic devices [58].

Overall, ceramic coatings offer significant advantages in prosthetic joint replacements, including reduced wear rates and excellent long-term biocompatibility. Ongoing research aims to further improve the mechanical properties and coating methods to enhance the performance and durability of ceramic-coated prosthetic devices.

4.4 Biomedical Sensors

Biomedical sensors are significant devices in the healthcare sector that enable monitoring of patients' physiological parameters and acquisition of critical information during medical diagnosis processes. These sensors are indispensable tools for early disease detection, treatment management, and effective healthcare monitoring. The performance, sensitivity, and reliability of biomedical sensors enhance the quality of patient care by ensuring accurate and trustworthy data acquisition. Therefore, the design and material selection of these sensors carry great importance.

The extensive adoption of ceramic coatings is a prominent choice to elevate the performance and longevity of biomedical sensors. These coatings can be achieved by combining diverse ceramic materials, thus effectively optimizing and enhancing the biocompatibility, mechanical robustness, chemical stability, and thermal properties of the sensors. Biomedical sensors, being devices that intimately interact with the

human body, place considerable importance on biocompatibility for their overall success and efficacy. In this regard, ceramic coatings present a favorable option, given that ceramic materials typically possess characteristics that align well with bodily tissues, consequently reducing the likelihood of adverse reactions [73].

Ceramic coatings, accomplished through the integration of ceramic materials featuring elevated hardness and strength properties, enhance the mechanical resilience of sensors. Moreover, the wear resistance offered by ceramic coatings enables sensors to withstand demanding usage, leading to reduced maintenance needs. An additional notable advantage resides in the thermal conductivity of ceramics, enabling sensors to attain precise and swift temperature measurements. Furthermore, the low thermal expansion coefficient of ceramic coatings contributes to heightened resistance of sensor components against thermal stresses.

Concurrently, Hydroxyapatite (HAp) emerges as a biocompatible material bearing a close resemblance to the mineral composition of natural bone. Its outstanding osteoconductivity capabilities facilitate and promote bone regeneration [8]. Notably, researchers have also explored the potential of other ceramic materials like zirconia and alumina for their application in sensor coatings [90].

Ceramic coatings find extensive applications on diverse components of biomedical sensors. Specifically, these coatings are commonly employed on sensor electrodes, detection elements, and cellular interfaces. In biomedical sensors, electrodes play a crucial role as they are responsible for detecting and transmitting electrical signals. When ceramic coatings are employed on electrode surfaces, they provide high conductivity and chemical resistance. Consequently, sensors can achieve precise measurements and obtain accurate data. Coating electrodes with ceramics allows sensors to be effectively utilized in applications involving electrochemical measurements and the detection of bioelectric signals [76].

Detection elements in biomedical sensors are employed to measure and monitor various physiological variables. Ceramic coatings are applied to these detection elements to impart essential properties such as biocompatibility and mechanical resilience. Ceramic coatings on detection elements aid in the collection of precise and reliable data by the sensors and contribute to their long-lasting functionality.

Some biomedical sensors are devices capable of interacting with other cells. Ceramic coatings are widely preferred in such sensors due to their advantageous biocompatibility properties. The application of ceramic coatings on cells minimizes their interaction with the external environment, thus facilitating accurate data acquisition. Additionally, the low toxicity attribute of ceramic coatings contributes to the preservation of cellular health, ensuring the acquisition of precise and reliable data.

The selection of different ceramic materials for ceramic coatings depends on the specific application areas. For instance, silver-based ceramic coatings are commonly employed in electrode applications, while ceramic coatings utilized as light sources may possess different sets of properties. Furthermore, various ceramic coating techniques are utilized based on the application areas and sensor design, aims to optimize the biocompatibility, conductivity, and other relevant characteristics of the coatings. So, ceramic coatings plays a vital role for enhancing the performance of biomedical sensors.

EKG sensors are employed to measure heart activity and detect heart rhythm abnormalities. Ceramic coatings are widely utilized on EKG electrodes. Particularly, silver-based ceramic coatings enable the precise and reliable acquisition of EKG data by detecting delicate heart signals through their high conductivity. The use of silver in EKG sensors enhances the biocompatibility of ceramic coatings. Given the critical importance of electrocardiography in detecting heart rhythm abnormalities and monitoring heart activity, silver-based ceramic coatings with high conductivity are preferred to ensure accurate and dependable data. Thanks to their high conductivity, biocompatible properties, and durability, silver-based ceramic coatings serve as an effective coating option for electrocardiography applications [63].

SpO₂ sensors non-invasively measure a patient's oxygen saturation. Ceramic coatings are applied on the light source and detection elements of SpO₂ sensors. These coatings enhance light transmittance, enabling accurate and precise oxygen saturation measurements. Zirconia-based ceramic coatings are commonly favored for SpO₂ (Blood Oxygen Saturation) sensors. Some of the ceramic coatings are using for sensors because of their high light transmittance and biocompatibility properties [73, 80].

Ceramic coatings have shown great potential in the field of hemoglobin sensors, offering unique properties such as biocompatibility and light transmittance. One approach involves the use of mussel-inspired polydopamine coatings on the surface of potentiometric ion sensors. These coatings, formed through the self-polymerization of dopamine, mimic the adhesion mechanism of mussels and enhance the biocompatibility of the sensors. The polydopamine coating reduces blood platelet adsorption while retaining the original sensing properties of the sensors [45].

An additional noteworthy application of ceramic coatings is found in the realm of hemoglobin sensors, which have been developed in conjunction with multiplexed electrochemical sensors. This innovative approach enables the detection of both glucose and hemoglobin utilizing a single electrode, leading to a reduction in sensor size and overall complexity [18]. The coatings on these sensors can be made titanium dioxide (TiO₂) or other which offer high light transmittance and biocompatibility. In addition, they are also used for ICP sensors alongside hemoglobin sensors. ICP sensors are commonly employed in the treatment and monitoring of neurological diseases and brain injuries. The use of these sensors is crucial for controlling intracranial pressure during neurosurgical interventions [45].

5 Conclusion

Ceramic coatings play a significant role in various applications and offer numerous advantages. They find common use in implant materials, biomedical sensors, dental applications, and prosthetics for hands and feet. Implant materials benefit from ceramic coatings as they enhance success rates and improve patients' quality of life due to their biocompatibility and durability. Zirconium oxide coatings, compatible with bones and tissues, contribute to implant success, while titanium dioxide

coatings are preferred for their durability and aesthetic properties. The application of ceramic coatings in biomedical sensors enhances sensor performance and sensitivity, enabling precise and dependable measurements. Especially, zirconia-based coatings exhibit high light transmittance and biocompatibility when applied to optical sensors and electrodes. In dental applications, ceramic coatings are widely favored for their aesthetic appeal and durability. Porcelain dental crowns create a natural appearance, satisfying aesthetic expectations, whereas zirconia coatings offer sturdy and durable solutions.

Ceramic coatings indeed play a vital role in improving the durability and biocompatibility of prosthetics designed for hands and feet. By being applied to artificial joint components and various mechanical parts, these coatings ensure that the prosthetics remain functional and reliable for an extended period of time. This longevity contributes significantly to the overall effectiveness and success of prosthetic devices for patients.

Various methods can applied ceramic coatings on diverse surfaces, including Physical Vapor Deposition (PVD), Chemical Vapor Deposition (CVD), and Electrophoretic Coating. Each technique comes with its own set of advantages and disadvantages in ceramic coating applications.

In conclusion, ceramic coatings stand as indispensable materials with wide-ranging applications, enhancing the quality of life for patients and making substantial contributions to healthcare services. Ongoing research and developments in ceramic coatings will continuously improve their effectiveness in the healthcare sector, thereby providing enhanced treatment options for patients in the future.

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Ceramic Scaffolds and Composites in Biomedical Applications



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Abstract This chapter presents a comprehensive exploration of the important role that ceramic biomaterials play in advancing the biomedical science. Ceramic biomaterials are celebrated for their unique combination of biocompatibility, mechanical strength, and versatile properties, making them a cornerstone in tissue engineering, regenerative medicine, and drug delivery systems. This chapter initiates by providing a fundamental understanding of ceramic materials, emphasizing their inherent characteristics that make them desirable in biomedical science. The discussion then turns to the design and fabrication techniques of ceramic scaffolds, elucidating their critical role in tissue regeneration. Furthermore, the integration of ceramics into composites is examined, demonstrating their capacity to enhance the mechanical and biological performance of biomaterials. The chapter highlights recent breakthroughs, challenges, and emerging trends in the field, equipping readers with a comprehensive overview of the current landscape. This chapter encapsulates the state-of-the-art developments, setting the stage for future innovations in ceramic biomaterials and their indispensable role in shaping the future of healthcare and regenerative medicines.

Keywords Ceramic scaffolds · Composites · Bone tissue engineering · Calcium phosphates · Bioglass

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1 Introduction

Over the past thirty years, tissue engineering has emerged as a highly promising strategy for the restoration and rejuvenation of tissues and organs that have been lost or impaired due to traumatic injuries, diseases, or the natural process of ageing [1–7]. One crucial part of tissue engineering is the utilisation of a synthetic framework known as a scaffold. This scaffold functions as a guiding structure in two or three dimensions (2D or 3D), facilitating the growth of soft and hard tissues *in vitro* and *in vivo*. The scaffold, characterised by its porous structure, offers a mechanically robust setting that is capable of accommodating the necessary cells and biological components. These components are typically introduced to the scaffold prior to implantation. The scaffold facilitates cell migration, adhesion, and growth, while also aiding in the organisation of the developing tissue when implanted *in vivo* [2, 8, 9]. The utilisation of “signalling” serves to further augment the advancements in tissue engineering. The process of signalling encompasses both biochemical and biomechanical signals that are delivered by the scaffold. These signals initiate mechanisms within the living organism that promote tissue regeneration. By influencing the cells to generate functional tissues, the signalling ultimately determines whether the scaffold successfully integrates into the surrounding tissue [10, 11]. The optimal scaffold design involves striking a balance between the requirement for extensive interconnected porosity to facilitate tissue in growth, nutrition transportation, and angiogenesis, and the ability to regulate resorption rates and achieve the necessary mechanical qualities, such as stiffness, strength, and fracture resistance [1, 2, 6, 9, 12–15]. The aforementioned attributes frequently coexist, leading to challenges in the design, characterization, and translation of synthetic implants for use in clinical settings. Various types of tissues, including skin, bone and cartilage have demonstrated effective regeneration [1, 7, 16–18].

A wide range of materials, including both natural and synthetic materials, as well as bioresorbable and permanent materials, have been extensively studied and modified for the purpose of constructing scaffolds. Bioceramics have been extensively studied because to their superior tissue response in comparison to polymers and metals [3, 7, 19–26]. Certain categories of bioceramics, namely alumina and hydroxyapatite (HA), are designed to function as permanent medical implants. As a result, these materials are engineered to prevent the release of their constituent elements into the human body. Additionally, they are anticipated to elicit no adverse reactions from the body’s immune system, commonly referred to as foreign body reactions. Alternatively, if designed as biomaterials that can be absorbed by the body (such as bioactive glasses), their ions (such as calcium, silicon, sodium, and phosphate) can undergo normal metabolic processes or be utilised for specific therapeutic purposes, such as stimulating the growth of new blood vessels and exhibiting antibacterial properties [27–30].

The application of bioceramics has traditionally been focused on the restoration of hard tissues, such as bones and teeth, due to their inorganic composition and mechanical hardness. Nevertheless, numerous research have also presented evidence

of the potential of bioceramics as a novel approach for the regeneration of diverse forms of damaged soft tissues [31, 32].

This chapter aims to describe the utilisation of ceramic biomaterials as scaffolds in the field of hard- and soft-tissue engineering. Initially, this chapter focuses on the fundamental framework prerequisites, followed by a comprehensive analysis of bioceramics employed in the fabrication of diverse scaffolds. Following this, the main manufacturing methods used for scaffold preparation are discussed, followed by an overview of potential future perspectives.

2 Criteria for Scaffolds in Bone/Cartilage Tissue Engineering

The exceptional mechanical properties of natural bone are strongly associated with its hierarchical structure spanning from the nano to the macro scale. This structure consists of meticulously organised inorganic and organic components at the nanoscale. During the process of bone biomineralization, hydroxyapatite (HA) nanocrystals are regularly and systematically deposited within the collagenous gap areas as shown in Fig. 1. Extensive research has been conducted on tissue engineering scaffolds in order to develop implantable bioceramic materials that can elicit the most suitable host response, tailored to the specific therapeutic requirements, while facilitating the formation and regeneration of intricate three-dimensional tissues. A number of universally acknowledged criteria that should define an optimal scaffold [2, 18, 28] as outlined in Table 1.

The area of bone tissue engineering utilises a combination of life sciences and engineering principles to develop engineered structures that restore, maintain, or enhance the function of bone tissue. This is achieved through the use of a substrate, or scaffold, which serves as both structural guidance and anchorage sites for cells (Fig. 2). By combining these scaffolds with living cells, the goal is to create a functional engineered structure for bone tissue as represented in Fig. 3 [34].

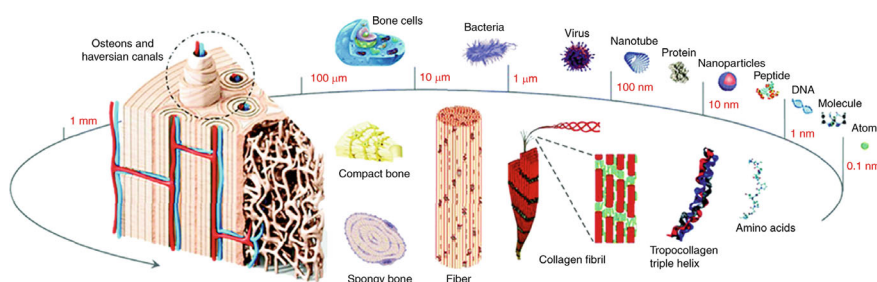


Fig. 1 Multidimensional hierarchical structure of bone tissue (reproduced with permission from [33])

Table 1 Necessary criteria for scaffold in bone/cartilage tissue engineering

Criteria	Description
Geometry	It should first address intricate three-dimensional (3D) imperfections by effectively filling them, and then directing the tissue towards aligning with the original 3D anatomy
Biocompatibility	The capacity to facilitate regular cellular functioning, such as molecular signalling mechanisms, without causing any harmful consequences on the local or systemic tissues of the host organism
Bioactivity	The objective is to promote expedited tissue adhesion to the surface of the implant, while minimising the formation of scar tissue. Additionally, the aim is to establish a durable and secure connection that prevents any small-scale movement at the interface and mitigates the occurrence of an inflammatory reaction
Stability/ biodegradability	The choice of scaffold material depends on the intended application. For long-term use, materials with high stability are necessary. In contrast, for temporary use, the scaffold should degrade slowly over a predetermined period and be replaced by the natural host tissue
Porosity	The scaffold should exhibit a porous structure that is linked, with a high ratio of surface area to volume. The pore size should be a minimum of 100 μm in diameter, which is considered optimal for bone healing. This pore size enables the penetration of cells, facilitates the creation of tissue inside the scaffold, promotes the development of blood vessels within the construct, and allows for the movement of nutrients
Mechanical strength	The scaffold's mechanical performance, influenced by the characteristics of the biomaterial and the porous structure, must meet the necessary requirements to endure implantation handling and provide adequate support for the loads and strains that the new tissue will eventually experience. Non-osteoarticular applications necessitate the presence of sufficient elastic compliance, characterised by low stiffness, in order to accommodate soft tissue
Biocompatibility	The scaffold material must have the capability to exhibit specific characteristics, such as the facilitation of angiogenesis, induction of cell differentiation, and exertion of antibacterial capabilities, through the controlled release of ions
Ease of fabrication	The scaffold should possess the ability to be conveniently customised in terms of dimensions and configuration to suit the specific needs where the newly formed tissue is intended to be implanted
Economic aspects	The scaffold ought to be manufactured via an automated methodology that ensures consistent replication. Additionally, it should be constructed and subjected to sterilisation procedures in accordance with internationally recognised standards for both commercial manufacturing and clinical application

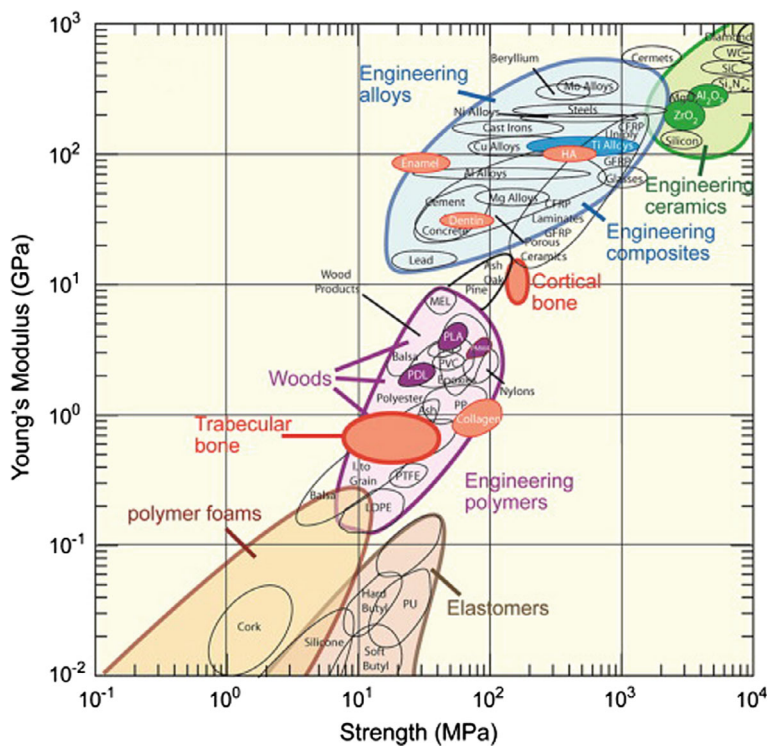


Fig. 2 Young's modulus versus strength chart of materials (reproduced with permission from [36])

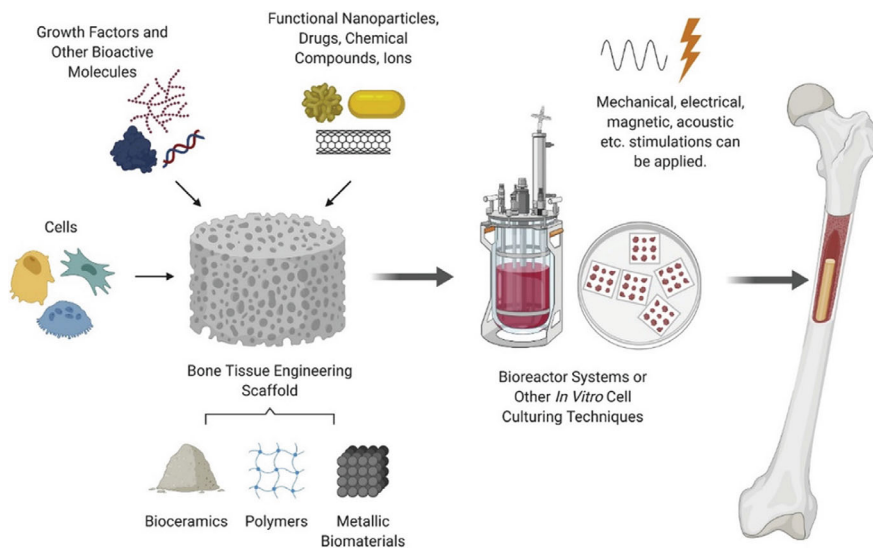


Fig. 3 Fundamentals of bone tissue engineering (reproduced with permission from [34])

One of the primary challenges in scaffold design is the need to balance competing requirements that arise from fulfilling the expectations of host tissue. This means that achieving a given requirement may have a negative impact on another requirement. The requirement to achieve a balance between the porosity and mechanical properties of scaffolds is a critical factor in ensuring the successful outcomes of load-bearing applications, such as bone tissue healing [35]. The characteristics of scaffolds are primarily influenced by the composition and microstructure of the materials utilised. Figure 2 presents a graphical representation of a material property chart that illustrates the strength and elastic modulus of both natural and synthetic materials. These materials typically possess a dense microstructure without any porosity, as indicated by Ref. [36]. The presence of a porous structure with a high degree of interconnectedness (usually characterised by a pore content exceeding 50 vol%) is crucial for facilitating the complete integration of the scaffold following its implantation. Nonetheless, the mechanical properties are influenced by porosity. The necessity to achieve a favourable result in scaffolds designed for load-bearing applications, such as bone tissue restoration, relies heavily on the careful management of scaffold porosity and mechanical properties [35]. Porous structure that is strongly linked, often with a pore content exceeding 50% by volume, in order to facilitate complete integration of the scaffold following implantation. The mechanical competency of a component is influenced by porosity, as an increase in the volume percentage of porosity leads to a gradual decrease in strength and stiffness.

When designing a bioresorbable scaffold, achieving mechanical competence is an additional challenge due to the inherent fragility of degradable materials as they degrade over time. There are two additional challenges that arise in the development of bioresorbable scaffolds. Firstly, it is important to ensure that the interface between the scaffold and the surrounding tissue remains strong and stable throughout the degradation process, as the scaffold is gradually replaced by the natural host tissue. Secondly, it is crucial to carefully align the rate at which the scaffold is resorbed with the expected rate of regeneration for the specific tissue being targeted. The facile achievement of metabolization of the degradation products of the biomaterial should be accomplished without eliciting any adverse local or systemic responses [37].

Another noteworthy element is to the constraint imposed by the mismatch in elastic modulus, which plays a critical role in ensuring the sustained efficacy of implant adhesion to both hard and soft tissues. Multiple investigations have shown evidence that the abrupt alteration in elastic characteristics at the interface between tissue and implant gives rise to significant stress gradients in the host tissue, ultimately resulting in the failure of the implanted material. The optimisation of all the physicochemical characteristics outlined in Table 1 presents a formidable challenge, primarily due to their intricate and partially unexplained interdependencies. The correlation between tissue integration rate and quality has been found to be influenced by scaffold pore size, porosity volume fraction, and pore interconnectivity [38]. Furthermore, it is essential to take into account the impact of strut microstructure and pore geometry on the capture and entrapment of growth factors, as well as their influence on scaffold functions. The complexity of determining the individual

impacts of parameters is heightened by the bioactivity exhibited by numerous bio ceramics. This bioactivity is primarily facilitated through two mechanisms: (i) direct effects involving the dissolution and subsequent release of ionic products, both in laboratory settings and within living organisms. This process leads to increased concentrations of soluble substances that directly interact with nearby cells or affect cellular behaviour by altering local pH levels. (ii) Indirect effects occur through the influence of molecular interactions between surfaces and proteins, entrapment of growth factors, and subsequent attachment and functionality of cells. Hing [39] has lately provided a significant depiction of these crucial matters with regards to enhancing scaffold design and manufacture.

One area of research that presents significant challenges involves investigating the methodologies for incorporating specific “biological” characteristics into tissue engineering scaffolds, with a specific focus on the utilisation of bioactive glasses. Previous studies have shown evidence that the promotion of new bone development is closely associated with the regulated discharge of dissolved ions, such as silica and calcium ions, from the deteriorating bioactive glass [40]. Several studies have demonstrated that bioactive silicate glasses and the dissolved ions they release have a positive impact on osteogenesis. This is achieved via influencing the proliferation, differentiation, and gene expression of osteoblasts [41, 42].

In a study conducted by Sun et al., it was demonstrated that the use of 45S5 Bioglass® has a positive effect on the proliferation of human osteoblasts. Specifically, when critical concentrations of silicon (Si) and calcium (Ca) ions are present, osteoblasts capable of differentiating into mature osteocytes begin to proliferate and facilitate the regeneration of new bone. Simultaneously, osteoblasts that are not in the appropriate phase of the cell cycle and unable to progress towards differentiation are induced into apoptosis by the ionic dissolution products of the Bioglass®.

The literature has engaged in a contentious argument regarding the disputed impact of particular ion dissolution products derived from bioactive glasses or Si-substituted calcium phosphates on the process of osteogenesis [37]. Previous studies have put forth the hypothesis that the presence of a substantial concentration of silicon in bioactive glass may play a significant role in promoting rapid growth of osteoblasts. This phenomenon has been observed particularly in the case of bioactive glasses formed from the melting process, as indicated by Xynos et al. [41]. Nevertheless, the study conducted by Bielby et al. [43] did not yield any statistically significant disparities in the growth rate of human primary osteoblasts when cultivated in conditioned cell culture media that included comparable levels of calcium (Ca), phosphorus (P), and sodium (Na) ions, but varied in the concentration of silicon (Si) ions released from a sol–gel bioactive glass. Hence, additional research is necessary to acquire quantitative understanding and validate the pathways by which ion dissolution products originating from bioactive glass can impact gene expression in bone cells.

According to recent research, it has been discovered that the regulated release of bioactive glasses’ ionic dissolving products at low concentrations can stimulate angiogenesis, which is a crucial factor in the regeneration of both hard and soft tissues [28]. Kanczler et al. [44] conducted a comprehensive analysis on the intricate

involvement of angiogenic and osteogenic variables in the adaptive response and interplay between osteoblasts and endothelial cells in the context of bone growth and repair.

3 Ceramics Used in Scaffold (Tissue Engineering)

Ceramics which finds applications in biomedical science popularly known as Bioceramics constitutes a broad category of engineered ceramic materials utilised for the purpose of repairing and reconstructing anatomical structures afflicted by disease or injury. The applications utilised in clinical practise encompass various forms, such as solid pieces employed in reconstructing middle ear ossicles or serving as load-bearing components in joint prostheses. Additionally, powders and granules are utilised for bone filling purposes, while coatings are applied to metal joint prostheses. Injectable formulations, known as bone cement, are also employed. Bioceramics can be categorised into three primary groups based on their tissue response: practically inert ceramics such as alumina and zirconia, bioactive ceramics such as bioactive glass, and resorbable ceramics such as β - and α -tricalcium phosphate (TCP) [15, 28, 45–47]. In the context of hip replacement and dental implants, inert ceramics are commonly employed as femoral heads, acetabular cups, and dental implants. However, their application as scaffolds is limited due to their inert nature, which induces the development of a fibrous capsule, approximately 1–3 μm in thickness, on the surface of the implant. According to Hench [45], in cases where there is no strong foreign body response, there is a lack of bonding between the implant and the host tissue.

The establishment of a durable link with the host tissue is a crucial factor in the selection of bioceramics for the fabrication of scaffolds. In this context, the utilisation of bioactive and bioresorbable ceramics is considered a significant and beneficial approach. Moreover, the latter entities demonstrate the additional benefit of undergoing gradual degradation over a specific timeframe, as they are gradually substituted by the natural host tissue. Consequently, these entities cease to exist once their function of serving as templates for new tissue formation has been fulfilled [16, 48].

The subsequent sections centre on the primary categories of bioceramics that are presently employed in the production of scaffolds. These materials are organised into distinct classes based on their microstructural characteristics, namely bioactive crystalline ceramics, bioactive glasses, glass–ceramics, and composites. The text briefly touches with applications and clinical advancements.

3.1 *Bioactive Crystalline Ceramics*

Several ceramic materials have demonstrated bioactivity; however, the most extensively researched category is bioceramics based on calcium phosphate. The exceptional properties of these materials can be attributed to two main factors. Firstly, they exhibit a remarkable resemblance in both composition and structure of the mineral phase found in bone. Secondly, they possess osteoconductivity, which refers to their ability to create a biocompatible interface that allows for the migration and bonding of bone tissue without the formation of scar tissue. There is a diverse array of calcium phosphate phases that can be observed in naturally occurring mineralized tissue. The classification of this group of calcium phosphate phases is commonly based on the molar ratio of calcium to phosphorus (Ca/P), the polymorphs (variants with the same chemical composition but different crystal structure), the presence or absence of structural water, and the formation of crystalline phases at high temperatures, such as tetracalcium phosphate.

One of the primary distinctions among the various calcium phosphate phases is in their varied solubility. The solubility of the calcium phosphates (CaP) follows a specific order at a physiological pH of 7.4 and a temperature of 37 °C. The order of compounds in terms of their relative composition is as follows: dicalcium phosphate anhydrous (DCPA) is greater than dicalcium phosphate dihydrate (DCPD), which is more than α -tricalcium phosphate (α -TCP), which is greater than β -tricalcium phosphate (β -TCP), which is greater than tricalcium phosphate (TCP), which is greater than Ca-deficient apatite (CDA), which is greater than octacalcium phosphate (OCP), which is greater than hydroxyapatite (HA) [24].

The major use of certain phases, namely DCPA, DCPD, α -TCP, and TCP, is as reactant phases in calcium phosphate bone cements. This is mostly due to their intrinsic high solubility at physiological pH. DCPD, DCPA, and OCP, despite not being conventionally categorised as ceramics due to their formation through aqueous precipitation at or near room temperature and their transformation into different calcium phosphate phases during high-temperature ceramic processing, have been the subject of investigation as potential substitutes for bone grafts [1, 28, 37, 39, 47, 49].

Among the calcium phosphate phases, Hydroxyapatite ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) exhibits a calcium-to-phosphate ratio of 1:67, which is consistent with its stoichiometry. In terms of crystallography, this synthetic compound closely resembles the apatite phase seen in natural bone. Due to its remarkable biocompatibility and osteoconductivity, hydroxyapatite (HA) has been effectively employed as a bone filler in various forms, such as cement or granules, as well as in coatings on artificial joints made of metal. Nevertheless, the utilisation of this material as a scaffold is restricted due to its inadequate mechanical qualities and very sluggish rate of resorption [50]. Porous ceramics are commonly employed in various applications, often integrated within a carrier material such as natural collagen or synthetic polymeric substances like polyethylene glycol (PEG). Additionally, they can also be utilised in the form

of cements. The many forms available have unique benefits, contingent upon the specific characteristics of the bone deficiency requiring treatment.

Alternatives to bone grafting made from porous calcium phosphates typically comprise of either hydroxyapatite (HA) or β -tricalcium phosphate (β -TCP), or a combination of these two phases to form biphasic calcium phosphates (BCPs). The solubility of β -TCP is significantly greater in comparison to that of HA. Both of these materials exhibit osteoconductive properties, facilitating the growth of new bone tissue by providing a conducive surface. The primary distinction between them lies in their varying rates of breakdown within a living organism [50]. When there is a need for expedited resorption of the bone graft, the use of β -TCP may be more advantageous compared to HA. However, a potential obstacle arises when β -TCP resorbs at a faster pace than the rate at which bone production occurs. The restricted solubility of HA ceramics may lead to the development of a material possessing an osteoconductive surface. Once the host bone forms on this surface, there is limited subsequent integration and absence of remodelling.

3.2 *Bioactive Glasses*

Bioglass was the pioneering material that established a link with living tissue particularly bone, resulting in the formation of a stable interface. These glasses have been found to initiate many biological reactions, including tissue regeneration and angiogenesis, while gradually disintegrating over a period of time [51]. This breakthrough marked the inception of the bioactive ceramics. The degradation mechanism of Bioglass involves dissolution in a liquid medium. Bioglass exhibits two distinct mechanisms of bioactivity in relation to bone repair. Firstly, the formation of a hydroxycarbonate apatite (HCA) layer on the glass surface occurs as a result of the glass dissolving and HCA precipitating onto it. This layer is believed to integrate with the collagen fibrils of the host bone, thereby promoting bone bonding [52]. Secondly, the bioactive glass possesses osteogenic properties attributed to the dissolution products of the glass, namely soluble silica and calcium ions. These products stimulate bone cells to enhance bone production [23]. The first bioactive glass, known as 45S5 Bioglass, is composed of 46.1 mol% SiO_2 , 24.4 mol% Na_2O , 26.9 mol% CaO , and 2.6 mol% P_2O_5 [53]. Numerous borate, phosphate and silicate glasses have been suggested for potential clinical relevance in various studies conducted in the past. These studies have been extensively examined in other literature sources [16, 28, 37, 42, 54–61].

The process by which the HCA layer is formed on the glass surface is facilitated by the presence of a solution. Cations present in the glass, such as Na^+ and Ca^{2+} , undergo a process of proton exchange with H^+ ions from the water in the blood or solution. This exchange results in the formation of a layer rich in silica and the creation of Si-OH bonds on the surface of the glass. The limited connection observed in the silica-rich layer results in the loss of a portion of the silica and facilitates the ongoing transportation of ions from the bulk of the glass. The blood already exhibits

elevated levels of calcium and phosphate ions. Additionally, an increase in these ions, along with a rise in pH resulting from the release of hydrogen ions from the solution, facilitates the deposition of calcium phosphate on the surface of the glass. This deposition occurs mostly on Si–OH groups, which serve as appropriate sites for the process. The amorphous calcium phosphate subsequently undergoes crystallisation when it assimilates hydroxide (OH) and carbonate ions from the solution or blood, resulting in the formation of hydroxyapatite (HCA).

3.3 *Glass–Ceramics*

The process of heating glass can result in its transformation into a partially crystalline material that encompasses a range of crystalline phases. The size and composition of these crystalline phases can be manipulated by adjusting the parameters of the thermal treatment. In general, the glass–ceramic material that is produced demonstrates enhanced mechanical qualities compared to its original glass form. These properties include an increased hardness, tensile strength, fatigue strength, and abrasion resistance. Scaffolds are commonly manufactured through the process of sintering, wherein glasses are subjected to temperatures higher than their glass transition temperature to induce localised flow. Several types of bioactive glasses, such as 45S5 Bioglass[®], undergo crystallisation just above their glass transition temperature. Consequently, bioactive glass scaffolds that have been sintered are frequently referred to as glass–ceramic scaffolds [28].

The scaffolds derived from 45S5 Bioglass[®] exhibit certain limitations due to the tendency of the underlying glass to crystallise prior to complete densification during the sintering process. This results in the formation of highly fragile porous products made of glass–ceramic material. Additionally, the bioactivity of the scaffolds appears to be slowed down somewhat because of the emergence of a crystalline phase composed of sodium, calcium, and silicate [62]. In an effort to address these limitations, some research groups have achieved noteworthy outcomes by suggesting alternate glass–ceramic materials. In a study conducted by Vitale-Brovvarone et al. [19], the researchers utilised a bioactive glass known as CEL2, which consisted of 45% SiO₂, 26% CaO, 15% Na₂O, 3% P₂O₅, 4% K₂O, and 7% MgO (mol.%). This glass was employed in the fabrication of foam-like glass–ceramic scaffolds that demonstrated a compressive strength of up to 1 MPa, with a porosity of 70% by volume. Furthermore, these scaffolds exhibited superior biological compatibility with bone cells. Subsequently, the same research group successfully optimised the process parameters, resulting in scaffolds with enhanced strength ranging from 5 to 6 MPa. This strength range falls within the typical values observed for cancellous bone, which typically ranges from 2 to 12 MPa [63, 64]. The compressive strength of scaffolds made of bone-like glass ceramic, utilising the experimental glass SCNA (57SiO₂–34CaO–6Na₂O–3Al₂O₃ mol.%), can achieve a value of 15 MPa with a porosity of

approximately 65 vol.%. This level of strength renders them appropriate for load-bearing purposes, while still maintaining a relatively moderate level of bioactivity [65, 66].

3.4 *Bio-inert Ceramics*

Alumina (aluminium oxide) and zirconia (zirconium oxide) are examples of commonly used bioceramics that exhibit bio inert properties in the field of biomaterials. The fabrication process of a medical device, or its component, typically involves the utilisation of bioceramics with high inertness. These bioceramics are commonly prepared by combining fine-grained particulate materials an organic binder and water, followed by compression in a mould. Following this, the temperature is increased in order to facilitate the evaporation of water, commonly referred to as drying, and to eliminate the binder through combustion. At significantly elevated temperatures, the component undergoes densification as a result of the fire process. Following the process of cooling to the surrounding temperature, it is possible to implement one or multiple concluding procedures, such as the application of polishing techniques.

In the absence of the densification stage, interstitial voids will persist between the particles, hence serving as potential imperfections when subjected to mechanical stresses. The phenomenon of pore closure, referred to as densification, is achieved through sintering. In case of bioceramics, solid-state sintering is the generally employed method for achieving densification. In certain systems, an increase in temperature can lead to the formation of liquid phases at grain boundaries, while the majority of the material remains in a solid state. This phenomenon, known as “liquid-phase sintering,” can result in densification. In this context, as the liquid infiltrates the interstices and permeates the voids, it will induce a cohesive force between the particles through capillary action, resulting in a reduction in the overall volume of the powdered mass (densification). The microstructure that arises from the process of “liquid-phase sintering” will include of diminutive grains derived from the initial powder compact, enveloped by a liquid phase. Upon the cooling of the compact, the liquid phase will undergo crystallisation, resulting in the formation of a finely textured matrix that encompasses the initial grains. Solid-state sintering is an alternative method for densifying a powder compact, which does not require the presence of a liquid phase. In this particular scenario, the atoms exhibit motion to occupy the interstices and pathways amidst the particles constituting the compacted powder. As a consequence, the crystalline grains undergo enhanced cohesion, resulting in a substantial augmentation in the density, strength, and resistance to fatigue of the ceramic object that has through the process of sintering. The densification rate during solid-state sintering is often slower compared to liquid-phase sintering due to the slower material movement in a solid state as opposed to a liquid state. The solid-state sintering technique is frequently employed in the formation of various bioceramics due to its ability to achieve a greater level of purity and consistency in fine-grained microstructures.

4 Composites Scaffolds

Scaffolds have been very effective in the fields of tissue engineering and tissue regeneration which relies heavily on the alignment of their structure and qualities with the specific tissue type and the mechanical forces it will encounter in its natural environment. Similar to the majority of ceramic materials, bioceramics possess the inherent drawback of displaying poor fracture toughness, resulting in brittleness. Consequently, this characteristic may impose restrictions on their applicability in load-bearing scenarios. Moreover, the elevated stiffness of bioceramics may impose limitations on their utilisation in non-osseous contexts, where it is crucial to ensure sufficient compliance with soft tissues [32].

A strategy that seeks to address these challenges is the integration of bioceramics and polymers to fabricate a composite scaffold, thereby capitalising on the unique properties of both materials. In general, the incorporation of bioceramics into the polymer matrix is a common practise aimed at enhancing the mechanical properties of the material. This involves the addition of fillers or coatings, which serve to raise the strength and stiffness of the polymer. Additionally, the presence of bioceramics effectively promotes improved bioactivity inside the material [67].

Bretcanu et al. [68] employed an alternate approach to produce porous composites. They utilised a bioceramic scaffold, specifically the 45S5 Bioglass®, as a porous inorganic matrix. To enhance the composite's properties, the scaffold was coated with poly(3-hydroxybutyrate) (P3HB). The polymer was intentionally used to enhance the structural integrity of the 45S5 Bioglass® scaffold. Specifically, the P3HB layer served as an adhesive, effectively binding the inorganic particles together in instances where the scaffold struts experienced deterioration. According to Chen et al. [62], the composite scaffold exhibited a compressive strength of up to 1.5 MPa, which was twice as high as that of the 45S5 Bioglass® scaffolds without any additional components, which had a compressive strength of up to 0.4 MPa.

The incorporation of mesoporous glass particles as a secondary phase in composites can contribute additional benefits, such as enhanced drug uptake and release [55, 69]. Composite scaffolds have been fabricated using both non-degradable and degradable polymers. However, it should be noted that stable polymers typically exhibit limited biocompatibility due to their tendency to develop a fibrous capsule upon implantation. Consequently, numerous endeavours have been made to develop composite materials by integrating biopolymers with bioceramics.

The initial composites that were examined consisted of hydroxyapatite (HA) or tricalcium phosphate (TCP) as the inorganic phases, and poly(L-lactic acid) (PLLA), poly(D/L-lactic acid) (PDLLA), poly(glycolic acid) (PGA), and their copolymers (PLGA) as the organic phases [70, 71]. HA/polyethylene porous composites, known as "Hapex" in the commercial sphere, are presently employed in clinical settings for the purpose of mending orbital floor fractures [72].

In recent times, there has been a shift in focus towards nano-bioceramic/polymer composites, as they possess the capability to enhance the contact with host tissue/cells [73]. One of the intriguing challenges in this context involves the development

of intelligent composite biomaterials that exhibit nanoscale interaction between the inorganic and organic phase. This enables the scaffold to degrade as a unified material, rather than experiencing disparate degradation rates between the glass and polymer phases. According to Jones and Hench [74], it has been emphasised that this close relationship facilitates the simultaneous engagement of cells with both phases, while the degradation of the scaffold occurs at a uniform rate.

It is worth noting the significance of “star gels,” a specific category of organically modified silicates known as “ormosils.” These materials consist of flexible arms encircling a pliable organic core that terminate in alkoxy-silane groups. During the sol–gel process, these alkoxy-silane groups are capable of forming a network similar to silica [75]. According to Manzano et al. [76], these hybrid materials exhibit bioactive characteristics and possess fracture toughness levels that surpass those of sol–gel glasses and same as cancellous bone. As a result, they hold potential for use in tissue engineering applications that necessitate favourable long-term fatigue performance.

5 Methods of Fabrication of Ceramic and Composites Scaffolds

One of the trickiest problems in biomedical science is deciding how to fabricate scaffolds and composites scaffolds so that they may be used as implants. Scaffolds have been made using a wide variety of conventional fabrication methods, such as electrospinning, gas foaming, solvent casting and particle leaching, phase separation, and melt mixing, solid freeform fabrication (SFF), foaming, organic phase decomposition, starch consolidation, and sponge replication [7, 17, 77, 78]. Conventional approaches have limitations in the fabrication of porous structures due to limitations in the ability to fully regulate the architecture of scaffolds, including pore size and interconnectivity [5]. However, the biocompatibility of scaffolds may be compromised by the use of solvents in several of these procedures [1]. Processing techniques can greatly influence many features of the scaffold, and these technologies offers to regulate the 3D structure of tissue engineering constructions. In reality, there is a sweet spot for strut thickness and orientation, pore size and distribution, interconnectivity, and overall porosity that may be achieved with any technique. Therefore, the best method must be carefully chosen to fulfil the needs of the targeted tissue [79]. In addition, the total cost of each fabrication method is different, with some being more suitable for the creation of high-value items while others being more cost-effective for mass manufacturing. In this section, the most common ways to make ceramic scaffolds and ceramic composites scaffolds was discussed along with their suitability and drawbacks.

5.1 Foaming

Creating scaffolds with pore sizes ranging from 20 μm to 1–2 mm is possible by first creating bubbles to transport gas via a ceramic suspension or colloidal sols, and then solidifying the mixture [6, 14]. Foaming methods can be broken down into two categories: (i) those that involve adding an external gas, such as through mechanical frothing, gas injection, or aerosol propellant, and (ii) those that involve the natural evolution of an in-situ gas. In direct foaming processes, stabilising and settling the wet foams is the most important stage. In order to preserve their porous shape during subsequent high-temperature sintering/ceramization, they must first be established.

In addition, the time between foam creation and foam solidification is long enough for many changes to occur in the bubble structure. For instance, after the nucleation phase, gas bubbles develop into polyhedral cells rather than maintaining their spherical shape [81]. Surfactants are typically utilised to stabilise the bubbles generated in the liquid phase to keep the cellular morphology and avoid the collapse of the foamed structure, as they lower the surface tension of the gas–liquid interfaces. Surfactants only give temporary stability; hence another mechanism is needed to maintain the system indefinitely [82]. There are numerous processing paths that can result in the inclusion of bubbles.

Ceramic powder and an H_2O_2 aqueous solution (the foaming agent) are combined in a mixer, poured into moulds, and baked at 60 °C. H_2O_2 decomposes at this temperature, and the oxygen released into the slurry often forms bubbles, giving rise to foaming. Based on the constituent powders, sintered samples can yield crystalline ceramics, bioactive glasses, and calcium phosphate scaffolds [83]. The percentage of porosity and pore size can be adjusted by changing both the H_2O_2 incorporation and the heat treatment. Pores are only connected to one another in a laminar fashion, which leads to inadequate interconnection in the direction perpendicular to the laminae [3].

Gel-cast foaming, which uses an organic monomer polymerized on-site instead of hydrogen peroxide, is another option. To facilitate in situ polymerization, a high-solid-load aqueous ceramic suspension containing an organic monomer that is soluble in water (such as acrylates) is created [60, 84]. The casting process is an essential step in the production of porous ceramics, and the latter two ingredients are required to regulate the induction time (the inactive time between the addition of reagents and the start of the polymerization reaction). To create wet ceramic foam, a foaming agent (surfactant) is added to the suspension, and the mixture is then mechanically agitated. After polymerization, the green body can be safely removed from the mold and taken to an oven, where it will dry, the polymer will be burned off, and the ceramic particles will be sintered. As a result of its solid struts and walls, the ceramic foam created by this process is far stronger than that obtained using more traditional methods.

However, as a result of the porosity, the resulting structure is inhomogeneous and has poor connectivity [82]. By manipulating bubble growth and lamella (cell wall) thinning during the induction period, strut thickness and cell size distribution

can be customised. This is most easily achieved by adjusting the concentrations of the initiator and catalyst, while it has been discovered that other parameters, such as temperature and pH, also have a substantial effect [82]. The capacity to create highly intricate porous scaffolds is another benefit of this method. In fact, casting eliminates the necessity for machining when sculpting shapes or profiles. In addition, the green foams, once cured, are sturdy enough to endure machining [81]. The foam replica approach (explained in Section “Sponge Replica Method”) has been used in conjunction with gel-cast foaming to create HA scaffolds with linked pores [85]. The use of gelling polymers (e.g., gelatin) that do not necessitate a catalyst and an initiator (e.g., gelation is possible with a reduction in temperature) can also be employed in gel-cast foaming; however, a freeze-drying phase is required prior to sintering [57]. Figure 2 depicts the internal structure of a gel-cast foamed scaffold.

5.2 Sol–gel Technique

Sol–gel foaming is a third option which combines wet synthesis (sol–gel) technologies with mechanical frothing. This process converts a solution containing preceramic precursors (sol) into a structure of silica with covalent bonds. For tissue in growth, a glass or glass–ceramic construct can be heated to create interconnected macropores (10–500 μm) and a mesoporous texture (2–50 nm channels) that increases surface response rates in vitro and in vivo (particularly the development of a HA layer on surfaces) by promoting cell adhesion and adsorption of biological metabolites [6]. Incorporating a surfactant into the sol that can serve as a model for self-assembly at the supramolecular level is one way to control the latter property; this process is also known as evaporation-induced self-assembly (EISA) [86]. First, a sol is made by combining distilled water with metal alkoxides like tetraethylorthosilicate and triethylphosphate, as well as salts like CaNO_3 and a hydrolysis catalyst like dilute acid. Then, the sol is foamed by vigorously agitating it with a gelling agent, a surfactant, and more distilled water; finally, it is cast into moulds and aged until it gels. However, the nanoporous structure of the material makes it extremely fragile, which is a major concern when it comes to the device’s safe implantation [48]. This method is effective in obtaining highly bioactive bone-like 3D scaffolds [6].

5.3 Starch Consolidation

Starch granules obtained from maize, rice or potatoes are used in this technique to serve as both a pore forming and a binder in the production of porous ceramics. The primary benefits of this processing method are its low cost and benign impact on the natural world. Starch granules, ceramic powder, and distilled water are combined in a mixing bowl and swirled constantly while the temperature is held between 60 and 80 $^{\circ}\text{C}$. Starch expands as it absorbs water in this temperature range, producing

a gel-like material that is then thermally treated after consolidation to burn-out the organic phase and sinter the ceramic matrix. Sintering makes it easier to regulate the final dimensions of a component because there are little dimensional changes during consolidation and drying [87]. The resultant glass–ceramic scaffolds have mechanical properties comparable to cancellous bone (2–12 MPa) (compressive strength of 6 MPa), but their porosity was too low (40 vol. %) and inadequately interconnected to be considered for ultimate clinical application [88, 89]. As a result, alternative polymer phases (besides starch) have been tested as a pore forming for bioactive glass scaffolds used in tissue engineering.

5.4 Organic Phase Decomposition

Another technique for making porous scaffolds is called organic phase decomposition (or the space-holder method). Synthetic (e.g., poly(methyl methacrylate) or polyethylene microbeads) or natural (for example, rice husk) solid polymeric phases are combined with ceramic powders in this technique [35, 48, 60]. The mixture is then compacted into a “green body” and subjected to high-temperature thermal treatment. When heated, the inorganic particles sinter while the polymeric particles breakdown, leaving a porous material with a negative duplicate of the original sacrificial template [35, 81, 89]. In order to prevent the porous structure from collapsing during the polymer removal step, which occurs during sintering and not pyrolysis, binders are typically incorporated into the mixture before the ceramic matrix is sintered [90].

The amount of gas produced during burning-out is substantially affected by the type of the sacrificial polymer, and the resulting ceramic foam can be either closed or open cell. However, because it is so challenging to keep the polymer spheres evenly dispersed, pore interconnectivity is typically quite poor [35, 60]. Scaffolds made using this technique can demonstrate exceptional durability in mechanical terms, on par with cortical bone, because of the presence of strong, dense struts [35]. A significant amount of the polymeric phase in the initial mixture is required to achieve a very porous structure. When this happens, a lot of gas forms when the ceramic heats, and that gas can expand and cause cracks in the body [58]. Therefore, the process must be carefully managed to prevent the development of flaws in the final component.

5.5 Sponge Replication

Since its invention, the sponge replication method has been widely adopted as the gold standard for making foam-like ceramic scaffolds for use in tissue engineering. The ease of use and adaptability of the technology, which may be used with any ceramic material that can be properly disseminated in a solution, are largely responsible for

its success. Bone tissue engineering scaffolds benefit most from having a network of ceramic networks (the struts) connects a series of interconnected gaps to form a reticulated open-cell structure, which closely mimics the 3-D trabecular architecture of cancellous bone. One of the main benefits of this technique is that the initial sponge can be readily trimmed and shaped to fit the deficiency in the tissue, meaning that, in theory, customised scaffolds may be made for each individual patient [88].

A synthetic (usually a polyurethane sponge) or natural (e.g., marine sponge) porous open-cell template is impregnated with ceramic powder that has been finely ground with a binding agent [e.g., poly(vinyl alcohol)], colloidal silica. Once the slurry has been evenly distributed throughout the sponge, it is squeezed to eliminate any surplus and allow the slurry to coat the sponge's individual struts. A porous ceramic with the same architecture as the sacrificial template (positive replica) is obtained by pyrolyzing the coated template after it has dried and then sintered at higher temperatures. Therefore, the polymeric template utilised has a direct effect on the morphological properties of the ceramic foam [91].

Creating a consistent coating on the polymeric structure is the most important part of the procedure. In particular, (1) impregnating suspension rheology and (2) its adherence to the struts of the polymeric sponge has a role. The suspension must be fluid enough to enter the sponge cells during compression and expansion, yet thick enough to prevent the leftover coating from draining. Notably, a structure with a particular degree of closed porosity is produced when extra slurry is not completely removed [81, 91]. Recently, the sponge replica method has been combined with the EISA method to create hierarchical porous bioactive glass scaffolds [55, 56], with a polyurethane foam and a surfactant serving as co-templates for the scaffold's macropores and mesopores, respectively. While the mesoporous structure gives these scaffolds a high bioactivity, it also makes them extremely fragile. Wu et al. [60] attempted to address the low compressive strength of these hierarchical porous constructions by depositing a silk coating on the strut, the results were insufficient to warrant their use in clinical settings.

5.6 Lyophilization (Freeze Drying)

Freeze-drying, scientifically referred to as lyophilization, is a commonly employed conventional method of fabricating ceramic scaffolds. This approach involves the cryogenic freezing of a suspension containing particles in a specific solvent, leading to the formation of a solid solvent. The freezing process occurs within a temperature range of -20 to -80 °C. The frozen material was subjected to sublimation using a lyophilizer, resulting in the formation of a solid scaffold characterised by a range of interconnecting macropores [7, 22, 26, 57, 82]. This sintering procedure subsequently enhances the mechanical strength of the constructs. The process of directional freezing of suspensions induces the growth of ice in a certain direction, hence leading to the creation of porous scaffolds characterised by an orientated microstructure. One advantage of an oriented microstructure is that it exhibits

increased scaffold strength in the direction of orientation, in contrast to a scaffold with a randomly oriented microstructure [92]. The freeze-drying technique is predominantly preferred in biomedical applications due to its utilisation of water solvents instead of other organic solvents for scaffold fabrication. However, it still poses challenges when it comes to creating well-defined structured scaffolds resembling vascular systems, which are commonly employed in biomedicine applications [2]. The utilisation of cytotoxic solvents in the blending process necessitates a substantial amount of energy. The scaffold that has been constructed necessitates multiple washings in order to eliminate the presence of harmful solvents. This process serves to reduce cell mortality and induce variations in pore diameters over an extended duration [32]. This process has been employed to prepare scaffolds using both 45S5 and 13–93 glass [93–95]. Nevertheless, scaffolds that are created from aqueous suspensions generally exhibit a lamellar microstructure, characterised by a pore width ranging from 10 to 40 μm . This pore size is generally deemed insufficient to facilitate tissue growth.

Past research have demonstrated that the introduction of an organic solvent, such as 1,4-dioxane, into the aqueous solvent [93, 96], or the utilisation of an organic solvent like camphene [94], leads to a transformation of the lamellar microstructure into a columnar microstructure and an augmentation in the breadth of the pores. Scaffolds composed of bioactive glass (13–93) have been successfully fabricated, exhibiting columnar microstructures and pore sizes ranging from 100 to 150 μm . Furthermore, apart from their enhanced strength, these orientated bioactive glass scaffolds have demonstrated the capacity to facilitate cellular proliferation and differentiation in laboratory settings, as well as tissue infiltration in vivo [93, 96].

5.7 Solid Freeform Method

Using a 3-D computer model as a starting point, “solid freeform fabrication,” also known as “rapid prototyping,” can produce scaffolds with a desired form and structure (including strut characteristics, pore arrangement, size, and distribution) through a series of layer-wise manufacturing strategies. To create this model, doctors used CT or MRI scans to rebuild the patient’s specific tissue abnormality in three dimensions. Using CAD, more specific information about the immediate surroundings may be crafted. Fabricating components with highly reproducible design and compositional variety is a major strength of SFF technology [97]. Functionally graded bioceramics and composites can be made with the use of these methods [98].

Scaffolds for use in tissue engineering can be made using a variety of SFF techniques [20]. Blending ceramic powders with a photocurable monomer is what makes stereolithography (SLA) possible. Layers are constructed immediately on top of previously cured layers by depositing more layers and scanning a UV laser over the top layer to cure the monomer, following the cross-section profiles of the CAD model. Sintering is then used to create the final product once the excess material that was not cured by the laser has been drained away [97]. It is well documented that SLA may

be used to fabricate HA and amorphous calcium phosphate scaffolds for hard tissue repair [20, 99]. A lithographic approach was recently proposed by Tesavibul et al. [100] to construct scaffolds produced from 45S5 Bioglass[®] with a highly organised pore layout. Sabree et al. [101] have described the stereolithographic construction of glass–ceramic scaffolds incorporating wollastonite with high-strength qualities. The process of selective laser sintering (SLS) uses a CO₂ laser beam to sinter successively thinner layers of ceramic powder to create three-dimensional objects. Powders are heated locally by directing a laser beam over the bed, a process guided by CAD data. This allows future layers to be constructed immediately on top of the sintered material, as the particles fuse together (Fig. 4). SLS technology has been used to manufacture scaffolds out of nano-HA, —TCP, and ceramic/polymer composites [97]. The construction of biphasic calcium phosphate scaffolds by SLS was also recently described by Gao et al. [22] (Fig. 5).

The third and potentially most useful technique is 3D printing, which was pioneered in the early 1990s at MIT. Using a printer head that travels in sync with the object profile being formed by a computer system, it joins powder granules in strategically placed areas by ejecting and depositing binder onto the powder surface. Then, a new coating of powder is applied using rollers. Once the entire object has been covered, the cycle is repeated with airflow to remove any loose powder. Sintering the pieces at high temperatures makes them sufficiently strong and allows the binder to be securely removed. Organic (such as starch-based) binders are also possible, as are water-based ones. With a regular 3D architecture and pore arrangement, 3D

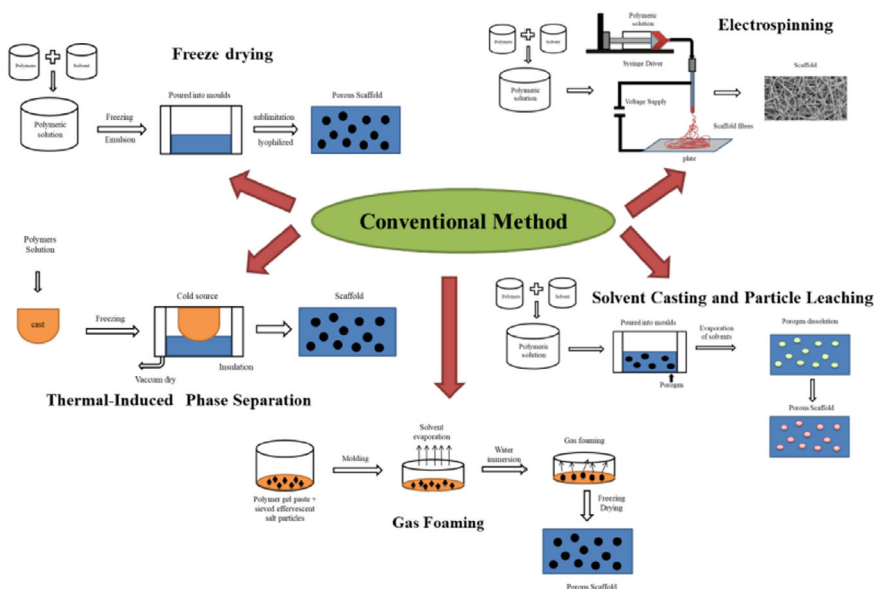


Fig. 4 Conventional methods of scaffold fabrication (reproduced with permission from [80])

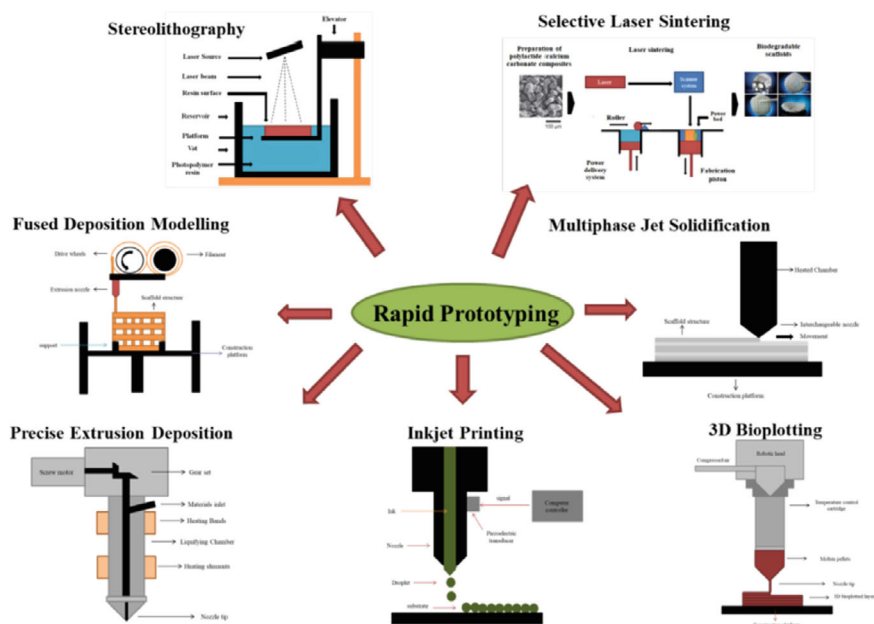


Fig. 5 Various advanced rapid prototyping techniques to fabricated scaffolds (reproduced with permission from [80])

printing has been used to process a wide range of ceramic materials for tissue engineering, including HA, calcium phosphates, calcium sulphate, bioactive glasses, and ceramic composites. However, extensive optimisation is required to process good quality parts with 3D printing for any new material/composition, and the associated cost of instrumentation is quite high.

Robotic casting and direct ink-write assembly are two examples of 3D printing methods. Bioactive glass scaffolds with a 3-D regular pore arrangement and exceptionally high mechanical performances in compression and flexure have been proposed for use in the replacement of cortical bone and load-bearing skeletal segments [16, 61]. MBG scaffolds have also been made via 3-D printing. Both Yun et al. [54] and Garcia et al. [21] used a double polymer template in conjunction with fast prototyping methods to create hierarchical 3-D porous MBG scaffolds. They created MBG scaffolds by combining MBG gel with methylcellulose, printing the mixture, and then sintering it at 500–700 °C to remove the polymer templates. Although the resulting MBG scaffolds have a homogeneous pore structure, the addition of methylcellulose, which results in some micropores, compromises their mechanical strength. Using a modified 3DP technique and poly(vinyl alcohol) as a binder, Wu et al. [60] reported an easy way to make hierarchical, multi-functional MBG scaffolds with tunable pore architecture, high mechanical strength, and the capacity to mineralize, making them ideal for bone regeneration. When compared to MBG (Mesoporous bioactive glass) scaffolds made utilising a

conventional polyurethane foam as a template, the compressive mechanical strength (16 MPa) of the 3DP MBG scaffolds obtained is approximately 200 times higher.

5.8 Short Glass Fiber Thermal Bonding

Glass fibres can be used to create porous 3D scaffolds. Porosity is created by the empty space between the fibres, which have sizes varying from the micrometre range to the millimetre range and are cut and deposited into a mold in a random pattern. After that, glass scaffolds can be made by thermally connecting (sintering) the glass fibres to stabilise the porous structure. By manipulating fibre size, sintering duration, and temperature, the scaffolds created in this way exhibit a high degree of pore interconnectivity [4, 102]

Other glass formulations, such as silicate (e.g., 13–93, 9–93) and borate (e.g., 13-99B3) bioactive glasses, as well as mixtures of them, have been proposed in the literature for fibrous scaffold production because 45S5 Bioglass® is difficult to draw into fibres without devitrification due to its narrow working range [103]. Available commercially as a graft material (porous morsels) for bone defect restoration is a porous scaffold made of glass fibres with nominal composition 11.1–12.0 Na₂O, 15.0–17.1 K₂O, 2.8–3.3 MgO, 12.7–15.2 CaO, 2.7–3.8 P₂O₅, 1.0–1.4 B₂O₃, 0.0–0.6 TiO₂, and 48.5–52.0 SiO₂ wt% is available commercially as a graft material for bone defect respiration [104].

6 Processing of Ceramic Composites Scaffolds

Electrophoretic deposition (EPD) is a versatile and promising method for producing bioceramic scaffolds coated with various polymers. Electrophoretic deposition (EPD) uses the electrophoresis mechanism, in which charged particles suspended in a solution move in response to an applied electric field, to deposit particles in an orderly form on a substrate, allowing for the development of both thin and thick films and coatings [105]. The EPD of mesoporous bioactive glass (MBG) onto a robust, almost inert glass–ceramic scaffold was described by Fiorilli et al. [106], yielding a bioactive high-strength load-bearing prosthesis in bone tissue engineering. Carbon nanotube (CNT) coatings produced via electrophoretic deposition (EPD) have been studied for their potential smart applications in tissue engineering. For instance, Meng et al. [100] cultured mesenchymal stem cells on 45S5 Bioglass®-derived glass–ceramic scaffolds, they found that the electrical conductivity of the CNTs could promote the proliferation and differentiation of the cell attached to the scaffolds, with or without electrical stimulation.

6.1 Additive Manufacturing

Complete control of architectural features like pore size, which has a major impact on the qualities of scaffolds, may soon be within reach thanks to additive manufacturing, a cutting-edge modern approach. This method is gaining popularity, especially for 3D-printed biopolymers due to the ability to create custom and intricate structures [15, 100]. Scaffolds must be designed and manufactured to imitate the structure of real bone because of the 3D architecture and geometry of native tissue settings. The term “3D printing” encompasses a wide range of techniques, from stereolithography (SLA) [5, 99, 101, 107], to fused deposition modelling (FDM) [2, 62, 81, 100], to selective laser sintering (SLS) and even to bioprinting. The implementation of these changes in the production of various materials is depicted graphically in Fig. 4.

Stereolithography is a widely recognised method of 3D printing that employs the principle of photopolymerization to fabricate three-dimensional objects. The SLA process employs a focused light source or a digital light projector operating at a certain wavelength, often ultraviolet (UV), to sequentially cure and solidify molecular chains in accordance with the STL file. Ceramic stereolithography encompasses the process of formulating a ceramic slurry that consists of ceramic particles characterised by micron/nanometric dimensions, a photocurable polymer, surfactants, and additives. The slurry is subjected to the irradiation of a focused light, which leads to the polymerization of the organic phase and the formation of ceramic particles that are encapsulated inside a cross-linked organic network [99]. In addition, the utilisation of additives like as dispersants can effectively address challenges inherent in the SLA (Stereolithography) process. For instance, dispersants can alleviate issues related to the dispersion of minute ceramic particles, which can otherwise lead to prolonged production time, reduced dimensional precision, and limited depth of cure. Additionally, it has been shown that the inclusion of additives in ceramic pastes serves to stabilise them and hinder the occurrence of particle agglomeration [15, 108]. In the context of 3D printing, heat treatment is commonly employed to eliminate the polymeric phase and solidify the ceramic particles present in the green portion.

The technique employed in the fabrication of HA/TCP composite scaffolds results in the development of scaffolds with a hierarchical controlled porosity structure [34, 45, 98, 109]. Polyfunctional acrylic resins and wax cast are types of photocurable polymers that are commonly employed in the manufacture of hydroxyapatite/tricalcium phosphate (HA/TCP) using this particular approach.

6.2 Inkjet Printing or Robocasting

The technique known as direct-ink writing or robocasting was initially developed by Joseph Cesarano and Cavert [110]. The ink deposition technique is utilised as a slurry-based 3D printing approach for the construction of three-dimensional structures featuring intricate geometries. During this procedure, a slurry consisting of

ceramic and organic materials is prepared to serve as the ink. Binders and lubricants are essential components of a suitable ink formulation for this particular technique, as they contribute to enhanced flow and convenience. Nevertheless, as a result of the limited concentration of ceramic granules present in the ink formulation, there is a susceptibility for quick evaporation, which subsequently causes the development of microcracks inside the 3D-printed component. Hence, the primary focus of the robocasting approach lies in the optimisation of the ink [111]. The ceramic composition of interest is dispensed through a nozzle and subsequently deposited layer-by-layer to construct the required structure. In order to remove the organic phase and enhance the mechanical integrity of the green structure, sintering is conducted at a comparatively elevated temperature [61, 111].

Extensive research has been conducted in the literature on the production of 3D porous HA/TCP composite scaffolds by the process of direct ink writing [112]. In order to achieve this objective, a ceramic ink that consists of a dispersed mixture of hydroxyapatite (HA) and tricalcium phosphate (TCP), biphasic calcium phosphate (BCP), or metastable calcium phosphate (CaP) powder is employed to fabricate a scaffold in a sequential layer-by-layer manner. Pluronic F-127 is commonly employed as a solution due to its characteristic of exhibiting a reverse thermal property. At low temperatures, this substance exhibits fluid-like properties, but at room temperature it transitions into a gel-like state. This gel-like state facilitates the convenient dispersion of the ceramic powder. Moreover, it is worth considering Darvan 821A as a strong contender for this objective, as it consists of ammonium polyacrylate and hydroxypropyl methylcellulose [113]. In addition, the utilisation of a polymeric porogen, which serves as an artificial defect, leads to increased porosity characterised by pore diameters that closely resemble those of the employed porogen. The robocasting process was employed to build a 3D printed HA/TCP scaffold with a porosity of 67%, using polymethylmethacrylate (PMMA) as the porogen [114]. Additionally, this technique presents a flexible strategy for the integration of pharmaceutical substances, wherein the sintering procedure can be substituted with a cross-linking stage to prevent the degradation of the encapsulated pharmaceuticals [115]. The process of organic combustion is often carried out within a temperature range of 400–600 °C, followed by sintering at temperatures of 1100–1200 °C. The scaffolds produced using this methodology had a porosity range of 45–67% and a pore size range of 150–620 µm.

7 Future Challenges in Ceramic Scaffolds and Composites

- *Biodegradability and Controlled Degradation:* Achieving the optimal balance between biodegradability and controlled degradation is an ongoing challenge. Fine-tuning ceramic scaffolds and composites to degrade at the right rate in line with tissue regeneration remains a priority. Controlling degradation can be particularly challenging in load-bearing applications where long-term stability is required.

- *Immunogenicity and Inflammatory Responses*: Managing immunogenicity and inflammatory responses to ceramic materials is a critical challenge. Developing ceramics that are less likely to trigger adverse reactions from the immune system and promoting a harmonious interaction between the implant and the host tissue are areas requiring further research.
- *Patient-specific Design and Mass Customization*: The trend towards patient-specific design in biomedical applications necessitates further developments in manufacturing techniques. Ensuring cost-effective and efficient methods for mass customization, especially in 3D printing, is a future challenge.
- *Optimized Mechanical Properties*: Balancing mechanical strength with porosity and ensuring that ceramic scaffolds meet specific mechanical requirements is a continuous challenge. These materials must withstand mechanical forces while providing an ideal environment for tissue in growth.
- *Wear Resistance and Fracture Prevention*: In orthopedic and dental applications, enhancing wear resistance and preventing fractures in ceramic composites is crucial. Developing materials that can withstand mechanical loads and resist wear over extended periods is an ongoing challenge.
- *Bioactive Integration*: The challenge of achieving superior bioactive integration of ceramics with host tissues will persist. Enhancing the surface design of ceramic materials to promote cell adhesion, proliferation, and differentiation is a subject of continued research.

8 Future Scopes

- *Advanced Material Development*: The future of ceramic scaffolds and composites in biomedical applications will involve the creation of advanced materials with superior properties. Research will focus on ceramics with improved biodegradability, customizable mechanical properties, and enhanced bioactivity. Novel composite materials with innovative combinations will also be explored.
- *3D Printing and Additive Manufacturing*: The integration of 3D printing and additive manufacturing techniques will become more prevalent. This technology will enable precise, patient-specific design and the fabrication of intricate ceramic structures that were previously challenging to produce.
- *Bioactive Coatings and Functionalization*: Future research will concentrate on enhancing the bioactive properties of ceramic scaffolds through coatings and functionalization. These technologies will facilitate more effective integration with host tissues, leading to improved therapeutic outcomes.
- *Multifunctional Composites*: The development of multifunctional ceramic composites will be a major focus. These materials will not only provide structural support but also offer drug delivery capabilities, sensing functionalities, or other advanced features. Multifunctional composites have the potential to revolutionize the field by addressing multiple healthcare needs in a single implant.

- *In Vivo Studies and Clinical Translation*: Extensive in vivo studies and clinical trials will be crucial for validating the safety and efficacy of ceramic scaffolds and composites. Bridging the gap between laboratory research and real-world applications will be vital for their widespread adoption in clinical practice.
- *Sustainability and Biocompatibility*: Sustainable sourcing of raw materials and environmentally friendly manufacturing processes for ceramics will gain prominence in response to heightened environmental awareness. Ensuring long-term biocompatibility and durability will continue to be a focus for researchers, aligning with the growing emphasis on eco-friendly practices in healthcare.

9 Conclusions and Future Perspectives

In this book chapter, we have comprehensively discussed the diverse and transformative world of ceramic scaffolds and composites in biomedical applications. These materials, with their exceptional biocompatibility, mechanical properties, and bioactivity, have emerged as key players in the field of regenerative medicine and medical device development. The versatility of bioceramic scaffolds and composites has significantly contributed to improving patient outcomes, reducing complications, and enhancing the overall quality of healthcare. We have discussed the challenges associated with achieving the ideal balance between biodegradability and long-term stability, managing immunogenic responses, and fine-tuning mechanical properties while maintaining the necessary porosity. These challenges, however, have not deterred the relentless pursuit of innovation in this field. Researchers and engineers have shown an unwavering commitment to addressing these issues and propelling the field of ceramic scaffolds and composites forward. The future of ceramic scaffolds and composites in biomedical applications holds tremendous promise, and we can anticipate several exciting avenues of development. In closing, the future of ceramic scaffolds and composites in biomedical applications holds great promise. These innovative materials, with their potential for customization, multifunctionality, and sustainability, are poised to revolutionize healthcare. As the field continues to overcome existing challenges and push the boundaries of material science, we can anticipate a future where ceramic scaffolds and composites play an even more significant role in enhancing the quality of life for countless individuals worldwide.

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Fiber and Ceramic Fillers-Based Polymer Composites for Biomedical Engineering



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Abstract Composites are essential materials with varying physical and chemical properties, used in various industries. Engineering performance of composites depends on the material, components, and interaction. Fiber-reinforced polymer is a composite material with superior mechanical and thermal properties, while biomedical composites include fiber-reinforced and particle-reinforced materials. Ceramic fillers, also known as fiber reinforcement or fiber additive, are solid particles made of ceramic materials that improve the mechanical, thermal, electrical, and other characteristics of composite materials. They are used in various sectors, including aerospace, automotive, electronics, and construction. Fiber reinforcement or fiber additive, are compounds that incorporate fibers into various goods to improve their qualities. They are commonly constructed of glass, carbon, agamid, or natural fibers such as cellulose and hemp. Ceramic fibers offer advantages such as strength, thermal stability, chemical resistance, electrical insulation, low thermal expansion, and abrasion resistance. However, ceramics are prone to cracking, processing difficulties, cost, limited design flexibility, and poor shock resistance. Ceramic fillers, fibers, and acrylics are prepared using various methods, including the sol–gel technique, solid-state reaction, hydrothermal synthesis, spray pyrolysis, electro-spinning, chemical vapor deposition, and spark plasma sintering. These methods are essential for creating ceramic products with controlled size, shape, and properties. Ceramic fillers, fibers, and acrylics are essential components in various industries, such as the juice industry, where they enhance packaging materials, equipment, and containers. They provide improved barrier properties, mechanical strength, and thermal stability, while fibers enhance filtration and reinforcement. Acrylics are used in coatings and sealants to

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protect packaging and maintain juice quality. In dentistry, ceramic fillers and fibers enhance dental restorative materials, while acrylics reinforce prosthetics and weakened tooth structures. Overall, composites play a crucial role in various industries, enhancing their properties, functionality, and longevity. Ceramic fillers and fibers are essential in various industries, such as aerospace, automotive, electronics, construction, and healthcare. They provide thermal insulators, dielectric materials, and coatings for corrosion resistance and high-temperature stability. In agriculture, they enhance structural integrity, durability, greenhouse construction, irrigation systems, and crop protection, contributing to modern agriculture's productivity, efficiency, and sustainability.

Keywords Chemical vapor deposition · Spark plasma sintering · Pyrolysis · Fiber-reinforced polymer · Ceramic fillers · Fibers · Acrylics

1 Introduction

Composites are distinct materials with varying physical and chemical properties, essential in daily life and various applications [1]. Engineering performance of composites depends on the material, components, and interaction. Fiber-reinforced polymer (FRP) is a composite material formed by a polymer matrix with fibers. The matrix provides superior mechanical and thermal properties, while reinforcement provides dispersed non-continuous phase. Fibers include glass, carbon, asbestos, paper, wood, and asbestos, while polymers include vinyl ester, epoxy, polyester thermosetting plastic, and phenol formaldehyde resins [2]. Engineering composites include cement, concrete, MMCs, ceramic, and polymer matrix composites, whereas biomedical composites include fibre and particle-reinforced materials [3]. Continuous matrix or base phase and Continuous reinforcing phase or filler materials make up composite materials. In order to improve qualities, these phases work together macroscopically. Composite materials include benefits including stronger fatigue strength, superior surface finishes, improved corrosion resistance, high tensile strength, and light weight. They are widely used in biomedical fields such artificial body parts, dentistry, and regeneration medicine. With the matrix phase being created from natural or synthetic polymers and the reinforcing elements being made from natural fibres, polymer composite materials exhibit good biocompatibility and can be employed in a variety of applications [4–6]. Natural fibres called “bio-fibers” are derived from biological sources, such as wood, regenerated cellulose, and crops. These composite materials are cheap, lightweight, biodegradable, recyclable, and biocompatible. Non-wood fibres like cellulose and lignin have greater physical and mechanical qualities than wood fibres, which have lower cellulose crystallinity. They have been employed since ancient civilizations and are used in industrial applications. Combining multiple materials, composite materials are able to maximize certain features and exhibit superior qualities over single components. Researchers are striving to create and construct composite materials that challenge conventional

materials like metals, alloys, and ceramic materials by having new mechanical behaviors, physical and chemical features, and processing technology. Most of the fundamental characteristics needed for body implants are present in composite materials, including a high specific elastic modulus, a strong strength to weight ratio, and excellent toughness to prevent crack propagation [7–10].

The fundamental function of ceramic fillers is to strengthen composite materials by more uniformly dispersing stress and enhancing strength, stiffness, and durability. They can also increase composites' resilience to wear, corrosion, and high temperatures, making them appropriate for use in harsh situations. Alumina, silicon carbide, and titanium dioxide are common ceramic fillers. Ceramic fillers are often blended with matrix material throughout the production process utilizing procedures such as mixing, compounding, or extrusion. Adjusting elements such as filler content, particle size, and distribution can alter the qualities of the final composite. Excess filler content, on the other hand, might cause issues such as increased viscosity during processing [11, 12].

Ceramic Fillers: Ceramic fillers are used in a variety of sectors, including aerospace, automotive, electronics, and construction. They can improve the structural integrity of aircraft components in aerospace. Ceramic-filled polymers in electronics can provide increased thermal conductivity for heat dissipation in electrical devices [13]. Ceramic fillers are used in the automobile industry to create lightweight yet sturdy parts that increase fuel efficiency and safety. Ceramic fillers are essential in the creation of new composite materials with improved characteristics. Because of their capacity to adjust mechanical, thermal, and electrical properties, they are critical in creating materials that can resist diverse and demanding circumstances in a variety of sectors. Ceramic fillers are solid particles comprised of ceramic materials that are used to improve the mechanical, thermal, electrical, and other characteristics of composite materials. These fillers are frequently used to improve the performance of composites made from polymer, metal, or ceramic matrices [14].

Fiber Filler: A fiber filler, also known as a fiber reinforcement or fiber additive, is a compound that incorporates fibers into various goods to improve their qualities. These fibers are generally constructed of glass, carbon, agamid, or natural fibers such as cellulose and hemp. The inclusion of fibers can enhance the mechanical, thermal, and other performance aspects of the host material dramatically. Fiber fillers are used in a variety of sectors, including construction, automotive, aerospace, textiles, and others. Fiber fillers are frequently used in the construction sector to increase the strength, durability, and fracture resistance of concrete and cementitious materials. The fibers assist in more uniformly distributing stresses throughout the material, lowering the possibility of cracks occurring and improving the overall structural integrity of the product. Fiber-reinforced concrete is widely employed in the construction of buildings, bridges, pavements, and other infrastructure projects. In the automotive sector, fiber fillers are utilized in the manufacturing of composite materials used for parts like bumpers, panels, and interior components. These fibers contribute to the light weighting of vehicles, leading to improved fuel efficiency and reduced emissions. Additionally, they enhance impact resistance and overall safety, making vehicles

more robust in collisions [15]. Advanced fiber fillers, notably carbon and glass fibers, are frequently used in aerospace applications. These materials are used to create parts for engines, wings, and fuselages of aeroplanes. Fiber-reinforced materials' superior strength-to-weight ratio is crucial for the aerospace industry because it enables the creation of light-weight yet robust structures that can resist the abrasive environment of flight. Fiber fillers are also useful in the textile sector [16]. Cotton, wool, and hemp have been used in textiles for generations, but synthetic fibers have gained popularity in recent decades due to their enhanced performance and adaptability. Polyester and nylon fibers are frequently mixed with natural fibers to improve the durability, flexibility, and moisture-wicking qualities of garments and other fabrics. Fiber fillers have also found use in the medical profession in a variety of applications. To facilitate tissue integration and healing, biocompatible fibers are used in medical implants and devices. These fibers may be programmed to deteriorate over time, enabling the body's natural healing mechanisms to take control while initially providing structural support. Fiber fillers significantly improve properties in various industries, including concrete, composites, textiles, and medical devices, contributing to safer, efficient, and sustainable products [17–19].

Ceramic Fiber Fillers: Fillers made from ceramic fibers are used to improve the mechanical, thermal, and electrical characteristics of ceramic composites. Ceramic composites are a type of advanced material composed of high-performance ceramic fibers embedded in a ceramic matrix. These fillers are critical to the overall performance and usefulness of the final composite material. This article will go through the definition, kinds, qualities, uses, and benefits of ceramic fiber fillers in depth. Ceramic fiber fillers are tiny, finely split particles of ceramic materials that are added to a composite matrix composed mostly of ceramics, polymers, or metals to change the characteristics of the material. These fillers frequently have unique features that are used to improve certain composite attributes like as strength, heat resistance, and electrical conductivity. Ceramic fiber fillers have different qualities depending on their composition and structure. These fillers, in general, have high melting points, great thermal stability, low thermal expansion coefficients, and strong chemical resistance. They are useful additions to ceramic composites due to their hardness, stiffness, and resistance to wear and corrosion [20, 21].

Acrylics: Acrylics are a versatile and popular type of paint that utilizes acrylic polymer emulsion as its primary binder. Since its inception in the mid-twentieth century, acrylics have gained immense popularity due to their ability to replicate various textures, offer a wide array of colors, and provide a quick-drying alternative to traditional oil paints. The name “acrylic” is derived from the chemical name of the resin used to create the polymer, which is composed of acrylic acid and methacrylic acid. Acrylic paints have a water-solubility when wet and become water-resistant when dried, allowing artists to manipulate the paint's consistency for various styles, from realistic portraiture to abstract expressionism. The rapid drying time of acrylics is a standout feature, allowing artists to work more efficiently, layer colors without waiting for extended drying times, and make alterations or corrections more easily. Acrylics can be applied to various surfaces, including canvas, paper,

wood, and fabrics, and are compatible with various additives and mediums. They can mimic the appearance of other media, such as watercolor or oil, while retaining their own distinct qualities. The color range of acrylic paints has expanded significantly, offering artists an extensive palette. Advancements in acrylic paint technology have led to the creation of acrylic gouache, a hybrid medium that combines the opacity of traditional gouache with the versatility of acrylics. Overall, acrylics have revolutionized the world of painting with their fast-drying properties, wide range of colors, and adaptability to various styles and techniques [22, 23].

2 Advantages and Disadvantages of CFFA

Advantages Ceramic Fillers [24, 25]

Strength—Ceramic fillers may greatly improve the mechanical characteristics of composite materials, resulting in high strength and stiffness.

Thermal Stability—Ceramics offer exceptional resilience to high temperatures, making them ideal for applications requiring intense heat or thermal cycling.

Chemical Resistance—Ceramic fillers are frequently resistant to corrosive chemicals, acids, and bases, which adds durability to the composite material.

Electrical Insulation—Ceramics are often good electrical insulators, which can be useful in situations needing electrical insulation.

Low Thermal Expansion—Ceramics' low coefficient of thermal expansion can assist decrease dimensional changes caused by temperature swings.

Abrasion Resistance—Ceramic-filled composites can provide better resistance to wear and abrasion, making them appropriate for high-wear applications.

Disadvantages Ceramic Fillers

Brittleness: Because ceramics are inherently fragile, they are prone to cracking or fracturing when subjected to impact or bending.

Processing Difficulty: Due to their hardness, ceramic fillers can be difficult to process into composite materials, necessitating specialized processes and equipment.

Cost: Ceramic materials might be more expensive than other filler alternatives, affecting the overall cost of the composite product.

Limited Design Flexibility: Ceramics are generally difficult to form and mold, restricting design options as compared to other fillers.

Poor Shock Resistance: Ceramics' brittleness can result in low shock resistance, making them unsuitable for applications where impact resistance is required.

Advantages Ceramic Fibers [26, 27]

Reinforcement: Fibers, such as glass or carbon fibers, can considerably improve a material's strength and mechanical qualities when integrated.

Weight: Fiber-reinforced materials may maintain high strength while being lightweight, which is advantageous in situations where weight is critical.

Flexibility: These materials can be flexible and resistant to bending or deformation depending on the fiber type and arrangement.

Corrosion Resistance: Certain fibers, such as glass fibers, are corrosion resistant, giving resilience to the material.

Disadvantages Ceramic Fibers

Anisotropy: Fiber orientation can result in anisotropic qualities, which means the material's properties change with direction, which might be undesirable in some instances.

Complexity of Processing: Incorporating fibers into a matrix material necessitates precise processing processes to achieve uniform distribution and good bonding.

Cost: High-performance fibers can be costly, thus raising the material's overall cost.

Environmental Impact: The manufacture and disposal of some fiber types, such as carbon fibers, raises environmental problems.

Advantages Ceramic Acrylics [28]

Weather Resistance: Acrylics are recognized for their exceptional weather resilience, which makes them appropriate for outdoor applications.

Transparency: Acrylics can be translucent, making them perfect for applications requiring clarity or visibility.

Processing: Acrylic materials are generally easy to produce, which allows for efficient production and molding.

Color Retention: Acrylics have the ability to hold their colour over time, keeping their look even after prolonged exposure to sunshine.

Disadvantages Ceramic Acrylics

Scratch Sensitivity: Acrylic materials are more susceptible to scratching than other materials.

Impact Resistance: While acrylics are robust, they are not as impact-resistant as other materials like as polycarbonate.

Thermal Instability: Acrylics have poorer heat resistance than certain other materials, which limits their usage in high-temperature applications.

Flammability: Acrylics are more flammable than certain other polymers, which might be a problem in certain settings.

3 Methods of Preparations

Ceramic Fillers, Fibers and Acrylics

1. ***Sol–Gel Technique***: entails the hydrolysis and condensation of precursor materials to make a sol, which is subsequently gelatinized to form a ceramic substance. It's a flexible approach that allows for exact composition and morphological control. The sol–gel method is a versatile technique for preparing ceramic materials, including fillers, by converting precursor solutions into a gel-like intermediate state and solid ceramic material through controlled drying and heating processes. The process involves dissolved metal alkoxides in a solvent, hydrolysis reactions, polymerization and gelation, aging and ripening, drying, and calcination. The gel's structure evolves, and the particles within it grow and rearrange, affecting the final properties. Controlled drying is essential to maintain the integrity of the gel's structure. The resulting ceramic material is characterized using techniques like X-ray diffraction and SEM, and can be used as fillers in various applications, such as composite materials and coatings. The sol–gel method allows for customization of parameters, making it highly versatile for various applications [29, 30].
2. ***Solid-State Reaction***: In this process, solid powders of different reactants are combined and heated at high temperatures to initiate a chemical reaction that results in the formation of the desired ceramic phase. The solid-state reaction method is a widely used process for producing ceramic fillers with tailored characteristics for specific applications. It involves selecting appropriate raw materials with the desired chemical composition, weighing and mixing them, sample compaction, sintering, cooling, and characterizing the final product. The success of this method depends on factors like raw material purity, mixing process, sintering conditions, and desired properties. This method is suitable for producing ceramic fillers with tailored characteristics for ceramics, composites, and advanced materials [31].
3. ***Hydrothermal Synthesis***: High pressure and increased temperatures in an aqueous solution are utilized under hydrothermal settings to stimulate the formation of ceramic crystals with regulated size and shape. The hydrothermal synthesis process involves preparing precursor materials, which react under hydrothermal conditions to form the desired ceramic filler. These materials are typically in the form of soluble salts, oxides, or other compounds. The precursor materials are mixed with a water-based solvent and placed in a high-pressure vessel called an autoclave. The autoclave is heated to the desired temperature and pressure, and the process is controlled by temperature, pressure, reaction time, and precursor concentrations. The hydrothermal environment promotes crystal growth, influencing the size, shape, and properties of ceramic particles. After the reaction time, the autoclave is cooled to prevent unwanted phases or structural defects. The resulting ceramic particles are collected from the solution and may undergo additional washing, drying, and calcinations steps to enhance

their properties. This process is widely used in industries like materials science, electronics, and catalysis for producing high-performance ceramic materials tailored to specific applications [32].

4. **Spray Pyrolysis:** A precursor solution is sprayed over a heated substrate in this approach. The solvent evaporates, leaving a deposit, which is then heated to produce a ceramic coating. Spray pyrolysis is a technique used to produce thin films, powders, or nanoparticles of various materials, including ceramic materials. It involves controlled decomposition of precursor solutions in the form of fine droplets. The process involves precursor solution preparation, atomization, droplet drying, thermal decomposition, particle collection, and characterization and testing. The process involves dissolving precursor compounds in a solvent, atomization, droplet drying, thermal decomposition, particle collection, and characterization using techniques like X-ray diffraction, SEM, and TEM. The process parameters, such as precursor concentration, atomization rate, furnace temperature, and gas atmosphere, need to be optimized to achieve desired ceramic filler properties. Variations in the spray pyrolysis process may exist depending on the material, equipment, and intended application [33].
5. **Electro-spinning:** A polymer solution containing ceramic precursors is electrostatically spun into nano-fibers in this approach. These nano-fibers may be heat-treated to become ceramic fibers. Electro-spinning is a technique used to create nanofibers from various materials, including ceramics. The process involves setting up a syringe with a ceramic precursor solution, creating an electric field between the spinneret and collector, and forming a liquid jet. This jet forms and solidifies the ceramic material, forming nanofibers. Fiber collection is then performed on a grounded collector, with morphology and alignment controlled by parameters like voltage, flow rate, and collector type. Post-processing steps may include heat treatment to remove solvents and organic components, and crystallization and ceramic phase formation. Ceramic nanofibers have various applications, including filtration, catalysis, sensors, and reinforcement in composites. The success of the electro-spinning process depends on the chosen precursor materials, solvent, voltage, flow rate, and other parameters [34–36].
6. **Chemical Vapour Deposition (CVD):** CVD is the chemical reaction of gaseous precursors on a substrate that results in the formation of a ceramic material. It is used to deposit thin ceramic coatings onto diverse surfaces. Chemical Vapor Deposition (CVD) is a technique used to produce ceramic materials by depositing thin films or coatings onto a substrate. It involves the chemical reaction of vapor-phase precursor compounds to create solid materials on a substrate surface. The process involves substrate preparation, precursor introduction, thermal decomposition, chemical reaction, film growth, and film thickness control. The process can be energy-driven through methods like resistive heating, induction heating, and microwave heating. Byproducts and waste are generated during the process, which can be carried away by the carrier gas. CVD offers precise control over film composition, thickness, and uniformity, making it widely used in semiconductors, coatings, and advanced materials

like ceramic fillers for composites. However, CVD can be complex due to the need for precise control over temperature, pressure, precursor flow, and reaction kinetics [37].

7. **Spark Plasma Sintering (SPS):** SPS is a fast consolidation technology in which a powder compact is subjected to pulsed electric current and pressure, enabling for rapid densification of ceramic materials. Plasma Sintering (SPS) is a consolidation technique used to prepare ceramic materials with improved properties, particularly for producing dense and high-quality ceramics. The process involves the application of pulsed direct current and uniaxial pressure simultaneously to rapidly heat and consolidate ceramic powders. The equipment used in SPS includes a graphite die, punches, a power supply unit, and a vacuum or controlled atmosphere chamber. The process involves loading ceramic powder into the die, assembly, heating, pressure application, and sintering. SPS achieves high heating rates, reducing the time required for sintering, resulting in fine-grained microstructures with improved mechanical properties. It is suitable for various ceramic materials, including oxides, non-oxides, and composites. SPS is used in various industries, including aerospace, electronics, energy, and biomedical applications, producing high-performance components like cutting tools, biomedical implants, and electrical insulators [38].
8. **Template-Assisted Methods:** These include the use of templates or molds to shape the ceramic precursor material into the required structure prior to sintering. Replica molding and sacrificial tinplating are two examples. Template-assisted methods are used to synthesize ceramic fillers with controlled size, shape, and properties, which are used in various industries like catalysis, electronics, and materials science. The process involves selecting a template material, coating the template, impregnation and adsorption, template removal, heat treatment (annealing), and template-derived ceramic filler. The resulting ceramic fillers are characterized using techniques like SEM and XRD to ensure they meet desired specifications. These fillers can be used in various applications, such as reinforcement in composite materials, catalytic supports, and electronic components. The success of the template-assisted method relies on careful selection of template material, precursor solution, heat treatment conditions, and characterization techniques [39].
9. **Melt Infiltration:** In this procedure, molten metal is infused into a porous ceramic preform. After solidification, a composite material with increased mechanical characteristics is created. Melt infiltration is a method for preparing ceramic matrix composites by infiltrating a molten metal into a porous ceramic preform. The process involves preparing a porous ceramic preform, selecting an infiltrant, preheating the preform, infiltrating the metal, solidifying and cooling, post-processing, and quality control. Melt infiltration offers tailorable properties, improved mechanical strength, and enhanced thermal properties compared to traditional ceramics. However, careful control of temperature, atmosphere, and processing parameters is necessary to achieve successful infiltration and desired composite properties [40].

10. **Slip Casting:** Slip Casting is the process of pouring slurry of ceramic powder and a liquid binder into a mold. The liquid is evacuated, leaving a solid green substance that may be treated and sintered further. Slip casting is a popular method for creating ceramic objects, involving a mixture of clay, water, and other additives. The process involves finely ground clay particles, controlled viscosity, deflocculation, mold preparation, pouring, casting time, drying, de-molding, finishing, and glazing. The clay particles form a layer on the mold's inner surface, determining the final thickness of the ceramic object. The mold is left to sit for a specific period, absorbing water and forming a thinner slip. The excess slip is poured out, leaving the clay layer on the mold to dry. The green ware is then removed from the mold, requiring additional drying and firing stages to become a finished product. After de-molding, rough edges or imperfections are smoothed out or refined using tools or sandpaper. Bisque firing is then used to transform the green ware into porous bisque ware, which can be dipped, sprayed, or brushed with glaze. The final firing is at a higher temperature to fuse the glaze particles into a glassy coating, making the ceramic body strong, durable, and waterproof [41].
11. **Extrusion:** Extrusion is the process of forcing ceramic pastes through a die to generate continuous shapes. After that, the forms are dried and fused to create ceramic goods. The extrusion method is a widely used technique for preparing ceramic fillers. It involves selecting appropriate raw materials, formulating the composition, mixing, de-airing, and extrusion. The mixture is fed into an extrusion machine, which uses a rotating screw to force the material through a specially designed die. The die design determines the shape and size of the extruded ceramic, with various shapes available. The extruded pieces are then dried to remove excess moisture, fired in a kiln at high temperatures, and cooled down to prevent cracks or warping. The final ceramic fillers may undergo finishing processes like glazing, polishing, or surface treatments. Quality control measures are taken throughout the process to ensure the final product meets desired specifications and properties. This technique is widely used in industries like ceramics, construction, and manufacturing for its precision control over shape and size, high production rates, and ability to create intricate cross-sectional designs [42].
12. **Powder-Liquid Mixing:** The most frequent approach is powder-liquid mixing. A liquid acrylic resin is blended with ceramic powder (often a combination of glass ceramics or zirconia). The slurry is then put in a mold or onto a prepared tooth structure to polymerize and solidify. The powered liquid mixing process for preparing ceramic acrylic involves gathering ingredients, measuring the required amounts, choosing a mixing container, starting at low speed, gradually adding ceramic powder, mixing until a homogeneous mixture is achieved, scraping and re-mixing, adjusting viscosity, performing quality checks, degassing (optional), resting for a short period, and conducting a final quality inspection. The process may vary depending on the type of ceramic powder and binder used and the intended application. The final quality inspection ensures the mixture meets the required specifications for the intended application. The process can

be applied to surfaces using casting, molding, or coating methods, following appropriate curing and drying procedures [43].

13. **Layering Technique:** Multiple layers of ceramic-filled acrylic are applied in this procedure. Each layer is independently polymerized, providing for complete control over the final product's color and translucency. This method is frequently utilized to create very cosmetic dental restorations. The layering technique for ceramic acrylic preparation involves layering different shades of ceramic material on a tooth-shaped acrylic base. This process involves selecting the right shade, applying an opaque layer, applying a dentine layer, and applying a translucent layer. Dental technicians use stains and characterization materials to mimic natural features. The layered ceramic-acrylic restoration is fired in a dental furnace at high temperatures, fuses the ceramic layers together, and then refined and polished. After firing, the restoration is tried in the patient's mouth to assess fit, appearance, and bite. Once approved, the restoration is permanently cemented onto the tooth structure using dental adhesive. This technique requires skill and expertise and aims to create restorations that blend seamlessly with the patient's natural dentition, ensuring a natural appearance and functionality [44].
14. **Computer-Aided Design/Computer-Aided Manufacturing (CAD/CAM) Technology:** This technology enables for the accurate manufacture of dental restorations. The ceramic acrylic material may be milled from a pre-sintered block before being sintered to its ultimate hardness in a high-temperature furnace. Ceramic acrylic is a hybrid material that combines the properties of ceramics and acrylics, resulting in a material with aesthetic appeal, strength, and flexibility. The CAM process involves computer software, precision machinery, and modern material science. The design is created using CAD software, which dictates the dimensions, aesthetics, and functionality of the desired part. CAM software converts the design into machine instructions, setting parameters like tool paths, speeds, and feed rates based on the material properties. Most ceramic acrylic components are milled using CNC machines, which precisely cut and shape the material based on the CAM software. Sintering is required for some ceramic components, while finishing involves polishing, painting, or surface treatments. Quality control measures ensure the part meets specifications and is free from defects. Ceramic acrylic can be used in various applications, including dental prosthetics, jewelry, and automotive components [45].

4 Material Used for Preparation of Ceramic Fillers, Fibers and Acrylics

Ceramic fillers are substances that are added to ceramics or other composite materials to improve their qualities. They are mixed with the underlying material to increase properties like as strength, hardness, thermal stability, and others. There are several types of ceramic fillers used, each with its own set of properties:

Silica (SiO_2): Silica is typical ceramic filler that improves the mechanical and thermal characteristics of ceramics. It is frequently used to improve hardness and resistance to thermal shock. There are many benefits to using silica (silicon dioxide, SiO_2) as a filler or nanofiller in polymer matrix composites, including improved biocompatibility and bioactivity. These substances promote biological processes for bone tissue applications, including calcium phosphate synthesis, porosity, and bio-resorption rate. SiO_2 particles metabolism and dissolution must be understood in order to fully comprehend their properties. SiO_2 nanoparticles in polyesters have benefits over other nano-fillers and show characteristics that make them perfect grafting and scaffolding materials. During the manufacturing of nano-composite, covalent connections can be created between macromolecular chains and fillers, enhancing stability, adhesion, and mechanical properties. The establishment of covalent connections between the hydroxyl end groups of polymer PBSu and the surface silanol groups from SiO_2 nanoparticles has been confirmed by nuclear magnetic resonance spectra (^{13}C -NMR) research leading to a substantial improvement in mechanical properties. The physicochemical properties of nano- SiO_2 in different forms, such as nanotubes and nanoparticles, also change, affecting the hydrophilic character of the material. The fact that silica is included into PLA/ SiO_2 nano-composites degrades more quickly than pure PLA suggests that silica speeds up PLA's biodegradation in the nano-composites. Silica may enhance water and enzyme molecules' attacks on the ester groups of PLA chains, lowering the polymer's molecular weight and causing the materials to disintegrate. Silica nanoparticles added to the polymer matrix encourage osteoblast-like cells to connect with surrounding tissue, boosting cell survival. While ortho-silicate acid ($\text{Si}(\text{OH})_4$) induces type I collagen synthesis in human osteo-blastic cells and cell differentiation, silicon can also play a role in bone formation and mineralization. The results are consistent with reports of silica materials utilised for bone regeneration, even though no discernible effects of SiO_2 incorporation on cell behavior could be seen. Mesoporous silica has the capacity to encapsulate pharmaceuticals and biological agents due to its regular, parallel pores, high specific surface area, low density, and good biocompatibility. The usage of these particles in pharmaceutical applications, especially in drug delivery systems, is widespread. The release properties of the composite may be impacted by the drug's incorporation into the silica xerogel or the polymer matrix during the sol-gel process. Core-shell architectures enhance regulated drug release and control of drug release by creating strong connections between silica and polymer. Mesoporous silica scaffolds may be produced by electro-spinning, conventional methods, or rapid prototyping. The ability of cells to retain osteo-blast like cells and express osteo-protegrin genes is improved by adding silica particles to hydrogels like CS or alginate. Nanosilica improves biological characteristics, biomineralization potential, and stiffness in polymer matrix composites without reducing mechanical strength. Potential uses of this strategy include bio-mineralization and cells that resemble bones [46–50].

Calcium carbonate: Common filler used in polyolefins (POs) to replace resin in applications is calcium carbonate (CaCO_3). HDPE bottle and packaging manufacturers utilize it to cut the price of raw resin. Increasing stiffness, hardness, and dimensional stability with fine CaCO_3 particles is possible, but it may also reduce tensile and impact strength qualities. CaCO_3 makes up 95–98% of commercial calcium carbonate products; the remaining percentage is made up of metal oxides. In comparison to untreated POs, treatment of CaCO_3 particles enables greater dispersion, simpler processing, and stronger impact forces. Stearic acids derived from fatty acids, maleic anhydride-grafted polymers, and silane-based compounds are suitable for coating CaCO_3 particles [51].

Alumina (Al_2O_3): Common ceramic filler is alumina. It boosts mechanical strength, wear resistance, and electrical insulation. Building materials, refractory materials, electrical and heat insulators, and electrical insulation all depend on the ceramic metal oxide alumina. It is a common choice for catalysts, catalyst support, and adsorbents due to its high strength, corrosion resistance, chemical stability, low thermal conductivity, and strong electrical insulation. To create alumina and corundum, preparation entails heating tri-hydroxides, gibbsite, and bayerite to temperatures above 1000 °C. These transition alumina are ideal for adsorbents, catalysts, catalyst support, and filtration membranes due to their high porosity, surface areas, and acidic characteristics. Several procedures, including melt growth techniques, extrusion, electro spraying, and electro-spinning, can be used to construct them into alumina fibres. The high surface areas of transition alumina are due to the presence of irregular pores, mainly microspores with diameters less than 2 nm [52, 53].

Zirconia (ZrO_2): Zirconia fillers are recognized for their exceptional strength and hardness, making them ideal for applications requiring long-term endurance. It has three crystal structures: cubic (c- ZrO_2), tetragonal (t- ZrO_2), and monoclinic (m- ZrO_2). Synthesis of t- ZrO_2 at moderate temperatures prevents expansion. Nano- ZrO_2 powders have advanced applications in refractories, abrasives, ceramic pigments, oxygen sensors, and catalytic materials. Wet-chemical synthesis approaches are used, but physical methods cannot meet nano size requirements and gas-chemical methods are too expensive for practical production. High purity ZrO_2 is a biomaterial with excellent natural white color, toughness, strength, and corrosion resistance, making it suitable for dental ceramics and biocompatible implant materials. However, processing and formation are challenging due to its high strength. Nano- ZrO_2 nanopowders offer various applications, such as filling, coating, and sintering raw materials. They considerably increase shear bond strength, flexural strength, and fracture toughness. They can also act as a porous covering to increase biocompatibility. Dental ceramics, implants, membranes, basements, and tissue engineering all use nano- ZrO_2 biomaterials to improve osseointegration by surface treatment and bio-activation [54].

Talc: Common PO filler, talc is a naturally occurring hydrated magnesium silicate mineral with variable effects on PE and PP characteristics. Because of the high aspect ratio of its plate-like particles, it improves modulus and decreases impact

strength. Talc comes in particle sizes ranging from 1 to 100 m and is utilised at up to 50% loading. For high-impact automotive TPO applications, fine talcs are essential. The bulk density of fine lamellar talc increases with talc grades that “compact” the bulk talc, minimizing trapped air and enhancing processing handling and feeding. Compacted talc has a bulk density that is nearly three times more than that of typical fine talcs, enabling melt processing of 30%-talc PP to be increased by 300%. There are “ultrafine” grades of talc with higher aspect ratios that can be used in car bumpers, body panels, dashboards, and interior trim to enhance the characteristics of PP and PP-based TPOs. These talc grades enhance the talc’s layered structure by lessening the impacts of sub-2- μ m talc particles’ stiffening and reinforcement. Rio Tinto Minerals and IMIFabi Spa have developed improved milling techniques that result in delaminated talc that keeps its platy structure and characteristics down to 1- μ m diameters. This compacted talc enables lighter PP and TPO parts while maintaining the same qualities as typical fine talc compounds at larger loadings. The benefits of each filler are combined and their shortcomings are covered up by mixing talc and calcium carbonate into one substance [55].

Titanium Dioxide (TiO_2): TiO_2 is used in ceramics to provide color and opacity while also improving mechanical qualities. Rutile, anatase, brookite, and TiO_2 (B) are the four different structural types of titanium dioxide (TiO_2), which is the metal’s natural oxide. TiO_2 (II) with the $-\text{PbO}_2$ structure, TiO_2 (H) with hollandite, baddeleyite with ZrO_2 , and cotunnite with PdCl_2 are examples of high-pressure forms. The chemical industry primarily produces rutile and anatase as microcrystalline minerals. Different morphologies of TiO_2 , such as nanoparticles, nanowires, nanotubes, and mesoporous structures, can be created. Hydrothermal/solvothermal, sonochemical, electrochemical, solgel, microwave field, and vapour phase are a few examples of synthetic techniques. As particle size reduces, TiO_2 specific surface area grows, affecting agglomeration behavior and interfacial characteristics. Polymer- TiO_2 nanocomposites can be improved through research that aims to reduce agglomeration and enhance distribution [56, 57].

Calcium Phosphate: Due to its chemical makeup and biocompatibility, calcium phosphate ceramics are frequently employed as alternatives to bone grafts. However, because of their fragility, their therapeutic applications are restricted to the skeleton’s non-load bearing areas. Due to their bioactivity, biodegradability, and biological responsiveness, calcium phosphates are utilised in bone repair. The Ca/P ratio, crystallinity, and phase composition affect bioactivity, degradation behavior, and osteo-conductivity. Tri-calcium phosphates are more soluble while synthetic HAP is more stable. Depending on the weight ratio of the stable/degradable phases, biphasic calcium phosphate (BCP) displays intermediate characteristics. Substituted CaP ceramics are a new development in the manufacture of calcium phosphates, particularly HAP. When compared to their parent materials, calcium phosphate ceramics are less soluble and bioactive, which results in altered biological reactions. While some are osteo-inductivity, the majority are osteo-conductive. Ceramics such as HAP, TCP, and BCP are frequently employed in biological applications. The development of calcium phosphate-containing composite materials, especially polymer-matrix

composites, is being pursued. Biphasic calcium phosphate ceramics are two-phase materials that combine the osteo-inductivity of -TCP with the low solubility and osteo-conductive nature of HAp. By adjusting the HAp/-TCP ratio, it is possible to alter the bioactivity, rate of resorption, and mechanical characteristics of these ceramics. Biphasic calcium phosphate ceramics can be altered by substituting ions, like including Sr, which accelerates the proliferation and differentiation of MG63 and HOS osteo-blast like cells. Additionally boosting biodegradation and bioactivity, magnesium substitution raises osteo-conductivity both in vitro and in vivo. The biodegradable synthetic polymers and copolymers PCL, PLLA, PLGA, collagen, and gelatin-pectin can all be modified using BCP ceramics. Compressive strength and Young's modulus of PLLA-based composites have improved with modifications. Higher compressive strength can also be achieved by directly grafting L-lactide onto the surface of BCP micro particles. A collagen/BCP composite (OsteonTM II collagen, available commercially) demonstrated good osteo-conductive characteristics with delayed rate of resorption, maintaining bone tissue regeneration space. It offers a consistent release profile, making it a good choice for a carrier of recombinant human BMP-2. In-vitro and in-vivo experiments revealed that the gelatin-pectin/BCP nano-composites scaffold was effective at promoting cell proliferation and the production of new bone [58–69].

Wollastonite: Wollastonite is calcium and silicon oxide mineral used as filler in reinforcing materials, increasing tensile and flexural strength, dimensional stability, and mold shrinkage. The size of its needle-like particles ranges from 5 to 20 m. In place of talc or glass fibre, the nonhazardous mineral fibre wollastonite has gained popularity as filler. Although it has characteristics that are comparable to those of glass fibres, its fiber-like shape can harm processing machinery. Automotive panels, housings, door handles, and appliances can benefit from the usage of wollastonite to reinforce PE and PP. It has stronger tensile, flexural, flexural modulus, and impact strength and equivalent mechanical characteristics to 15% talc-filled PP. Wollastonite offers the same HDT, flex modulus, and tensile strength as 20% glass fibre alone and can also be used as a partial replacement for glass fibre. Improved dispersion, processing, impact resistance, surface gloss, dimensional stability, and scratch resistance qualities result from surface treatment with silane-based coupling agents [70–74].

Magnesium Oxide (MgO): Magnesium oxide can improve ceramic refractoriness and electrical insulation. A key inorganic ceramic material with superior optical, thermodynamic, electrical, electronic, mechanical, and chemical properties is magnesium oxide (MgO). It can be used as a catalyst, an additive, air purification adsorbent, a metal stabilizer, clear filler, a surface conditioner, a biomedical application, or to clean up toxic waste, among other things. Spinning disc reactors, chemical reactions, reverse micellar, laser ablation, and thermal decomposition are a few of the traditional processes used to create MgO nanoparticles. The sol–gel process is easier and provides high purity, greater specific surface areas, and smaller particle sizes. This study focuses on the synthesis of MgO nanocrystals with weak bases NH_4OH and Na_2CO_3 and strong bases KOH and NaOH with a range of normalities. X-ray

diffraction (XRD) and SEM analysis were used to characterize the production of MgO nanoparticles and identify their shape and crystal structures [75].

Barium Sulphate (BaSO_4): Ceramics typically utilize this filler to increase density and radiation absorption capacity. Due to its high specific gravity, X-ray opacity, inertness, and whiteness, barium sulphate, generally known as barite, is commonly used filler in a variety of industries. It has been applied to research crystal growth, precursor mixing, precipitation mechanisms, and morphology. Due to their distinctive structural, electrical, optical, magnetic, and chemical capabilities, nanoparticles with nanoscale dimensions are attracting growing amounts of scientific and technological interest. However, due to their high surface activity and ease of adsorption, nanoparticles can readily combine into bigger ones despite the difficulty in producing pure ultra-fine particles. Current research in nanomaterials focuses on regulating particle size, preventing aggregation, and redistributing them throughout the medium. Current research focuses on synthesis of smaller particles and inorganic additive powders with good dispersing properties in water for stable suspensions [76, 77].

Glass fibers: Ceramics are filled with glass fibres to increase their tensile strength and hardness. The capacity of bioactive glasses (BGs) to regulate biological and chemical characteristics at the molecular level makes them useful materials for tissue engineering applications. Sol–gel or melt-quenching techniques can be used to create these glasses, with gel-derived BGs exhibiting enhanced bioactivity and cellular responsiveness. Controlled phase composition, structure, texture, microstructure, and surface chemistry are all possible using the sol–gel method. To enhance biological responsiveness and surface reactivity, BGs can be doped with therapeutic oxides and trace elements. For tissue engineering applications, research is concentrated on creating silicate and borate/borosilicate BGs as well as resorbable phosphate glasses. Silicate bioactive glasses (SBGs) are frequently utilised as fillers in polymer-based composites for bone tissue engineering and are the subject of extensive research for biomedical applications. Hench et al. created the first melt-derived silicate SBG, Bioglass® 45S5, which is frequently employed as a modifier for biodegradable synthetic polymers and copolymers. In addition to their bonding abilities, SBGs also produce ionic dissolution products, osteoblastic and stem cell gene expression, stimulate angiogenesis, have antibacterial and anti-inflammatory characteristics, and release calcium. Chemical composition, volume fraction, size, and distribution of a bioactive phase can all affect how bioactive a composite is. Glass modifiers can enhance the bioactivity of poly (L-lactide)-based scaffolds by improving composite bioactivity [78–84].

Carbon Fibres: Carbon fibres can be used to ceramics to increase mechanical qualities while keeping the weight low. Carbon fibers offer an attractive alternative to traditional implantology materials like stainless steels and titanium alloys. They offer low thermal conductivity, easy shape formation, and resistance to corrosion and ion diffusion. Mechanical properties, such as tensile strength and resistance to UV radiation, can be further enhanced with lacquer layers and phenolic resins. However,

carbon fibers have drawbacks, such as low UV radiation strength and resistance to temperatures above 200 °C [85, 86].

Silicon Carbide: Silicon Carbide fillers are recognized for their strong thermal conductivity and outstanding mechanical qualities, making them ideal for high-temperature applications. With great hardness, strength, chemical and thermal stability, melting point, oxidation resistance, and erosion resistance, silicon carbide is a versatile non-oxide ceramic. It is perfect for abrasion and cutting applications as well as high power, high temperature electronic components. Although the classic Acheson process, which is based on carbothermal reduction, has been commercialized, it has a lot of steps, requires a lot of energy, and uses subpar materials. Alternative techniques for producing SiC have been documented, including mechanical alloying, liquid phase sintering, sol–gel, physical vapor deposition, and chemical vapor deposition. Based on the synthesis techniques, the ensuing mechanical, structural, and electrical properties are reviewed. Silicon carbide (SiC) is a wide band gap semiconductor suitable for high temperature, power, and radiation conditions. It has high thermal conductivity and breakdown electric-field strength, with a 3.3-fold increase in 6H-SiC polytypic at 300 K. Silicon carbide, naturally found in meteorites, is man-made through the Acheson process, producing poly-crystalline SiC suitable for grinding and cutting applications [87].

Boron Nitride (BN): Because of its excellent thermal conductivity and lubricating qualities, BN is useful in applications requiring heat dissipation and low friction. Robust intralayer bonding and weak vander Waals forces make BN a highly mechanically robust, electrically insulating, and thermally conducting material. It is thermally and chemically stable due to its white colour and transparent surface. Its stability, however, makes it challenging to interact with other compounds. Researchers have looked into using polymers and organic particles to functionalize BN. Pre-ceramic polysilazanes have been employed as coating materials, and silane coupling agents create strong connections between organic and inorganic substances. These substances are made up of silicon atoms, groups that can be hydrolyzed, linkers, and functional groups for organs. This study looks into how to improve the affinity between the filler and matrix by coating A-BN, an aggregated binder. An epoxide group in GPTMS is employed to make a thermal conductive route. PSZ and GPTMS bridge inorganic and organic materials, preventing A-BN from losing shape and functionalizing it with epoxide groups. The resulting polymer composites are analyzed for morphology and thermal conductivity [88].

Polymer Matrix: Tissue engineering uses biodegradable polymeric materials, which can be divided into two primary categories: synthetic polymers like poly (lactic acid), poly (glycolic acid), poly (-caprolactone), and poly (3-hydroxybutyrate) and natural-based polymers like proteins or polysaccharides. Sensitive linkages are broken during biodegradation, permitting polymer erosion. Biological recognition of natural polymers exists, but the availability and concentration of the enzymes determine how quickly they degrade in vivo. Chemical composition, configurational structure, molecular weight, polydispersity, crystallinity, and material shape all control

how quickly synthetic polymers degrade. For some applications, synthetic polymers provide strong mechanical strength and adaptable characteristics. However, they lack cell-recognition sequences and have hydrophobic surfaces. For biomedical applications, composites with excellent formability are created utilizing a variety of techniques, assuring the necessary characteristics and microstructures [89].

5 Application of Ceramic Fillers, Fibers and Acrylics

Ceramic Fillers, Fibers and Acrylics finds wide applications in various fields like in agriculture, dentistry, juice industry and engineering. The applications are shown in Fig. 1. The details are discussed as under—

1. **In Juice Industry:** Ceramic fillers, fibers, and acrylics are essential components in the juice industry for improving packaging materials, equipment, and containers. Ceramic fillers provide improved barrier properties, mechanical

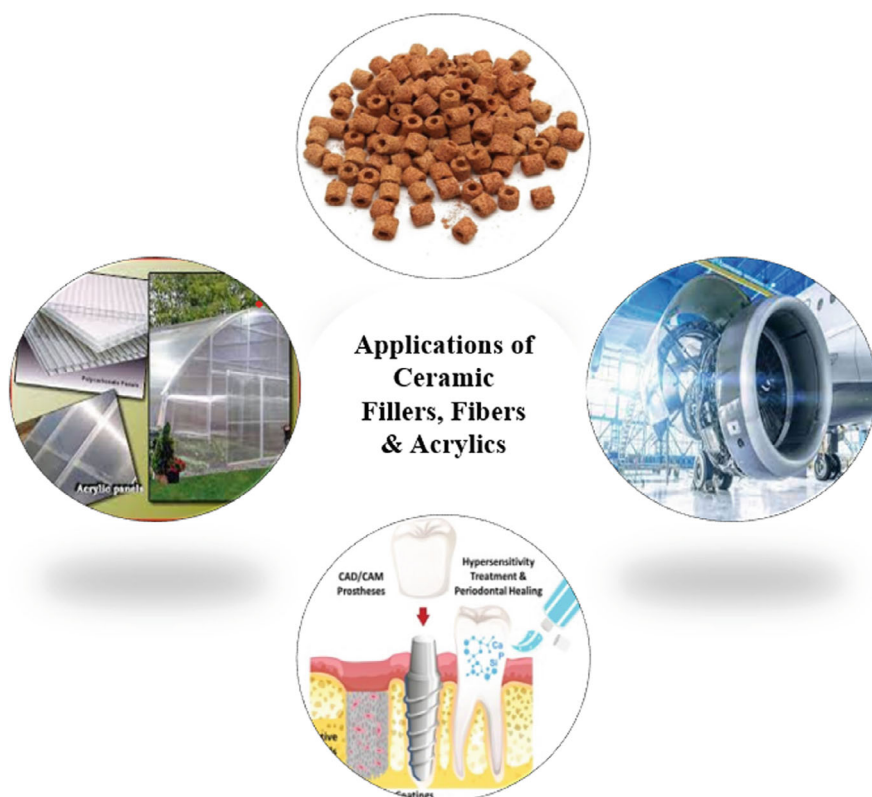


Fig. 1 Application of ceramic fillers, fibers and acrylics in different fields

strength, and thermal stability, while fibers enhance filtration and reinforcement by removing particulates, pulp, and sediment. Acrylics, on the other hand, are used in coatings and sealants to protect packaging and maintain juice quality. These materials play a crucial role in ensuring the safety, shelf life, and overall appeal of juice products.

2. **In Dentistry:** Ceramic fillers, fibers, and acrylics are essential in dentistry for various applications. Ceramic fillers enhance dental restorative materials, while fibers reinforce prosthetics and weakened tooth structures. They are used in tooth-colored restorations like composite fillings and ceramic crowns. Acrylics are used in various dental applications, including removable dentures, temporary restorations, orthodontic appliances, mouth guards, and repairs. These materials play a crucial role in modern dentistry, improving the functionality, aesthetics, and longevity of dental treatments [90].
3. **In Engineering:** Ceramic fillers, fibers, and acrylics are essential in enhancing material properties in various industries, including aerospace, automotive, electronics, construction, and healthcare. They enhance mechanical, thermal, and electrical properties of materials, making them suitable for various applications. Ceramic fillers can reinforce polymers, metals, and ceramics, creating composite materials with improved strength, stiffness, and wear resistance. They are also used as thermal insulators in high-temperature environments, dielectric materials in electronic components, and coatings for corrosion resistance and high-temperature stability. Ceramic fibers possess excellent thermal stability and mechanical strength, making them suitable for high-temperature insulation, reinforcement in composites, aerospace components, and thermal protection systems. Acrylics are versatile synthetic polymers used in structural components, adhesives, coatings, and medical devices due to their biocompatibility, transparency, and ease of fabrication [91].
4. **In Agriculture:** Ceramic fillers, fibers, and acrylics play a crucial role in enhancing material properties, enabling applications in various industries such as aerospace, automotive, electronics, construction, and healthcare. They are used in composite materials, thermal insulation, dielectric materials, coatings, and fibers. Ceramic fibers possess excellent thermal stability and mechanical strength, and are used in high-temperature environments, aerospace components, and thermal protection systems. Acrylics are versatile synthetic polymers with various engineering applications, including structural components, adhesives and sealants, coatings and paints, and medical devices. In agriculture, ceramic fillers, fibers, and acrylics are used in various applications due to their thermal and mechanical properties. They improve the structural integrity and durability of agricultural equipment, tools, and structures, enhancing greenhouse construction, irrigation systems, storage tanks, soil moisture sensors, and crop protection. Ceramic fibers are also used in fire prevention, animal enclosures, and fertilizer encapsulation. Acrylics are versatile synthetic polymers with applications in agriculture, including mulch films, plant protection, fertilizer encapsulation, and erosion control. These applications showcase how ceramic fillers, fibers, and

Table 1 Patents related to ceramic fillers, fibers and acrylics

S.No.	Title of patent	Patent number	Date of patent	Assignee	Inventors
1	Methods for producing metal carbide materials	10954167	March 23, 2021	Advanced Ceramic Fibers, LLC	John E. Garnier, George W. Griffith
2	Single phase fiber reinforced ceramic matrix composites	10793478	October 6, 2020	Advanced Ceramic Fibers, LLC	John E. Garnier
3	Boron carbide fiber reinforced articles	10208238	February 19, 2019	Advanced Ceramic Fibers, LLC	John E. Garnier, George W. Griffith
4	Metal carbide fibers and methods for their manufacture	9803296	October 31, 2017	Advanced Ceramic Fibers, LLC	John E. Garnier
5	Carbon fiber-reinforced silicon carbide composite and method for producing the same	JP2009227565A	2012-12-05	Showa Denko Materials Co Ltd	Kazuya Baba, Makoto Ebihara and Mitsuaki Unno

acrylics contribute to modern agriculture, improving productivity, efficiency, and sustainability [92].

Patent—Some of the patents related to Ceramic Fillers, Fibers and Acrylics are listed in Table 1.

6 Conclusion

Composites are distinct materials with varying physical and chemical properties, essential in daily life and various applications. The fundamental function of ceramic fillers is to strengthen composite materials by more uniformly dispersing stress and enhancing strength, stiffness, and durability. Ceramic fillers are used in a variety of sectors, including aerospace, automotive, electronics, and construction. Fiber filler, also known as a fiber reinforcement or fiber additive, is a compound that incorporates fibers into various goods to improve their qualities. Fillers made from ceramic fibers are used to improve the mechanical, thermal, and electrical characteristics of ceramic composites. Ceramic composites are a type of advanced material composed of high-performance ceramic fibers embedded in a ceramic matrix. Acrylics are a versatile

and popular type of paint that utilizes acrylic polymer emulsion as its primary binder. Since its inception in the mid-twentieth century, acrylics have gained immense popularity due to their ability to replicate various textures, offer a wide array of colors, and provide a quick-drying alternative to traditional oil paints. The method of preparation includes sol–gel technique, solid-state reaction, hydrothermal synthesis, spray pyrolysis, electro-spinning, chemical vapor deposition, spark Plasma Sintering etc. The materials used for preparation, their applications and patents are discussed in this chapter. In future, the in-vivo models, regulatory aspects are to be considered for broader applications in science and allied fields for biomedical applications.

Acknowledgements The authors are also grateful to the Department of Science and Technology (DST-FIST) Letter no-SR/FST/COLLEGE/2018/418, New Delhi for providing financial assistance.

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3D Printing of Ceramics and Fiber-Based Composites for Biomedical Applications



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and T. P. Vinod

Abstract The use of 3D printing technology for the fabrication of ceramics and fiber-based composites has gained significant attention in recent years due to their potential applications in the biomedical field. This book chapter presents a comprehensive report of the state-of-the-art developments in 3D printing of ceramics and fiber-based composites, and their potential use in biomedical applications. The focus is on the properties of these materials, such as their biocompatibility, mechanical strength, and thermal stability, which make them ideal for use in biomedical applications such as tissue engineering, drug delivery, and implant design. This chapter also discusses the challenges and limitations of 3D printing of ceramics and fiber-based composites, including the need for precise control of the printing process and the development of new materials with improved properties. Overall, the potential of 3D printing technology for the fabrication of ceramics and fiber-based composites for use in various biomedical applications is highlighted and insights into the current state-of-the-art in this rapidly evolving field are attempted.

Keywords 3D printing · Ceramics · Fiber composites · Bio-medical applications

1 Introduction

3D printing, commonly known as Additive Manufacturing (AM), is a fabrication method that works by printing two dimensional (2D) or one dimensional (1D) layers of materials one on top of the other to create a 3D shape [1]. The printing is performed following a digitally designed pattern and this technology can transform a digital geometrical representation into a real object, offering the fabrication of a wide variety

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of structures and complex geometries [2]. The designed 3D structures are manufactured layer-by-layer using computer-controlled translation steps (Fig. 1) based on data from 3D computer models [3, 4].

After the discovery of the first stereolithographic printer by Charles Hull in 1984, 3D printing technology has been found to be of significant utility in many industries, such as in biomedical, aeronautics, robotics, electronics, industrial products, and even the food industry (Fig. 1b) [5].

The selection of materials for 3D printing is primarily based on the specific application and the fabrication process involved. The available options encompass a diverse array of materials, ranging from hydrogels, thermosets, and thermoplastics to ceramics, carbon composites, and metals, with potential for combinations thereof

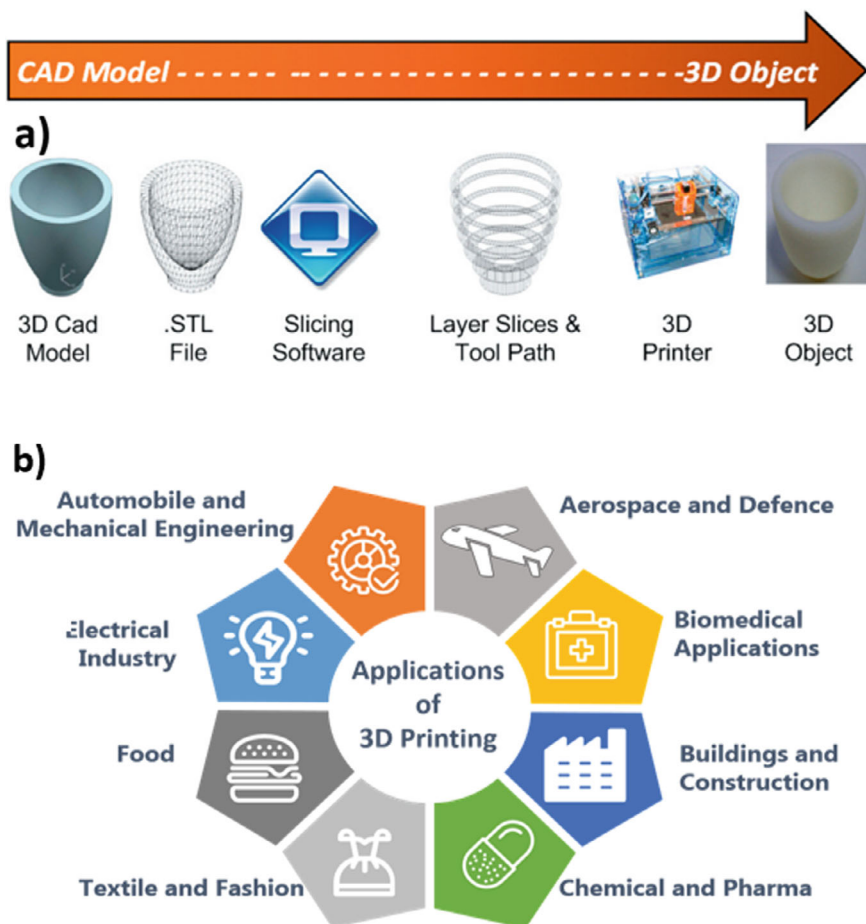
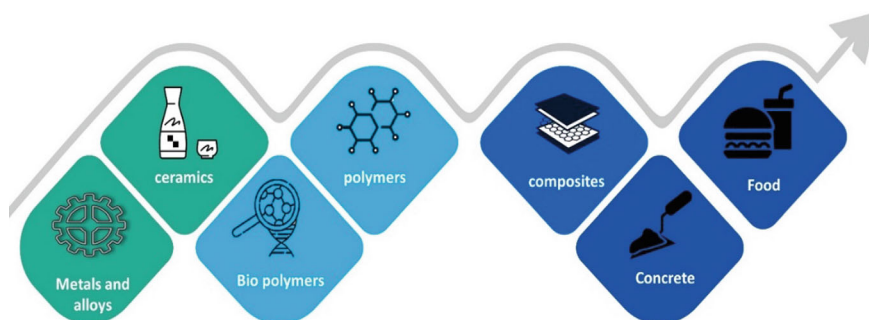


Fig. 1 **a** Schematic representation of the 3D printing process. Reproduced with permission from Ref. [4], © 2022 MDPI. **b** Major applications of 3D printing



Materials used in 3D printing

Fig. 2 Different types of materials used in 3D printing technology

(Fig. 2; Table 1) [6]. The selection of materials for 3D printing with metals is somewhat restricted due to processing constraints and difficulties in achieving the desired bulk-like material properties [7]. Traditional production methods were based on rich supply chain management and time consuming steps whereas robotized 3D printing avoid the current material roll-to-roll production method and relies on CAD programming to print items using various materials, reducing the supply chain management [8, 9]. A 3D printer can print without the assistance of human support and speeds up production while lowering expenses. 3D printing is also utilized in low-volume manufacturing, where a small run of finished items is the primary goal, allowing for faster response and modification of parts than in high-volume manufacturing [10].

The availability of printable materials (metals, thermoplastics, carbon-based fiber composites, ceramics, and even live cells) has generated numerous 3D-printing fabrication techniques, including fused deposition modeling (FDM), direct ink writing (DIW), stereolithography apparatus (SLA), etc. [16]. The techniques selected for the production depends on the particular applications of the components and the material used.

Additive manufacturing (AM) can create fully functioning parts out of various materials, including metals, ceramics, polymers, and their mixtures in the form of composites, hybrids, and functionally graded materials [17]. Soft polymer materials are also used in recent years due to advancements in robust 3D printing technology [18]. Another class of electronically conductive materials that received much attention in recent years are carbonaceous materials and composites. Carbon-based materials such as graphite, graphene, graphene oxide (GO), reduced graphene oxide (rGO), carbon nanotubes (CNT), carbon blacks, and active carbons are widely used for preparation in 3D printing [19]. Due to these advancements in 3D printing materials, multifunctional devices, biomedical implants, components, and even human organs can now be 3D printed [20].

An important application of 3D printing in the field of health is the provision of printing patient specific anatomical structures. In the biomedical field, 3D printers

Table 1 Materials and fabrication techniques used in 3D printing

Materials	Examples	Fabrication method	Physical properties	References
Metal and alloy	Aluminum alloys, cobalt-based alloys nickel-based alloys	Powder bed fusion	High stiffness High recovery rate It can withstand high temperatures	[11]
Biopolymers	Polysaccharides, starch, cellulose, alginate, pectin, chitosan, Xanthum gum, carrageenam Protiens, collagen, silk fibron, gelatin, keratin, casein, soy protein	FDM Direct inkjet writing Inkjet printing Stereolithography	High viscosity Excellent cell adhesion	[12]
Ceramics	Alumina Zirconia Al_2O_3 ZrO_2 LiO_2	Inkjet (suspension) Powder bed fusion Paste extrusion	High mechanical strength. Hardness Good thermal and chemical stability	[13]
Concrete	Cement, sand, geopolymers, and fibers	Extrusion Power bed	Low viscosity Low static yield stress	[14]
Composites	Epoxy Resin Composites Nylon composites Polylactic acid composites	Fused filament fabrication (FDM)	Stiffness Hardness Tensile strength	[15]
Polymers	Polylactic acid (PLA) Acrylonitrile butadiene styrene (ABS) Polypropylene (PP)	Stereo lithography FDM Inkjet printing	Flexibility Hardness Viscoelasticity	[3]

have been utilized for applications including the creation of tissue without damaging living cells, the manufacture of blood vessels, dental implants, and special prosthetics. Furthermore, this technology is also being researched for the purpose of repairing or replacing defective organs such as the kidneys and the heart. Additionally, this technology allows for the creation of organs that will perform the same biological functions as their original counterparts. Currently, it is a rapidly expanding research area devoted to utilizing its findings in a wide range of biomedical applications.

3D printing is a versatile approach in the advanced manufacturing industry, as shown in Fig. 3. Many countries have adopted this technology, particularly in the health care manufacturing sector. As indicated in Fig. 3a, there is rapid development happening in the field of 3D printing ceramics, especially in the biomedical area, due to the fact that ceramics are biocompatible. Country wise statistics of the growth in

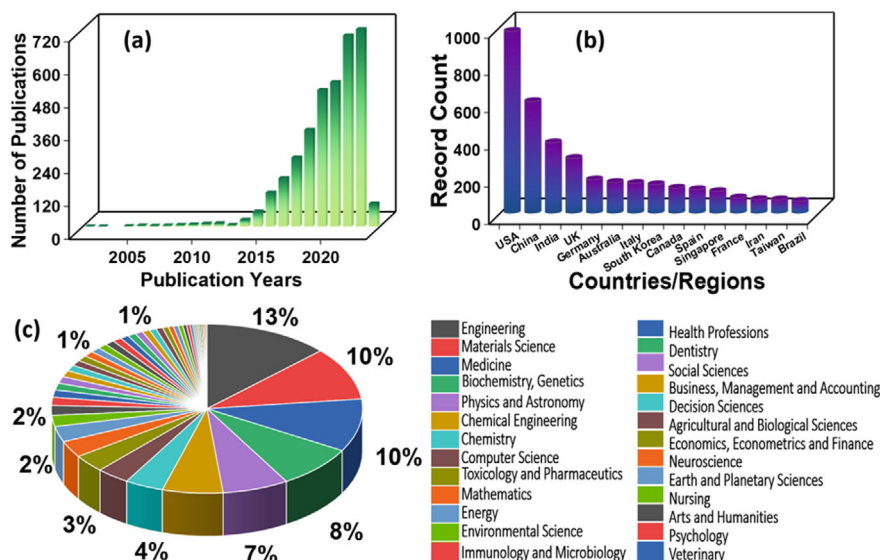


Fig. 3 Comparison of the publications **a** of articles **b** ranking by countries, **c** research area category for the keyword “3D printing and biomedical/health care” from 2001 to 2023. Data from Scopus as of February 2023

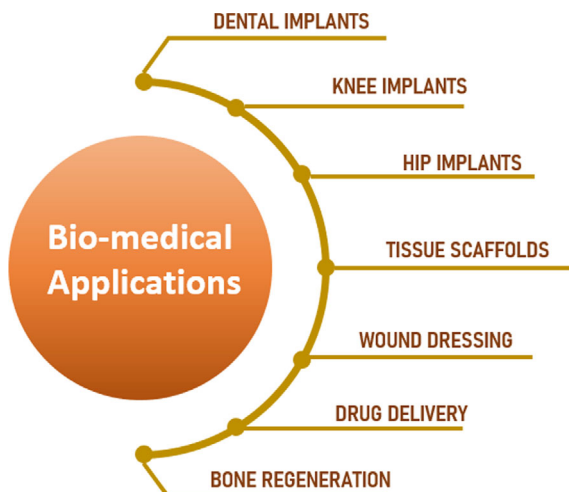
the research on 3D printing can be seen in Fig. 3b. Observing Fig. 3c, it can be seen that researchers from the fields of engineering, material science, and medicine were active in ceramic applications of 3D printing. The success of additive manufacturing is determined by how successfully this manufactured ‘object’ serves its intended commercial biomedical function. In this book chapter we aim to provide a detailed overview of the use of 3D printing of ceramics and fiber-based composites in various biomedical applications.

2 Significance of 3D Printing in Biomedical Applications

In order to prepare complicated structure and microstructure instruments, the 3D printing technology uses various composites suitable for the biomedical applications. Additionally, some medical devices have complex shapes, precise structures, and high antibacterial requirements [21]. The application of 3D printing in biomedicine is rapidly expanding, and some traditional biomedical devices are expected to be replaced by 3D printing products (Fig. 4).

Currently, 3D printing is a major event that will assist medication and clinical associations in creating more unambiguous prescriptions, facilitating the development of clinical installs, and altering the way that authorities and experts prepare strategy [22]. 3D printing allows us to visualize unique life structures, create clear models,

Fig. 4 Biomedical applications of 3D printed ceramic materials



cautious assistants, stents, prosthetics, drug delivery devices, and more [23]. 3D printing technology can potentially be used to replace, restore, maintain, or improve tissue function. The porous structure network in the 3D printed replacements tissue is biocompatible, has appropriate surface chemistry, and has excellent mechanical strength [24]. In some cases, cartilage or bone that has been damaged or diseased can be repaired with 3D printing technology [25].

3D printing is a revolutionary innovation that is being studied for its potential in solid health. In full-scale knee arthroplasty, the capability of enlisted tomography-based 3D printed understanding express moves [26]. Neurosurgeons can employ 3D printing models in the learning process to assist them practice surgical skills. AM will be extremely beneficial to the pharmaceutical sector. As a result, drug manufacturing and delivery systems will undergo significant changes. In 2015, the Food and Medication Administration approved the first additive manufactured drug [27]. On-demand manufacturing of customised medicines will be possible, both for dosages and for specific pharmacogenetic profiles [28]. Simulating a specific patient's pathological condition in 3D can enhance accuracy, save trainers time when performing clinical procedures, and provide opportunities for surgeons to receive hands-on training [29].

3 Biomedical Applications of 3D Printed Ceramic Materials and Fiber-Based Composites

The application of 3D printing of ceramic materials and fiber-based composites in biomedicine is rapidly expanding. Various fundamental requirements must be met for a material to be ideally used in 3D printing procedures, (i) pressure-driven extrusion

must take place through a nozzle with a specific diameter and flow rate (ii) the extruded product must also maintain the correct shape, (iii) the extruded product must act as a bridge and also serve as a mechanically sound substrate (iv) during the transition to the final state, the developed structure must be dimensionally stable [30]. From all other materials, ceramics and fiber-based composites are extensively used and printed into completely functional pieces using 3D printing technology due to their potential applications in biomedical fields [13].

3.1 *Ceramics*

Ceramics are used in a variety of applications, such as the chemical industry, manufacturing, electronics, biomedical, and aerospace. Some of the properties that make them exceptionally suitable materials are their excellent tensile strength and toughness, good chemical and thermal stability, and viable thermal, optical, electrical, and magnetic performance. The use of 3D printing in the production of ceramic components opens up whole new avenues for solving difficulties and overcoming challenges [31]. In addition to their chemical stability and biocompatibility, ceramics have excellent corrosion restriction behavior as well as wear resistance. The mechanical strength of these materials decreases during reabsorption, which is a major disadvantage [32].

The applications of 3D printed ceramics and fiber-based composites in body implants are revolutionizing the field of orthopedics and dentistry due to their excellent biocompatibility and ability to be customized to fit into human body structure precisely [33]. Among them Dental implants, medical products used to replace missing teeth and hold artificial teeth in place. The use of biocompatible materials in this implants allow it to attach to the bones in a much easier way [34]. A hip implant is a medical device that is designed to regain mobility and reduce pain from conditions like osteoarthritis in patients. A femoral neck fracture, for example, is one of the most common causes of osteopain, which is usually associated with osteoarthritis, osteonecrosis, hip developmental dysplasia, and femoral neck fractures. Total Hip Replacement (THR) is the surgery that is needed in such cases. The durability and design features are the things to be considered while choosing an implant for the patient [35].

Knee implant is a medical device that replaces damaged bone and cartilage with different components to recreate the surface of the joint. There are three main parts that may be replaced in total knee arthroplasty the bottom part of the femur, the upper part of tibia, and the patella back side. This procedure is referred to as total knee arthroplasty (TKA), for which metals are usually used [36]. Cobalt–chromium, for example, can cause infection, loosening, instability, or pain when used with higher content. More than 2% of total knee arthroplasty are caused by metal-related pathology, according to the Australian Arthroplasty Register 2016 [37]. As a result of this unnatural, hinge-like motion, metal knee implants put a high level strain on the parts of ligaments and muscles that support the knee, causing different problems to arise in the future. In the first clinical trials, survivorship was verified using

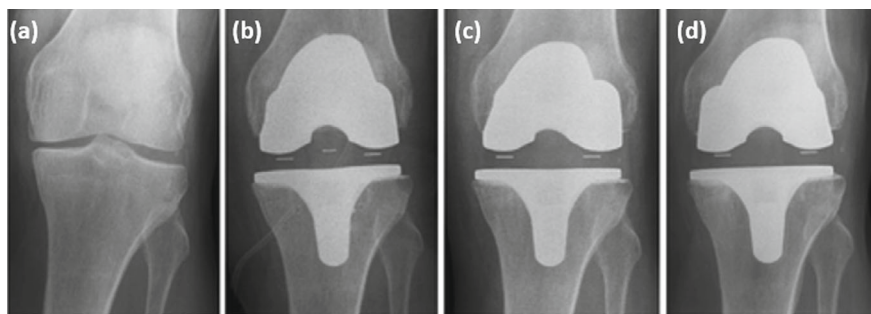


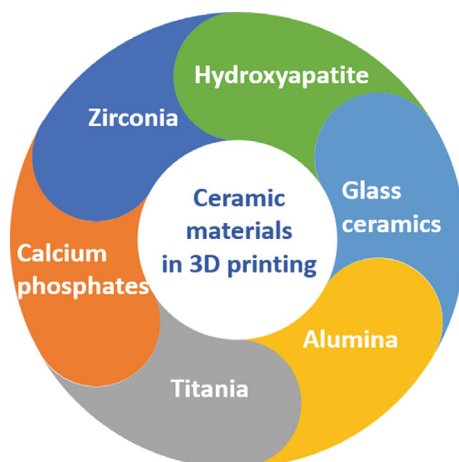
Fig. 5 Radiographs of metal-free ceramic knee implant **a** day of surgery **b** 3 months **c** and 12 months **d** after surgery. Reproduced with permission from Ref. [39], © 2016 BioMed Central

five-year or ten-year follow-ups [38]. Morrison et al. [37] conducted a study aimed to improve bearing materials for knee replacements by testing various types of ultra-high molecular weight polyethylene (UHMWPE) against oxidized zirconium (OxZr) and cobalt-chromium (CoCr) components. The results indicated that OxZr surfaces enable lower radiation doses to achieve reduced wear without significantly compromising mechanical properties, unlike CoCr. Subsequently, as a progression, a ceramic tri-condylar implant has been developed by for the purpose of evaluating its long-term durability and clinical outcomes over a 15-year period. Meier et al. [39] found that ceramics were clinically harmless and an effective alternative to metal-based systems (Fig. 5). They were fitted with a Knee Implant made by Peter Brehm GmbH, Weisendorf, Germany, the BPK-S Integration. The use of ceramics in conjunction with 3D printing technologies and metallic implants seems appropriate in light of all this.

The application of 3D printing of ceramics in tissue scaffolds has gained significant attention in the field of tissue engineering. Ceramic-based scaffolds have desirable properties such as biocompatibility, bioactivity, and osteoconductivity, which make them suitable for bone tissue engineering. The ability to 3D print these scaffolds allows for precise control over their design, porosity, and mechanical properties, making them an attractive option for regenerative medicine. Another major issue in the field of health care today is defects and functional disorders of the bone. A huge clinical and socioeconomic need for bone restoration has arisen as a result of the ageing population and social development [40, 41]. This one is a sophisticated, well-coordinated biological process in the production of new bones during a normal fracture. The techniques for bone regeneration have quickly improved with the invention of three-dimensional (3D) bioprinting [42]. Regenerative medicine has a branch called “bone tissue engineering” (BTE) that aims on new treatments for fractures that can be fixed with 3D-printed living tissues. Since it mimics the natural function of bone, the scaffold plays a crucial role in BTE.

3D printed ceramic materials have gained popularity in recent years due to their unique properties and potential applications. Additionally, ceramic materials have excellent biocompatibility and high resistance to heat, wear, and corrosion,

Fig. 6 Ceramic based materials used in 3D printing



making them ideal for use in biomedical, aerospace, and energy applications. Among various ceramic materials, the most commonly used ceramics are zirconia (ZrO_2) and Alumina (Al_2O_3) (Fig. 6; Table 2) due to their potential applications in bio-medical field.

3.1.1 Titania

A form of titanium dioxide called Titania, discovered in the eighteenth century, is commonly used in dental and orthopedic implants [48, 54]. Stainless steel and titanium are commonly used metals, but this inorganic material has excellent biocompatibility, bioactivity, and stability, making it a good replacement material. It is important to keep in mind that even though these materials are strong mechanically, they can lead to bone resorption and stress shielding between implants and surrounding bone tissue [54]. A major drawback of this device is that it needs to be modified to improve osseointegration. This material is primarily intended to be used as bone implants. For high-density cancellous bone, elastic moduli range from 0.28 GPa to 1.86 GPa, which is within the range of 0.28 GPa and 1.86 GPa. Titanium ceramics sintered at various temperatures (1000 to 1400 degrees Celsius) have elastic moduli between 1.22 GPa and 6.87 GPa. In addition to dental applications, titanium composites have also been used in biomedical applications as antimicrobials, toothpaste, and ointments [48, 49]. Ceramic coatings are often applied with titanium alloy for hip implants to enhance corrosion resistance [55]. Heer et al. [56] studied the effects of additive manufacturing on a $\text{Ti}_6\text{Al}_4\text{V}$ implant coatings. Followed by this Hiara Micheletti and her team investigated the utilization of Ti-6Al-4V for local drug delivery, using a dual-scale surface topography. The topography was achieved by combining the inherent microscale roughness of $\text{Ti}_6\text{Al}_4\text{V}$ samples fabricated through selective laser melting with the nanoscale roughness of TiO_2 nanotubes obtained through electrochemical

Table 2 3D printed ceramic based materials and their bio-medical applications

S. No.	Ceramic materials	Characteristics	Products	Bio-medical applications	References
1	Zirconia	Good mechanical strength, and hardness, capable to resist corrosion, good insulator	Yttria-stabilized tetragonal zirconia polycrystalline	Body Implant, Tissue scaffolds	[43, 44]
2	Alumina	Cheap, high mechanical strength, high-temperature and pressure resistance, corrosion resistance, good dielectrics	Inert alumina ceramics, nanoporous alumina	Body implants, bone regeneration	[45–47]
3	Titania	Good biocompatibility, bioactivity, and stability	Alumina–zirconia–titania composites	Dental and orthopedic implants, good cell viability	[48, 49]
4	Bioactive glasses	Used in osteogenesis, osteoinduction, good combination with bone and soft tissue	Bioactive glass ink; bioactive borosilicate glass (BG) scaffolds	Tissue scaffolds	[50, 51]
6	Hydroxyapatite	Good biocompatibility and bone conductivity	Hydroxyapatite coatings, poly (glycolic acid)/ hydroxyapatite composite scaffolds	Tissue scaffolds	[52, 53]
7	Calcium phosphates	Biocompatibility, bone conductivity, and absorbability	Beta-tricalcium phosphate based bioinks, 3D printed calcium phosphate cement (CPC)	Repair of jaw bones, scaffolds	[44, 45]

anodization [57]. Massimo Pellizzari and his team fabricated cylindrical samples of ultra-low Young's Modulus β -Ti Alloy using laser powder-bed fusion additive manufacturing technology. They reported that these samples shows significant mechanical properties with good cell viability and no cytotoxicity [58] (Fig. 7).

3.1.2 Zirconia

Zirconia dioxide, also known as “cement steel,” was identified in 1789 [59]. The pigment was used in ceramics during the eighteenth century. Humphry Davy tried

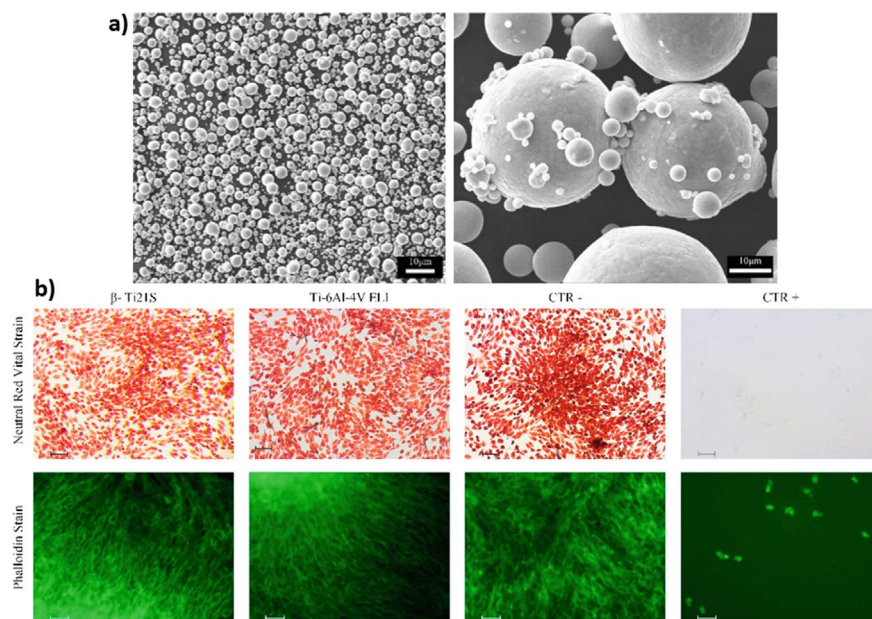


Fig. 7 **a** SEM images of 3D printed cylindrical samples of β -Ti Alloy, **b** microscopic images of cell viability tests. Reproduced with permission from Ref. [58], © 2020 MDPI

to separate it using electrolysis in 1808 but failed. Heating potassium and potassium zirconium fluoride forms this metal, and further purifications leads to its pure state. The pioneer biomedical studies of this material was published in 1969 by Helmer and Driskell [60]. Among the crystals of zirconia, three patterns can be observed: monoclinic (M) at room temperature, cubic (C) at 1170 °C, and tetragonal (T) at 2370 °C. Zirconia can be categorized into four types fully stabilized Zirconia, tetragonal Zirconia polycrystals, partially stabilized Zirconia and dispersed Zirconia ceramics. A fully stabilized zirconia polycrystal consists mainly of cubic phase due to the high dopants present. The next one consists almost entirely of tetragonal phase stabilized by yttrium or cerium oxides. There are two types of partially stabilized zirconia: cubic-phase with interior tetragonal precipitates, and ceramic matrixes with tetragonal zirconia dispersions. In addition to reducing the wear rate of implants, this material has excellent biocompatible, low toxicity corrosion resistance, and has appropriate mechanical properties for manufacturing medical devices, which are some of the advantages of using it in 3D printing [61, 62]. The highest bending strength and toughness in fracture make yttria (Y_2O_3)-stabilized zirconia an ideal material for making dental, knee, or hip prostheses [43, 44].

In case of dental implants, for its proper adherence with bone, it needs to be coated with a particular coating. Bio-integration occurs when the tissue bonds to the implant. It has historically been common for titanium dental implants to be coated with hydroxyapatite (HA). Zirconia implants have started being produced

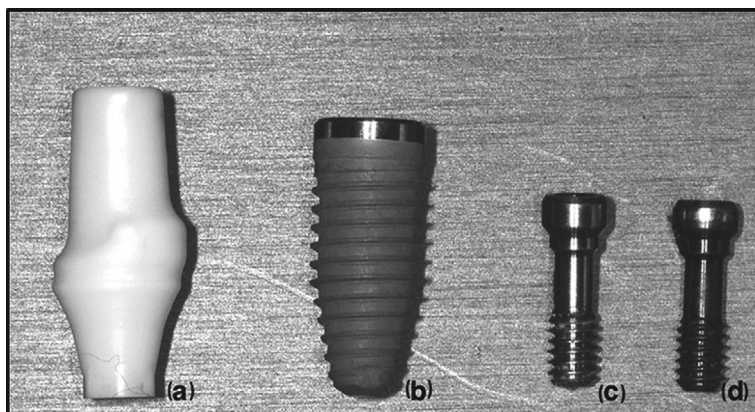


Fig. 8 Components of the implant system: **a** zirconia abutment, **b** implant fixture, **c** aftermarket abutment screw, and **d** OEM abutment screw. Reproduced with permission from Ref. [64], © 2020 Nature

lately. As mentioned, their integration is faster since their union is chemical, rather than mechanical, as in titanium. Furthermore, as metallic materials can lead to peri-implant infections. As Gahlert and Roehling [63] suggest, zirconia parts may be a viable solution for such infections. The components of the implant system consist of a zirconia abutment, implant fixture, aftermarket abutment screw, and a OEM abutment screw (Fig. 8) [64].

Zirconia dental implants were printed using DIW by Lee and Jiang [65]. There were no cracks or delaminations found on the implant parts. A similar zirconia root analogue implant was prepared by Anssari Moin et al. [66]. Zirconia dental crowns were fabricated using direct inkjet printing (DIP) with a suspension containing 27% zirconia. A three mole percent yttria partially stabilized zirconium oxide (3Y-ZrO) was used in 3D printing hip implants by Zhu et al. [67]. An implant with good effective antibacterial properties and finite structure was developed through the integration of additive manufacturing with antibacterial nanomodification. Stanciuc et al. [56] 3D printed zirconia-toughened scaffolds for hip arthroplasty using material extrusion. Porosity in micro and macro levels were observed in the 3D printed ZTA scaffolds. Furthermore, human primary osteoblasts have high level osteogenic marker expression in 3D-ZTA compared to 2D-ZTA controls.

3.1.3 Alumina

Alumina, also known as aluminum oxide (Al_2O_3), was discovered by Pierre Berthier in 1821 [68]. Henri-Etienne Sainte-Claire Deville and his partners, Charles and Alexandre Tissier, produced the first industrial aluminum in 1856. By 1865, an Austrian chemist named Karlo Joseph Bayer invented a cheap and feasible method of producing alumina. By crushing the bauxite, mixing it with sodium hydroxide, and

seeding it with crystals, aluminum hydroxide precipitates [68]. Activated alumina, smelter grade alumina, and calcined alumina are all produced in alumina kilns by driving off the water. When alumina is heated to 1200 °C, it changes into— Al_2O_3 , a stable oxide. Alumina has been used to implant dental implants and to perform total hip arthroplasty procedures. The properties of Alumina make it unique; it has a low electric conductivity, a high melting point, a high strength and elastic modulus, as well as excellent wear resistance. It has a density of approximately 97%, extreme hardness, a Mohs hardness of nine and high corrosion resistance [45–47].

Alumina parts were manufactured using stereolithography by Wu et al. [69] using particles with different particle sizes. SLA can print ceramics with good performance using powders with a bimodal particle distribution and vacuum debinding processes. Using SLA, Dehurtevent et al. [70] have recently achieved dental crowns made of alumina. Their study investigated the physical and mechanical properties of crowns with three different building orientations (XY, ZY, and ZX). The fused filament fabrication technology (FFF) was used to fabricate dental implants made of alumina with infiltrated glass [71]. According to the study, adding alumina to hip implant increased its wear resistance by about 90%, suggesting that this material could be used to articulate load-bearing implants' surfaces.

A combination of decellularized extracellular matrix and poly(ϵ -caprolactone) PCL fibres for bone mimetic scaffolds were also reported. Ceramic scaffolds can either be made of biodegradable ceramics. Because of their durability and great mechanical strength, zirconia and alumina are used in dental and musculoskeletal bone regeneration. Figure 9 shows a 3D-printed bioactive Ca_3SiO_5 bone cement scaffolds with nano surface structure for bone regeneration [72]. Porous ceramics also can be manufactured using 3D technology which has various advantages for creating lightweight, multipurpose materials that are customized to the requirements of the patient. This can be fabricated using fused deposition modeling (FDM), which effectively promotes bone ingrowth and regeneration. A bone scaffold constructed from calcium phosphate and starch-based composites was fabricated by Koski et al. using solid freeform fabrication [73]. When dopants like strontium (Sr), magnesium (Mg), iron (Fe), and silicon (Si) are added to ceramic scaffolds, it is shown that these materials have the ability to promote osteogenesis eventually leading to complete bone regeneration [74]. The combination of CaP and Fe/Si/Sr/Mg are also very much feasible for fabrication because of its osteogenic effect.

3.1.4 Bioactive Glass

It has a high porosity, high compressive strength, and uniform interconnected macropores. Human bone marrow stromal cells can express osteogenic genes in response to it. As well as being biologically active, osteogenesis, osteoinduction, and well-suited for tissue, it has a variety of functions. Bioactive glasses promote tissue regeneration due to their good bioactivity, biocompatibility, and non-cytotoxicity [50, 51]. Bioactive glass is known for its potential to act as a drug delivery system for therapeutic ions and growth factors. However, it cannot be used alone for scaffold preparation due

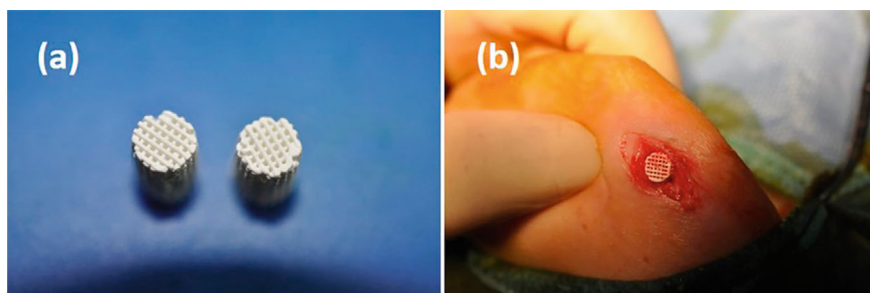


Fig. 9 Images of surgery before (a) and after (b) scaffolds were transplanted into femur defects. Reproduced with permission from Ref. [72], © 2017 ACS

to its loss of amorphous properties at high sintering temperatures. To overcome this limitation, researchers have studied polymer-bioactive glass composites to create superior biomimetic scaffolds that combine the biocompatibility, biofunctionality, and biodegradability of bioactive glass with the mechanical properties of polymers [75]. Although concerns about the toxicity of photosensitive binders and burnout of polymers during high-temperature sintering have limited their use, extrusion-based additive manufacturing is now the preferred method for 3D printing of scaffolds [76]. By combining chitosan with bioactive glass, researchers have developed a biomaterial with improved mechanical and biological properties. In a recent study, bioactive nanoglass was dispersed in distilled water and mixed with a chitosan solution before being 3D printed into a bone scaffold with aligned macrochanneled pore structures. The resulting scaffold exhibited ideal microenvironments for pre-osteoblastic cell growth and cytoskeletal network formation, making it a promising biomaterial for bone tissue engineering [77].

3.1.5 Hydroxyapatite

Bones and teeth contain hydroxyapatite, which is an inorganic component. Its products include coatings of hydroxyapatite and composite scaffolds made of poly (glycolic acid) and hydroxyapatite. It has a low bone induction effect, is brittle, and has a slow degradation rate [52, 53]. The excellent biocompatibility and bone repair applications of Hydroxyapatite (HA) bioceramics have attracted significant attention in recent years. Projection-based 3D printing (3DPP) offers a promising method for fabricating bioceramic scaffolds with complex geometry, high accuracy, and efficiency.

A study conducted by Huifeng Shao et al. demonstrated that the 3DPP technique can manufacture HA bioceramics with uniform morphology, complex structure, and high accuracy. The resulting HA scaffolds possess mechanical strength similar to that of human cancellous bone, and when cultured with osteoblast precursor cells, the scaffolds exhibit strong biocompatibility and can promote osteoblast adhesion,

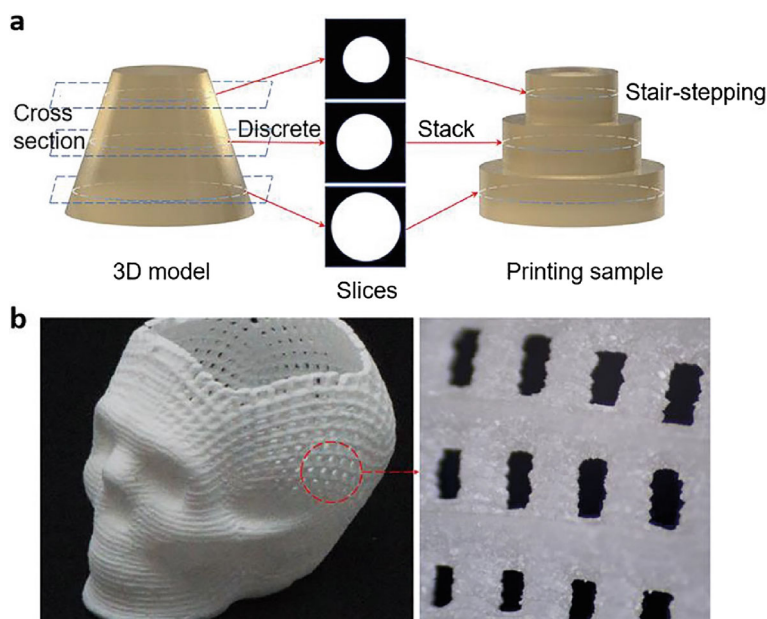


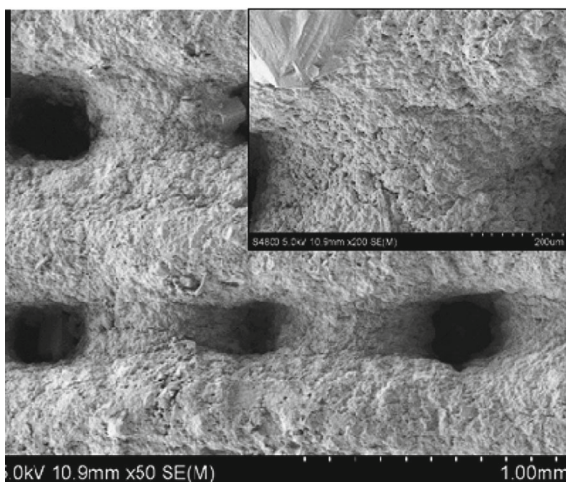
Fig. 10 **a** Stair-stepping of the 3DPP samples, **b** side view of ceramic sample. Reproduced with permission from Ref. [78], © 2022 Elsevier

proliferation, and differentiation. These results highlight the potential of the 3DPP technique for preparing bioceramic scaffolds, and the HA scaffolds produced using this method show promising potential for use in human bone regeneration repair (Fig. 10) [78].

3.1.6 Calcium Phosphates

Calcium phosphates are synthetic bone substitutes that have similar compositions to bone minerals. They are well tolerated, bioactive, bone conductivity, and absorbable. The degradation rate of calcium phosphate is much less. It has low toughness and critical compressive strength. The main products are beta-tricalcium phosphate-based bioinks and calcium phosphate cement (CPC) [79, 80]. For the repair of jaw bones, scaffolds with personalized sizing, bone regeneration, and antibacterial properties are necessary. A recent study proposed using 3D printing to produce degradable calcium phosphate scaffolds with antibacterial capabilities for jaw bone regeneration. The researchers utilized berberine and calcium phosphate powders to create printing inks, which were used to construct porous scaffolds via direct extrusion 3D printing. Additionally, sodium alginate was cross-linked in situ to further stabilize the scaffold. The 3D printing technique allowed for precise customization of the scaffolds' size, shape, and porosity (Fig. 11) [81].

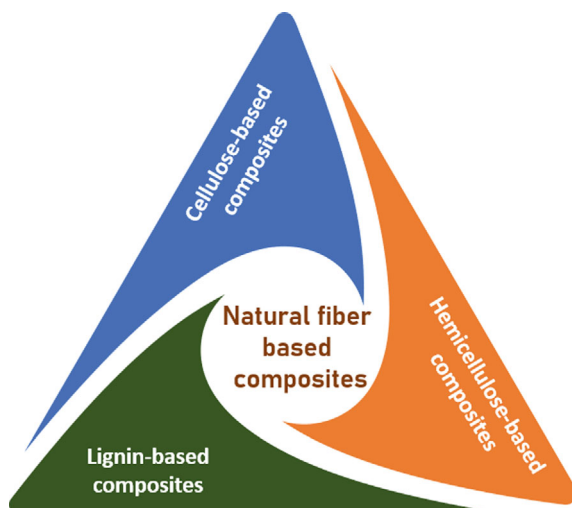
Fig. 11 Surface morphology of calcium phosphate scaffold. Reproduced with permission from Ref. [81], © 2020 Elsevier



3.2 *Natural Fibre-Based Composites*

In the research and application of natural fiber-based composites, natural fibers and their derivatives are among the most commonly used biomass and polymers. Moreover, 3D printing provides a novel approach for developing and promoting natural fiber-based composite materials and provides a platform for developing biomass materials for intelligentization and industrialization [1]. The natural fibers include fibers from bamboo and wood, straws, shells of rice and nuts, etc. which are byproducts of agriculture and forestry. Natural fiber composites are a type of biomass and polymer composites that are made by adding natural fibers as reinforcements and other agents that act as compatibilizers and flexibilizers to polymers and gels. A green and sustainable economy needs materials that are low density, have high specific strength and modulus, are light, have high affinity, and are biodegradable. As a result of replacing synthetic fibers with natural fibers, a number of factors need to be considered, including variation in the substrate composition, material characteristics, anisotropic behaviours, thermal instability, and changeable moisture absorption effects. A variety of natural fibers contain cellulose, hemicellulose, and lignin, which can be used in 3D printing to fill, reinforce, or modify polymer matrixes (Fig. 12) [82, 83]. Fiber is advantageous in the field of biomedicine for several reasons. Firstly, it is non-cytotoxic, meaning it is compatible with cell growth and proliferation and demonstrates biocompatibility. Secondly, it is biodegradable, allowing for the printing structure to degrade without the need for manual intervention. Finally, its exceptional mechanical properties make it suitable for use as printing ink or as a reinforcing agent in a polymer matrix, resulting in better mechanical performance of composite materials. These remarkable properties make 3D-printed fiber composites highly suitable for various biomedical applications, including medical devices, tissue engineering, and wound dressing.

Fig. 12 Natural fiber based composite material used in 3D printing



3.2.1 Cellulose-Based Composite Materials

It is a linear molecule with a macromolecular structure. It contains a glycosidic bond with the molecular formula $(C_6H_{10}O_5)_n$ as well as a polymerization degree of between 6000 and 10,000. Because of the free hydroxyl groups on its molecular structure, this product is strongly hydrophilic. Combining cellulose with polymer can not only improve mechanical properties, but also improve dimensional stability, including water absorption and volume expansion [84]. According to Murphy et al., the properties of a natural composite materials like thermal, mechanical, electrical, etc. were affected by its surface modification through titanium couplers. They studied this by using CNC/PLA wires prepared through extrusion with twin screws and casting using different solvents [85]. In the composite materials, CNC acted as a nucleator, dramatically improving PLA crystallinity and a substantial increase in storage modulus. It has been shown that CNC surface modification has the greatest impact at a concentration of 3%. Aside from reducing the water sorption of composite materials, it has also proven to be effective in ensuring the stability of 3D printed materials [86].

Cellulose-based 3D printed materials have shown great potential for biomedical applications due to their biocompatibility, biodegradability, and ability to support cell growth. These materials have been utilized to create a range of structures, such as scaffolds for tissue engineering, drug delivery devices, and surgical implants. In addition, the antimicrobial properties of cellulose-based materials can be harnessed to create wound dressings or other devices that prevent infection. The ability to 3D print cellulose-based materials also enables the creation of complex geometries and customized shapes, facilitating patient-specific treatments. Ongoing research in this field aims to optimize the properties of cellulose-based materials for specific biomedical applications, paving the way for exciting advancements in regenerative

medicine, personalized healthcare, and beyond [87]. In the preparation of medical equipment, it is crucial to consider factors such as thermal stability and antimicrobial properties. However, cellulose materials are not inherently compatible with antibacterial substances. To confer antimicrobial properties, composite inks or matrix materials can be supplemented with antimicrobial agents. Pattinson and Hart utilized a simple mechanical mixing process to create ink with a suitable viscosity, consisting of cellulose acetate and acetone. This ink was then extruded through a nozzle to form miniature forceps that could be solidified by the evaporation of acetone. The addition of an antibacterial agent to the composite inks was tested by depositing *Escherichia coli* bacteria suspended in PBS buffer solution onto disks fabricated using the ink. After 20 h of bacterial culture under a fluorescent lamp, the number of surviving bacteria was reduced by 95%, providing evidence of successful loading of the antibacterial agent onto the composite material [88]. Additionally, Kamdem et al. studied the impact of adding CNF to an acetic acid and chitosan solution, evaluating the effects on mechanical strength and viscosity of the composite ink [89].

3.2.2 Hemicellulose-Based Composite Material

Among polysaccharides, hemicellulose is the second most abundant. A hemicellulose is a complex glycan composed of pentoses, hexoses, and glucuronates [90, 91]. Approximately 25% of softwood hemicellulose is galactoglucomannan (GGM). Xu et al. fabricated 3D printed scaffolds by thermally separating GGM from the mechanical pulp of *Picea abies* and dissolving it in dimethyl sulfoxide (DMSO). After solubilizing the PLA with dichloromethane (DCM) and mixing uniformly, it was melted and squeezed them to filaments [92]. Researchers found that hemicellulose was up to 25% of scaffolds when they were 3D printed. GGM was found to make up to 20% of the sample. GGM in the composite material prevented smooth printing due to excessive amounts.

Hemicellulose-based 3D printed materials have potential biomedical applications, including as scaffolds for tissue engineering, wound dressings, and drug delivery devices. Their biocompatibility, biodegradability, and ability to support cell growth make them attractive options for personalized healthcare and regenerative medicine. Ongoing research aims to optimize the properties of hemicellulose-based 3D printed materials for specific biomedical applications. Hemicelluloses extracted from corn cobs have demonstrated selective proliferative effects, inhibiting the proliferation of tumor cells while not affecting fibroblast proliferation and even leading to macrophage proliferation. A recent review has highlighted the drug delivery potential of hemicelluloses, specifically in the colon, by leveraging their insolubility at the acidic conditions found in the stomach. Ongoing research is exploring the use of hemicelluloses for targeted drug delivery, offering a promising avenue for medical applications [93-95].

3.2.3 Lignin-Based Composite Material

Lignin-based composite material are characterized by their 3D spatial structure, diverse and complex chemical bonds between structural units, and its poor thermostability, which make them a very useful component of biomass [95]. As a result of the addition of lignin, the composite material will be significantly more crystallized and more thermally stable, which is especially important for applications requiring high thermal efficiency. Several studies have been conducted in the literature on the use of 3D printing to produce lignin. A study carried out by Gkartzou and colleagues investigated the phase morphology, mechanical and thermal properties of Kraft lignin/PLA composite filaments obtained by varying their component ratios. The interfacial distance between the lignin and PLA and the relative slippage resulted in the composite materials becoming more brittle, leading to a decrease in the area of the stress–strain curve that is plastically deforming and disappearance of the yield point in the process [96, 97].

Lignin-based 3D printed materials have promising biomedical applications, including as drug delivery carriers and tissue engineering scaffolds. Their antioxidant activity and ability to modulate the hydrophilicity of resulting matrices make them an attractive option for biomedical applications. With ongoing research, lignin-based 3D printed materials hold potential for a range of medical application. Recently, lignin has garnered significant interest as a potential drug delivery carrier and for biomedical applications, primarily owing to its antioxidant activity. A study examining the engineering of PLA-lignin nanofibers found that increasing the lignin content enhanced the antioxidant activity, but also inhibited cell proliferation at higher doses [98]. Therefore, to achieve good biocompatibility, it is essential to maintain a balanced lignin concentration. The hydrophilicity and hydrophobicity of the matrix surface play a crucial role in cell adhesion. To modulate the hydrophilicity of the resulting matrix, hydrophobic lignin can be incorporated into hydrogels. Additionally, lignin-based nanoparticles are emerging as a promising option for drug delivery. When hydrogel inks are developed for printing, stable lignin-based nanosystems could offer a viable solution for medical applications [100, 101].

4 Conclusion

In conclusion, 3D printing technology has emerged as a promising approach for the fabrication of ceramics and fiber-based composites for use in various biomedical applications. The ability to create complex structures with high precision and accuracy has opened up new avenues for tissue engineering, drug delivery, and implant design. The biocompatibility, mechanical strength, and thermal stability of these materials make them ideal for use in biomedical applications. However, there are still several challenges and limitations that need to be addressed, such as the need for precise control of the printing process and the development of new materials with improved properties. Nonetheless, the potential of 3D printing technology for the

fabrication of ceramics and fiber-based composites in the biomedical field is enormous, and ongoing research and development efforts are expected to further advance this field. It is expected that 3D printing technology will continue to revolutionize the biomedical industry and provide innovative solutions for improved patient care and treatment.

[68]

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Zein Based Polymer Composites for Biomedical Applications



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Abstract This chapter provides a comprehensive coverage of zein as a natural polymer, with a focus on its properties that are pertinent to biomedical applications. Additionally, the chapter investigates into the specific techniques for synthesising, processing, and characterising zein composites. This chapter will provide an overview of the diverse polymer matrices and reinforcement materials utilised in zein composites for biomedical applications, along with an examination of the various fabrication techniques employed. The aim of this study is to offer a thorough comprehension of the potential of zein-based polymer composites in various biomedical applications such as controlled drug delivery, tissue engineering scaffolds, wound healing, imaging and diagnostics, and 3D printing. This research endeavour is expected to contribute to the progress of biomedicine and personalised healthcare.

Keywords Zein · Natural polymer · Processing · Characterising · Drug delivery · Wound healing

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1 Introduction

Zein is a naturally occurring polymer that is obtained from maize and is classified under the prolamin group of proteins. The natural alternative to synthetic polymers has garnered considerable attention owing to its distinct properties and diverse range of applications. The biodegradability of zein is considered to be a significant advantage [1]. Zein, as a natural polymer, possesses the ability to undergo biodegradation through natural mechanisms, thereby rendering it ecologically sustainable [2]. This characteristic distinguishes it from synthetic polymers that are obtained from petrochemicals and tend to endure in the environment for prolonged periods. The property of zein being biodegradable renders it a desirable option for utilisation in scenarios where emphasis is placed on sustainability and environmental consciousness [3]. The source material for Zein is maize, which is a sustainable and replenishable resource. The substance in question is derived as a secondary output of maize processing, thereby minimising waste and rendering it an environmentally viable option for diverse applications. The consistent supply of zein is ensured due to the abundance and renewability of maize, which adds to the attractiveness of this natural polymer.

Zein exhibits notable characteristics of being non-toxic and possessing edibility. The U.S. Food and Drug Administration (FDA) has classified it as Generally Recognised as Safe (GRAS). Zein has been utilised in numerous food applications, including coatings for confectionery, chewing gum, and pharmaceutical capsules, with a well-established record of safety [4]. The non-toxic and biocompatible properties of zein render it a viable option for deployment in domains that entail food contact or pharmaceuticals, wherein safety is a critical concern [5]. The film-forming ability of Zein is exceptional, rendering it a highly appropriate material for the purposes of coatings and encapsulation. Upon dissolution in ethanol or other appropriate solvents, zein exhibits the ability to generate a dense solution that can be utilised for the production of films or the application of coatings onto diverse substrates [6]. The zein films present several benefits, including exceptional moisture resistance, properties of oxygen barrier, and safeguard against UV radiation [7]. The adaptability of zein films can be enhanced by the addition of additives or by blending zein with other polymers, thereby broadening its range of potential uses in various fields, including but not limited to food packaging, drug delivery systems, and cosmetic formulations [8]. Zein exhibits a unique characteristic of hydrophobicity. The inherent hydrophobic nature of Zein results in its exceptional barrier characteristics against water vapour and moisture [9]. The unique characteristic of zein films and coatings renders them highly advantageous for employment in packaging applications, owing to their ability to prevent the detrimental impact of moisture and water vapour on the shelf life and quality of the packaged commodities. The hydrophobic nature of zein can be augmented by the inclusion of hydrophobic agents or by constructing multilayer architectures, thereby conferring superior safeguarding and conservation properties. Moreover, zein demonstrates compatibility with a diverse array of additives, thereby enabling the integration of functionalities such as antimicrobial agents, antioxidants, and flavourings. The ability to be flexible allows for the creation of

zein-based products that offer additional value and improved characteristics that are customised to meet specific needs [10]. The properties of Zein render it appropriate for diverse biomedical applications. Zein's biocompatibility and biodegradability render it a promising contender for drug delivery systems and scaffolds in tissue engineering [10]. Zein has the potential to undergo various processing techniques, including the formation of nanoparticles, microparticles, or electrospun fibres. These forms can be utilised for the purpose of encapsulating and administering drugs or bioactive compounds, while also allowing for the regulation of release profiles. Additionally, zein has the potential to undergo chemical or enzymatic modifications in order to enhance its properties or incorporate novel functionalities. The mechanical strength and stability of zein films can be improved by crosslinking, thereby rendering them appropriate for use in scenarios that necessitate heightened durability [11]. To summarise, Zein is a naturally occurring polymer that possesses distinctive characteristics, rendering it a desirable substitute for artificial polymers. The broad spectrum of applications of this substance can be attributed to its biodegradability, which is derived from renewable maize sources, as well as its edibility, film-forming ability, hydrophobicity, and compatibility with additives. Zein provides sustainable solutions with guaranteed safety and performance across various industries, ranging from food packaging to pharmaceuticals and biomedical applications. With the progression of research and development in the realm of natural polymers, it is probable that zein will assume a progressively noteworthy function in the sustainability of materials in the future.

2 Significance of Zein-Based Polymer Composites in Biomedical Applications

The utilisation of Zein-based polymer composites has garnered considerable attention in the field of biomedical research owing to their distinctive characteristics and potential for diverse therapeutic and regenerative medical applications [12]. The importance of zein-based polymer composites in the realm of biomedicine is underscored by several critical factors.

The biocompatibility of Zein is attributed to its natural origin from maize, which renders it intrinsically compatible with biological systems. Upon being incorporated into polymer composites, zein exhibits biocompatibility, thereby reducing the likelihood of unfavourable reactions upon interaction with biological systems. The aforementioned characteristic holds significant importance in the field of biomedical research, particularly in cases where harmonious interaction with living tissues and cells is imperative.

The potential of Zein-based polymer composites in controlled drug delivery systems has been thoroughly investigated. The incorporation of therapeutic agents, such as drugs or bioactive molecules, into the composite matrix of zein composites

can enable efficient regulation of the release kinetics of said substances. The utilisation of zein composites enables accurate dosing, targeted therapy, and extended release, thereby enhancing the efficacy of treatment.

Zein-based polymer composites have demonstrated potential as scaffolds for tissue engineering purposes. The composite materials of zein exhibit a porous structure that offers a conducive milieu for cellular attachment, proliferation, and differentiation. Furthermore, it is possible to customise the mechanical characteristics of zein composites to correspond with the desired tissue, thereby furnishing architectural reinforcement throughout the process of tissue restoration. The property of zein to undergo biodegradation facilitates the gradual disintegration of the scaffold as fresh tissue develops, thereby obviating the necessity for surgical extraction.

The potential of zein-based polymer composites in wound healing and skin regeneration applications has been investigated by several researchers. The application of Zein composites has been found to be effective in the formation of a protective barrier over wounds, thereby impeding the onset of infections and expediting the process of wound healing. In addition, the integration of bioactive substances, growth factors, or antimicrobial agents into zein composites has the potential to facilitate tissue regeneration, diminish scarring, and augment wound closure.

Zein-based polymer composites have the potential to be designed with imaging or diagnostic functionalities for various applications in the field of medical imaging and diagnosis. The utilisation of zein composites for diverse imaging modalities, such as magnetic resonance imaging (MRI) or computed tomography (CT), can be achieved by integrating contrast agents or nanoparticles into the composite matrix [13]. The aforementioned capability allows for the creation of composite materials that serve multiple functions, including therapeutic and diagnostic applications. This, in turn, promotes the advancement of personalised medicine and targeted treatments.

The utilisation of Zein-based polymer composites has exhibited promise for the implementation of 3D printing in the field of biomedicine, particularly for the printing of intricate structures. Zein composites possess adjustable rheological characteristics and biocompatibility, rendering them suitable for deployment as bioinks for the production of intricate three-dimensional architectures with meticulous regulation of geometry and porosity [14]. This facilitates the development of implants, tissue constructs, and drug delivery systems that are tailored to the individual patient.

Polymer composites based on zein exhibit significant promise in diverse biomedical contexts. Due to their biocompatibility, controlled drug delivery capabilities, tissue engineering potential, wound healing properties, diagnostic capabilities, and 3D printing versatility, these materials have garnered significant interest in the field of advancing therapies, regenerative medicine, and personalised healthcare [15]. Further investigation and advancement in the domain of zein-derived polymer composites are anticipated to propel advancements in the biomedical sector and enhance patient results.

3 Zein: A Versatile Natural Polymer

From a chemical perspective, zein is a protein polymer that consists of a sophisticated arrangement of amino acids. Zein's primary structure is composed of a series of amino acids, with a notable abundance of hydrophobic amino acids like proline and glutamine [7]. The hydrophobic amino acids present in zein are responsible for its overall hydrophobicity. The structure of Zein is distinguished by the prevalence of α -helical secondary structures, which are established through hydrogen bonding among the peptide backbone. The distinctive characteristics and functionalities of zein are attributed to its secondary structure. Zein exhibits insolubility in water on account of its hydrophobic characteristics at the chemical level. It has a tendency to coalesce and undergo precipitation in aqueous surroundings [16]. Zein has the capability to dissolve in a range of organic solvents, including ethanol, isopropanol, or a combination of water and organic solvents, which facilitates the creation of coatings or solutions [17]. The hydrophobic nature of zein is attributed to the disposition of hydrophobic amino acids in its protein conformation. The aforementioned characteristic of zein is responsible for its remarkable ability to act as a barrier against moisture and water vapour. As a result, zein is deemed appropriate for utilisation in scenarios where resistance to moisture is a prerequisite. Zein has the potential to undergo diverse chemical modifications and reactions, as viewed through a chemical lens. Crosslinking can be employed as a means to augment the mechanical properties, stability, and durability of the material [18]. Chemical alterations can also be utilised to incorporate particular functionalities or enhance compatibility with other substances. Moreover, zein demonstrates compatibility with a diverse array of additives and functional molecules. The utilisation of zein-based materials enables the integration of antimicrobial agents, antioxidants, and flavourings, thereby broadening the scope of potential applications and functionalities.

Zein exhibits biodegradability, implying its susceptibility to decomposition through natural mechanisms within a certain period. Zein degradation is facilitated by enzymatic activity that cleaves the peptide bonds present in the protein structure. The biodegradability of zein presents a noteworthy environmental benefit, as it has the potential to mitigate waste and environmental contamination in contrast to synthetic polymers that lack biodegradability. As a whole, the distinctive characteristics of zein, such as its hydrophobicity, insolubility in water, compatibility with additives, and biodegradability, can be attributed to its chemical composition and structure. Comprehending the chemical facets of zein is imperative in order to enhance its processing, alter its characteristics, and formulate innovative materials for diverse applications.

4 Structure and Properties of Zein

Corn kernels comprise diverse protein types, constituting approximately 10% of the grains' desiccated weight. Figure 1 shows the different areas and structures of zeins. The protein composition of cereals is contingent upon the genotype (i.e. species and variety) as well as the prevailing growing conditions (e.g. soil quality, climatic conditions, and fertilisation practises). Corn proteins are categorised into four groups based on their solubility properties [19]. These groups include albumins, which are soluble in water, globulins, which are soluble in aqueous saline, prolamins, which are insoluble in water but soluble in 70% alcohol, and glutelins, which are insoluble in both water and alcohol. The protein Zein exhibits amphiphilic characteristics, displaying both hydrophobic and hydrophilic properties. Zein, a protein found in maize, comprises predominantly hydrophobic amino acid residues, constituting slightly over 50% of its composition. Notably, it contains a significant proportion of leucine (20%), proline (10%), and alanine (10%). However, it also contains a relatively high proportion (21–26%) of glutamine, which is a hydrophilic amino acid [20]. Despite being derived from corn gluten, which is a renewable and cost-effective source, the production of zein is not prevalent or extensive. This is attributed to the comparatively high expenses associated with the conventional extraction method [21]. The established method for protein extraction involves the utilisation of an aqueous-alcohol solution. The sample is subjected to centrifugal clarification followed by refrigeration to induce precipitation of zein. Augmenting extractions and precipitations enhances the purity of zein. Upon desiccation, zein undergoes a transformation resulting in the formation of a powdery substance with a yellowish hue. Several research studies have been conducted with the aim of minimising or eradicating the quantity and frequency of solvents utilised in the extraction procedure. The categorization of Zein is based on variations in molar mass and solubility, resulting in the identification of three distinct fractions, namely α -, β -, and γ -zein [22]. The commercial extraction process yields a higher quantity of the α -zein fraction, which accounts for approximately 80% of the total prolamine content in corn. This fraction exhibits a molar mass within the range of 21–25 kD. The fractions of β -zein and γ -zein constituted merely 10–15% and 5–10%, correspondingly, contingent on the genotype of the origin.

5 Biocompatibility and Biodegradability of Zein

The safety and environmental impact of materials utilised in diverse applications, particularly in the biomedical domain, are determined by two crucial attributes: biocompatibility and biodegradability. Zein, a plant-based protein that is commonly present in maize, has garnered considerable interest in recent times. Zein exhibits distinctive characteristics that render it a desirable option for diverse applications,

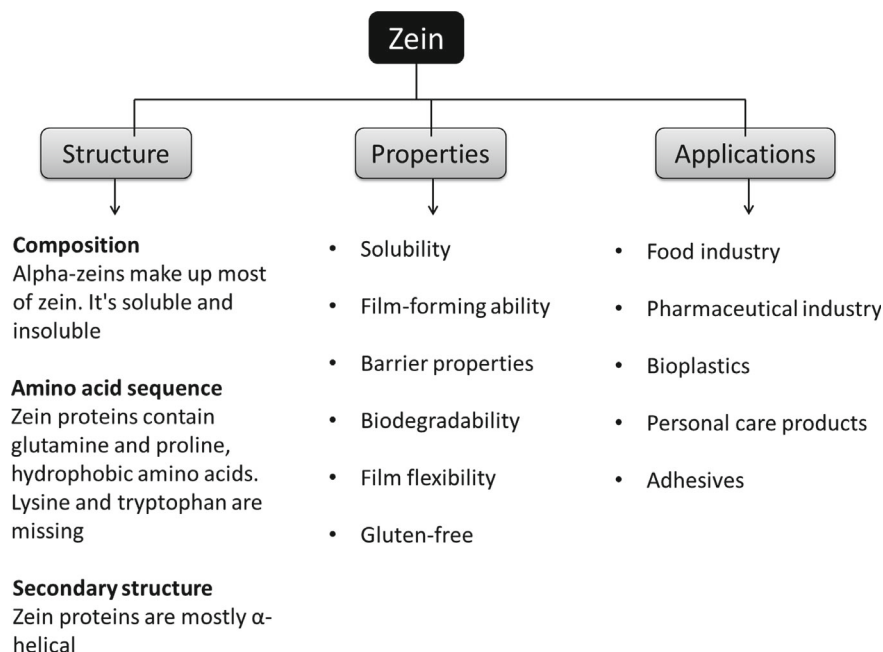


Fig. 1 Consolidated structure–property and applications of zein based hydrocolloids

such as drug delivery systems, tissue engineering, and food packaging. This paragraph aims to examine the biocompatibility and biodegradability properties of zein and evaluate its potential advantages and disadvantages.

The term biocompatibility pertains to the capacity of a substance to coexist with living organisms or tissues without inducing any deleterious outcomes. The biocompatibility of Zein is noteworthy, rendering it a highly viable contender for employment in biomedical contexts. The biocompatibility of the substance can be attributed to its natural protein origin, specifically its presence in corn. This characteristic serves to minimise the potential for immunogenic reactions and toxicity. Upon interacting with biological systems, materials composed of zein demonstrate negligible cytotoxicity, indicating their lack of detrimental effects on cellular viability and functionality. The inherent characteristic of zein renders it a viable option for incorporation into drug delivery systems, as it has the ability to encapsulate pharmaceutical agents and facilitate their controlled release without eliciting any untoward responses. Zein possesses a noteworthy benefit in terms of its biodegradable properties. The term biodegradability pertains to the capacity of a substance to undergo decomposition through natural mechanisms, such as enzymatic or microbial reactions, resulting in the formation of less complex and non-hazardous compounds. The high biodegradability of Zein can be attributed to its proteinaceous composition. The degradation of zein occurs upon exposure to various environmental conditions, including moisture, heat, and microorganisms, resulting in the liberation of its constituent amino acids. The

process of degradation is advantageous as it aids in mitigating the buildup of waste and environmental contamination, thereby positioning zein as a sustainable substitute to synthetic materials. The advantageous feature of zein lies in its biodegradability, which makes it a suitable material for various applications including food packaging. The non-biodegradable nature of conventional petroleum-based plastics utilised for packaging purposes presents substantial environmental obstacles. The utilisation of Zein-derived films or coatings presents a viable and environmentally sustainable option in lieu of traditional packaging materials. The zein films exhibit remarkable barrier characteristics against oxygen and moisture, thereby prolonging the shelf life of food products that are packaged. Furthermore, zein films have the ability to undergo natural degradation upon disposal, thereby reducing the environmental impact that is typically associated with plastic waste.

Notwithstanding the favourable biocompatibility and biodegradability properties exhibited by zein, it is imperative to acknowledge that certain limitations associated with this material necessitate attention and resolution. Zein presents a challenge due to its mechanical strength being comparatively inferior to that of synthetic polymers. The aforementioned constraint imposes a restriction on its applicability in specific contexts that necessitate the utilisation of sturdy and long-lasting substances. Scholars are currently investigating various techniques to enhance the mechanical characteristics of zein, including the amalgamation of zein with other polymers or the integration of reinforcing agents. Moreover, the water solubility of zein may pose a constraint in specific applications. The limited solubility of Zein in water imposes limitations on its utilisation in scenarios where resistance to moisture is of paramount importance. Considerable advancements have been made by scholars in altering the configuration of zein via chemical or physical means to augment its hydrophobic characteristics and ability to withstand moisture. Zein exhibits favourable biocompatibility and biodegradability characteristics, rendering it a highly desirable material for a diverse range of applications. Due to its natural origin, low toxicity, and capacity to decompose into non-toxic constituents, this substance is a viable contender for biomedical uses, such as tissue engineering and drug administration. Furthermore, the biodegradable nature of zein renders it a sustainable substitute for traditional packaging materials, thereby contributing to environmental conservation efforts. Despite the limitations of zein, current research and development endeavours are focused on surmounting these challenges and broadening the range of its potential applications. Zein exhibits promising potential in providing sustainable and biocompatible material solutions, owing to its continued advancements.

6 Reinforcement Strategies for Zein-Based Composites

Polymer reinforcement techniques involve the incorporation of reinforcing materials to enhance the mechanical properties of polymers. The process of fibre reinforcement entails the incorporation of fibres, namely glass, carbon, or aramid fibres, into the polymer matrix with the aim of enhancing the strength and stiffness of the composite

material. The technique of particulate reinforcement involves the incorporation of particles such as silica or metal powders into a material in order to enhance its mechanical properties, specifically its hardness and resistance to wear. The process of enhancing the strength of a polymer matrix through the incorporation of slender, singular crystal whiskers is referred to as whisker reinforcement. The utilisation of these methods is prevalent in various sectors, including aerospace, automotive, and construction, for the production of polymer composites that exhibit enhanced strength, toughness, and other favourable characteristics.

The selection of reinforcing materials for zein composites necessitates careful consideration of both the distinctive properties and characteristics of zein and the intended properties of the ultimate composite. Zein is a type of polymer that is protein-based and biodegradable, and it is obtained from maize. In comparison to synthetic polymers, it exhibits relatively lower mechanical strength. The utilisation of natural fibres, including jute, hemp, and flax fibres, as reinforcing agents in zein composites is a viable option. The aforementioned fibres exhibit commendable mechanical characteristics, such as elevated strength and stiffness, and have the potential to enhance the composite's overall strength and toughness. Natural fibres present several benefits, including cost-effectiveness, low density, and environmental sustainability. Cellulose Nanocrystals (CNCs) are sub-micron scale particles that are obtained from cellulose. Due to their remarkable mechanical characteristics and elevated aspect ratio, they exhibit a great potential for reinforcing zein composites. The incorporation of CNCs into composites has been shown to improve their tensile strength, modulus, and barrier properties, all while preserving their biodegradability. The incorporation of nanoclay, like montmorillonite, into zein composites has been found to enhance their mechanical characteristics and thermal endurance [23–25]. The incorporation of nanoclay layers within a composite material serves to impede the propagation of cracks and augment the material's stiffness. Additionally, they provide enhanced gas barrier characteristics and heightened resistance to flames. Carbon nanotubes (CNTs) exhibit remarkable mechanical characteristics, such as elevated strength and stiffness. The integration of carbon nanotubes (CNTs) into zein composites has been found to yield a substantial improvement in their mechanical properties. Carbon nanotubes (CNTs) exhibit electrical conductivity, rendering them advantageous for applications that necessitate electrical characteristics. Bioactive fillers such as hydroxyapatite or tricalcium phosphate can be incorporated into zein composites to achieve specific functionalities. The incorporation of fillers has the potential to augment the bioactivity and biocompatibility of composites, rendering them viable for utilisation in the fields of tissue engineering and drug delivery [26–41]. When selecting reinforcing materials for zein composites, it is important to take into account various factors, including but not limited to compatibility with zein, cost, availability, desired properties of the composite and specific application requirements. The performance evaluation and reinforcement material optimisation of composites necessitates the conduction of experimental characterization and testing.

2.3. Types of reinforcements: nanoparticles, fibers, and fillers.

7 Surface Modification Techniques for Improved Compatibility

The colloidal stability, extensibility, and fragility of zein products are adversely affected by the surface properties and solvent behaviour of ZN molecules [42]. Prior research efforts were primarily directed towards comprehending the conformational configuration of zein. However, more recent investigations have expanded the purview to encompass its involvement in the development of intermolecular cross-links as a constituent of heterogeneous systems [43]. The process of protein solubilization entails the disruption of various types of interactions that contribute to protein aggregation, such as disulfide, hydrogen, van der Waals forces, ionic, and hydrophobic interactions. In order to comprehend the interaction patterns of zein, it is imperative to first examine the process of rehydration and dispersion of the protein in appropriate solvent systems. The chemical properties of zein are predominantly inert, and its structure is primarily globular in nature. The solubility of zein is facilitated by its molecular composition in non-aqueous (primary) solvents, including but not limited to propylene glycol, glacial acetic acid, lactic acid, formic acid, and methyl alcohol. The compound exhibits solubility in alcohol-water blends, including methanol, ethanol, isopropyl alcohol, and acetone. The surface charge characteristics of zein enable its molecular interaction with other entities, thereby promoting the formation of complexes. The diverse physicochemical properties exhibited by these complexes have facilitated their extensive utilisation in various applications. The primary hindrance in utilising zein as a functional protein in the domains of food and biomaterial nanotechnology is its suboptimal functional efficacy. Significant attention has been directed towards zein modifications with the aim of introducing novel and enhanced characteristics, such as surface and material binding properties. The distinctive polymerization characteristics of zein can be attributed to its amphiphilic nature when compared to other proteins. The manipulation of protein polymerization and disintegration can be utilised to elicit advantageous chemical and biological characteristics. Table 1 presents a comprehensive overview of composite systems based on zein and the corresponding interaction mechanisms that have been identified.

8 Processing Techniques for Zein-Based Composites

The incorporation of reinforcing materials and the formation of desired structures in zein-based composites are facilitated by processing techniques, which are of paramount importance in their development. The mechanical, thermal, and functional properties of composites are determined by the dispersion, alignment, and interfacial interaction between zein and the reinforcing materials, which are influenced by various techniques.

The technique of solution casting is commonly employed in the production of composites that are based on zein. The present technique involves the dissolution or

Table 1 Zein-based composites and their interaction mechanisms

Polymer used	Solvent system	Method of preparation	Mechanism	References
Tannic acid	70% ethano	Emulsion gelation	Zein-Tannic acid network formation	[44]
Flavonoids	85% ethanol	Dispersion	Hydrophobic interaction between glucosyl group of flavonoids and zein	[45]
Gelatin	–	Maillard reaction	Electrostatic and hydrophobic interactions	[46]
Sodium caseinate	pH 7.0	Film casting	Steric stabilization, hydrophobic interaction, and H-bonding	[47]
Chitosan	70% ethanol	Ultrasonication	Partial unfolding and H-bonding	[48]
Zein hydrolysate	Water	Emulsion	Electrostatic interactions, Covalent or non-covalent interaction	[49]
Soluble soybean polysaccharide	75% ethanol	Dispersion	Hydrophobic interaction	[50]
Carotenoids	Glacial acetic acid	Electrospinning	H-bonding, electrostatic and hydrophobic interactions	[51]
Chitosan	80% ethanol	Cold plasma treatment	Intermolecular interactions	[52]
Caseinate	80% ethanol	Dispersion	Hydrophobic interactions	[53]
Konjac glucomannan	80% ethanol	Dispersion	Molecular entanglement	[54]
Poly (vinyl alcohol)	70% ethanol	Film casting	Electrostatic interaction	[55]
Tannic acid	70% ethanol	Emulsion	Hydrophobic interactions	[56]
Konjac glucomannan	80% ethanol	Film casting	Steric stabilization	[57]
Sodium caseinate	3M sodium hydroxide	Dispersion	Hydrophobic interaction	[58]

(continued)

Table 1 (continued)

Polymer used	Solvent system	Method of preparation	Mechanism	References
Epigallocatechin gallate (EGCG), quercetagenin (Q) and chlorogenic acid	70% ethanol	Dispersion	Covalent and non-covalent complexation	[59]
Propylene glycol alginate	70% ethanol	Colloidal dispersions	Non-covalent interactions	[60]

dispersion of zein and reinforcing agents in a solvent that is appropriate, such as water or ethanol, to generate a uniform solution. Subsequently, the resultant solution is applied onto a planar substrate, for instance, a glass plate, and desiccated to eliminate the solvent, leading to the formation of a composite film. This methodology facilitates convenient regulation of the thickness of the composite and is appropriate for the fabrication of thin films or coatings. Attaining optimal dispersion and homogeneity of the reinforcing agents within the zein matrix can pose a significant challenge.

The process of melt mixing entails the fusion of zein and reinforcing materials in a molten state. The composite is subjected to processing methodologies such as extrusion or injection moulding. The process of extrusion entails the application of pressure to a molten composite material, which is then passed through a die to generate uninterrupted profiles, such as tubes or rods. In contrast, the process of injection moulding entails the introduction of liquefied composite material into a cavity of a mould, followed by its solidification, thereby yielding intricate geometries. The process of melt mixing facilitates the fabrication of composites based on zein, which can be obtained in various shapes, including but not limited to films, fibres, or moulded objects. The technology provides benefits in relation to its capacity for expansion and adaptability in terms of customization of shape and size. The precise regulation of processing temperature is imperative to prevent zein deterioration and guarantee adequate dispersion of the reinforcing agents.

The process of compression moulding is frequently employed for the mass production of composites based on zein. The present technique involves the placement of a blend of zein and reinforcing agents within a mould cavity, followed by the application of heat and pressure. The application of heat and pressure facilitates the malleability of zein, enabling it to conform to the contours of the mould and ultimately yield a solid composite possessing the desired geometry. Compression moulding is a viable method for manufacturing intricate-shaped, larger-sized components in bulk. This approach presents benefits in relation to cost efficiency and elevated rates of production. Attaining homogenous dispersion of reinforcing agents and preserving their orientation during the moulding procedure can pose a difficulty.

The electrospinning method is a versatile approach that is utilised for the production of composite fibres based on zein. These fibres exhibit a diameter range that spans from the nanometer to micrometre scale. During this procedure, a solution

comprising of zein and the reinforcing materials is subjected to electrostatic spinning through a slender nozzle. The application of high voltage to the nozzle results in the generation of a charged polymer solution jet, which subsequently undergoes solidification into fibres during its transit towards a collector that is grounded. The composite fibres that ensue possess a substantial ratio of surface area to volume, intricate morphology, and regulated alignment. The utilisation of electrospinning technique enables the production of composite fibres based on zein, which exhibit improved mechanical, thermal, and functional characteristics. This technology has various applications in diverse fields, including but not limited to filtration, tissue engineering, and drug delivery.

Additive manufacturing, commonly referred to as 3D printing, has garnered considerable interest due to its ability to produce intricate structures while maintaining meticulous regulation over the allocation of materials. Composite filaments or pastes based on Zein, which incorporate reinforcing materials, can be developed and employed as feedstock in 3D printing. The utilisation of layer-by-layer deposition in composite material fabrication enables the production of intricate geometries and tailored structures. The utilisation of 3D printing technology facilitates the creation of composites based on zein, which can be customised to exhibit specific characteristics, including but not limited to mechanical robustness, porosity, and controlled drug release kinetics. This methodology exhibits significant potential.

Apart from zein-polymer combinations, there exist other materials that exhibit potential for being combined with zein or zein-polymer blends, namely inorganic materials, to create composites [61]. Bioceramics, which are inorganic materials, exhibit resemblances to the mineral constituents of bones. This similarity has the potential to improve the attachment and growth of cells, making bioceramics a promising option for bone regeneration techniques. Furthermore, the integration of inorganic bioactive phases has the potential to facilitate the adhesion between zein-matrix composites and bone tissue [62]. Bioceramics such as hydroxyapatite (HA), calcium phosphate, bioactive glasses, and natural clays (e.g. montmorillonite, sepiolite, palygorskite, bentonite, etc.) are among the frequently utilised inorganic fillers [63]. This discussion inspects the amalgamation of zein with inorganic fillers that are frequently utilised, encompassing a diverse range of systems documented in scholarly literature, with a primary emphasis on their implementation in the field of bone tissue engineering.

The researchers Qu et al. conducted a study wherein they utilised the salt leaching method to produce composite scaffolds composed of hydroxyapatite (HA)-zein for the purpose of bone tissue engineering [61]. The interconnectivity of the pores located on the surface and within the scaffolds was found to be satisfactory. An increase in osteoblastic differentiation of human bone marrow stroma cells was observed on the surface of the scaffold in comparison to those on a pure zein scaffold. Zhang et al. fabricated composite fibres consisting of ultrafine nano-hydroxyapatite (nHA) and zein via the electrospinning technique. The findings indicate that the incorporation of nHA in the fibres led to an increase in their crystallinity, which in turn resulted in favourable mechanical characteristics. The preparation procedure for HA-zein scaffolds was modified by Zhang et al. [64] through the implementation of two distinct

agitation methods prior to electrospinning. Conversely, the amalgamation of zein with synthetic polymers like PCL, as previously indicated, can amplify the regulated degradability and mechanical robustness of scaffolds. Salerno and colleagues (70) conducted a characterization of the mechanical, physical, and biological properties of scaffolds made from PCL-thermoplastic zein (TZ)-HA [65]. The initial step involved the blending of PCL with thermoplastic zein, which was synthesised through *de novo* thermoplasticization of zein. Subsequently, HA micro particles were dispersed in the PCL-TZ blend to confer bioactivity to the scaffold. The study revealed that PCL-TZ-HA scaffolds manifested notable advancements in biological properties, including superior cell adhesion, growth, and osteogenic differentiation. Additionally, these scaffolds exhibited enhanced mechanical properties when compared to other PCL-based scaffolds. Zein-clay nanofibers were produced through electrospinning by Torres-giner and Lagaron [63]. The researchers opted for diverse clay substances. Ruiz-Hitzky et al. employed a range of biopolymers, such as chitosan, pectin, alginate, xanthan gum, ι -carrageenan, gelatin, and zein, along with nanoclays, including sepiolite, a naturally occurring microfibrinous magnesium silicate, to create nanobiocomposite materials through ion-exchange mechanisms, by incorporating them with layered host material (hydroxides) [66]. The suitability of the properties of the bionanocomposite materials produced was purportedly applicable to a diverse array of uses, including biosensors, tissue engineering scaffolds, drug delivery, and gene transfection systems.

9 Zein-Based Composites for Biomedical Applications

The application of Zein-based composites has garnered considerable interest in the sector of biomedicine. An example of this is the utilisation of zein nanoparticles, wherein zein is merged with pharmaceutical agents to fabricate specialised drug delivery systems. Nanoparticles serve as a protective mechanism for drugs, preventing their degradation and facilitating targeted delivery to particular anatomical locations within the body. In contrast, Zein hydrogels exhibit remarkable mechanical strength and water-absorbing capability, rendering them appropriate for controlled drug release and tissue engineering purposes. The composite scaffold comprising of zein and chitosan has been reported to facilitate cellular proliferation and mineralization in bone tissue engineering. The integration of poly(lactic-co-glycolic acid) (PLGA) with zein has been found to facilitate the gradual release of drugs, rendering it a suitable option for extended therapeutic interventions. Finally, the combination of zein and polyethylene glycol (PEG) has been found to produce composites that exhibit controlled drug release profiles. The aforementioned instances underscore the adaptability of composites based on zein in diverse biomedical contexts, thereby facilitating the development of more advanced systems for drug delivery and tissue engineering methodologies.

9.1 Drug Delivery Systems

The utilisation of Zein-based drug delivery systems has surfaced as a propitious strategy for the regulated and focused discharge of therapeutic agents. The protein Zein, which is obtained from maize, exhibits numerous advantageous properties that render it a desirable substance for employment in drug delivery systems. Zein possesses a significant benefit in terms of biocompatibility, thereby ensuring minimal unfavourable reactions when employed in medical applications. The source of derivation for this option is renewable and sustainable, thereby rendering it an eco-friendly alternative [67]. Furthermore, Zein exhibits biodegradability, thereby facilitating the secure removal of the delivery mechanism from the human body post drug discharge. All the advantages of zein based systems used in drug delivery have been elucidated in Fig. 2.

The film-forming properties of Zein play a crucial role in the advancement of drug delivery systems. The substance has the ability to generate consistent and enduring coatings, thereby serving as an exceptional shield against moisture, oxygen, and UV radiation. These factors are of utmost importance in maintaining the stability and effectiveness of pharmaceutical agents. Zein is a highly versatile material for a broad

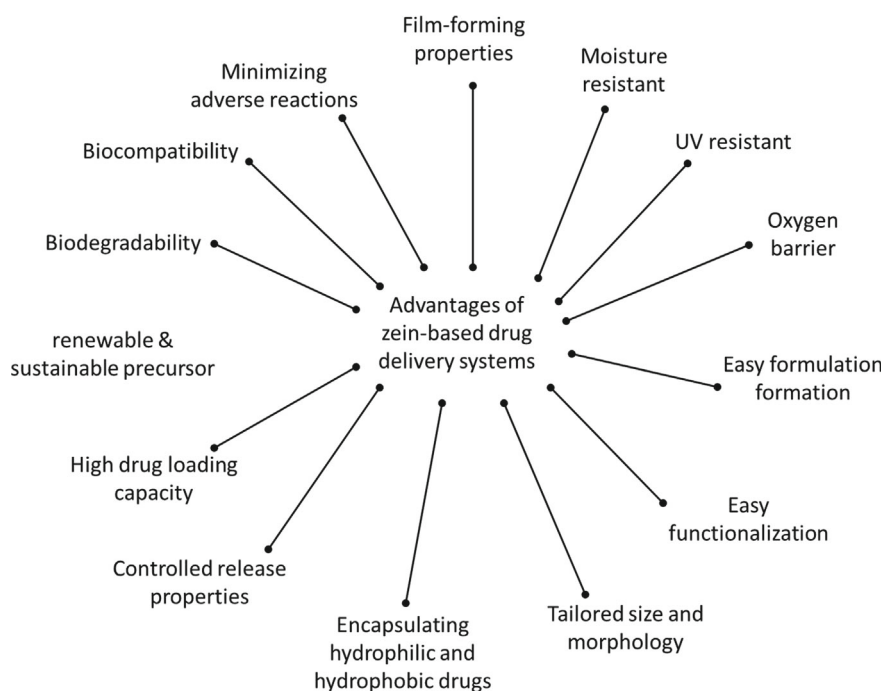


Fig. 2 Various advantages of zein based polymer systems used in drug delivery applications

spectrum of therapeutic applications, owing to its ability to readily accommodate a diverse range of hydrophilic and hydrophobic drugs within its films.

Zein has been employed by researchers to fabricate diverse drug delivery systems, such as nanoparticles, microparticles, and films [68]. Various methods such as solvent evaporation, nanoprecipitation, or emulsification can be employed to fabricate Zein nanoparticles, which enable the incorporation of pharmaceutical agents into the nanoparticle framework. Nanoparticles present a multitude of benefits, including but not limited to enhanced drug solubility, extended release, and increased stability. The surface of these entities can be modified with targeting ligands to achieve site-specific drug delivery, thereby enhancing their functionalization.

Zein-based microparticles represent a promising strategy for drug delivery. Various methods such as spray drying, coacervation, and electrostatic deposition can be employed to fabricate Zein microparticles. The microparticles exhibit notable drug loading efficacy and controlled release characteristics. In addition, the dimensions and structure of these entities can be customised to meet particular therapeutic needs [69]. The utilisation of Zein microparticles has exhibited favourable outcomes in the administration of various drugs, encompassing anticancer agents, anti-inflammatory drugs, and antimicrobial agents.

The utilisation of Zein-based films as drug delivery systems has garnered significant interest. The production of these films can be readily achieved through the application of zein solutions or suspensions onto firm substrates. The utilisation of Zein films has been found to be a proficient approach for targeted drug delivery, particularly in the context of wound healing interventions. It is possible to incorporate pharmaceutical agents that facilitate tissue regeneration and wound healing into these devices, which can enable the controlled and prolonged delivery of drugs at the site of injury [70]. Zein films possess desirable characteristics of flexibility and biocompatibility, rendering them a suitable alternative for the purpose of transdermal drug delivery. Zein exhibits remarkable drug delivery characteristics and presents prospects for additional functionalization. The surface of the material can be altered to enhance drug encapsulation efficacy, augment stability, or facilitate drug release that is responsive to stimuli. In addition, the integration of zein-based drug delivery systems with other materials, such as polymers or lipids, can result in the development of composite systems that exhibit improved properties and functionalities. To sum up, the utilisation of zein-based drug delivery systems has demonstrated significant promise within the realm of pharmaceutical research and development. Zein exhibits biocompatibility, biodegradability, film-forming properties, and versatility in formulation techniques, making it a promising platform for the controlled and targeted delivery of various therapeutic agents. The further development of drug delivery systems based on zein is anticipated to make a substantial contribution to enhancing drug effectiveness and patient results in the coming years.

9.2 Zein Nanoparticles as Drug Carriers

The typical characteristics and capacity to improve drug delivery systems have rendered Zein nanoparticles a subject of considerable interest as drug carriers. The utilisation of Zein, a protein extracted from maize, presents several benefits including biocompatibility, biodegradability, and the capacity to encapsulate drugs with both hydrophilic and hydrophobic properties. The fabrication of zein nanoparticles encompasses diverse methodologies such as solvent evaporation, nanoprecipitation, and emulsification [71]. The utilisation of these methodologies facilitates the creation of homogeneous nanoparticles that exhibit regulated dimensions, surface properties, and drug encapsulation capability.

The utilisation of zein nanoparticles is advantageous due to their capacity to enhance the solubility and stability of inadequately soluble pharmaceutical compounds. The application of zein nanoparticles is of significant value for drugs that exhibit low bioavailability or therapeutic efficacy, as it can effectively address these limitations and enhance their pharmacological performance.

In addition, zein nanoparticles provide a mechanism for the sustained and regulated delivery of pharmaceutical agents, thereby facilitating extended therapeutic outcomes and reducing the need for frequent administration [72]. The modulation of the release rate of the drug that is encapsulated can be achieved by modifying the composition of the nanoparticle formulation. This can be done by adjusting the concentration of zein, the drug-to-polymer ratio, and the inclusion of supplementary excipients or surface modifiers. The ability to regulate drug release kinetics provides opportunities for tailored and individualised drug treatments, which can enhance treatment efficacy while reducing adverse effects.

The biocompatibility of zein is a pivotal determinant in its efficacy as a pharmaceutical carrier. Zein is sourced from natural origins and demonstrates minimal toxicity, rendering it appropriate for a range of biomedical uses. The biodegradability of the nanoparticles guarantees their safe metabolism and subsequent elimination from the body upon drug release [73]. The reduced immunogenicity of zein nanoparticles owing to their biocompatibility renders them suitable for diverse drug delivery systems such as parenteral, oral, and transdermal routes.

Furthermore, the drug delivery capabilities of zein nanoparticles can be augmented through additional functionalization beyond their intrinsic properties. The application of surface modification techniques, such as polymer coating or conjugation with targeting ligands, has been found to enhance the stability, targeting specificity, and cellular uptake of zein nanoparticles. The aforementioned alterations facilitate the administration of drugs to a specific site, thereby mitigating non-specific impacts and augmenting drug concentration at the intended site of activity.

The utilisation of Zein nanoparticles has demonstrated encouraging outcomes in diverse therapeutic domains. Zein nanoparticles have been utilised in cancer therapy to transport chemotherapeutic agents, thereby enhancing drug solubility and minimising systemic toxicity. Zein nanoparticles have been utilised in the field of infectious diseases to encapsulate antimicrobial agents, thereby facilitating targeted

delivery and sustained release [74]. This approach has been shown to improve the efficacy of these drugs against bacterial or fungal pathogens.

Additionally, the utilisation of zein nanoparticles has been investigated as a means of transporting bioactive substances, including antioxidants, nutraceuticals, and peptides. The utilisation of zein nanoparticles for the encapsulation of these compounds has been found to augment their stability, bioavailability, and controlled release, thereby rendering them appropriate for dietary supplements or functional food applications.

In summary, the utilisation of zein nanoparticles has surfaced as a propitious approach for drug administration owing to their biocompatible and biodegradable nature, as well as their capacity to encapsulate a diverse array of drugs. Zein nanoparticles are a promising option for enhancing therapeutic efficacy and reducing adverse effects due to their ability to control drug release kinetics, improve drug solubility, and potential for surface modifications. Further exploration and advancement in the domain of zein-derived drug conveyors exhibit significant promise in enhancing drug administration mechanisms and ultimately augmenting patient welfare.

9.3 Zein-Based Microspheres and Nanocapsules

Microspheres and nanocapsules made from zein have gotten a lot of attention in the field of drug delivery because they have unique properties and can be used in many different ways. Zein is a natural protein made from maize. It has a lot of great qualities that make it a great choice for making microspheres and nanocapsules [69]. These systems offer a promising platform for the controlled release and targeted delivery of therapeutic agents, which can improve the effectiveness of treatment and help patients stick to their treatment plans.

Zein microspheres are round particles with a diameter in the micrometre range. They can be made by spray drying, coacervation, or electrostatic deposition, among other methods. Because zein is so flexible, it can be used to encapsulate a wide range of drugs, including those that are hydrophilic, hydrophobic, or even macromolecular. Zein microspheres have a lot of benefits when it comes to drug delivery. First of all, they can hold a lot of drug, which means that a lot of drug can be put inside the particles. This is especially helpful for drugs that have a low therapeutic index or need a slow release. Second, zein microspheres protect the drug inside the capsule, keeping it from breaking down and keeping it stable. Lastly, zein microspheres have controlled release kinetics, which means that the drug is released slowly and steadily [75]. The porous structure of zein microspheres makes it easier for drugs to move out of the particles, which leads to a steady release of drugs over a long period of time. Because of these qualities, zein microspheres can be used to deliver drugs with different therapeutic needs, such as sustained release, targeted delivery, and drug release at a specific site.

Nanocapsules, on the other hand, are made up of particles that are smaller than a micron and have a core and a shell. There are different ways to make zein nanocapsules, such as by emulsification, solvent displacement, or interfacial deposition. The core of the nanocapsules can hold a drug that doesn't like water, and the zein shell protects the drug and controls how it gets out. The structure of nanocapsules has many benefits for drug delivery [76]. First, the zein shell makes the drug inside it more stable, so it doesn't break down and lose its therapeutic effect. Second, zein nanocapsules can make it easier for drugs that don't dissolve in water to do so, making them more bioavailable and effective. Also, the structure of the nanocapsule keeps the drug from being broken down by enzymes, which lets it get to the target site quickly. Also, ligands or functional groups can be added to the surface of zein nanocapsules to make them deliver drugs in a more targeted way [77]. This change to the surface makes it easier for drugs to build up at certain places, which improves their therapeutic effect and reduces their off-target effects.

The properties of microspheres and nanocapsules made from zein can be improved by adding more excipients or changing the surface of the particles. For example, adding polymers or surfactants can make the particles more stable, control how the drug is released, and make the release last longer. Co-encapsulation of multiple drugs or combination therapies within zein microspheres or nanocapsules is also possible, allowing for synergistic effects or drug release in steps.

One of the best things about microspheres and nanocapsules made from zein is that they are biocompatible and biodegradable. Zein comes from a natural source and is well-tolerated by the body, so it doesn't cause many side effects. Because zein is biodegradable, the particles can be safely removed from the body after the drug is released. This means that there are no worries about long-term accumulation or toxicity. These properties are important for making drug delivery systems that are safe and work well.

Microspheres and nanocapsules made from zein can be used in a wide range of therapeutic areas. In the treatment of cancer, zein microspheres or nanocapsules have been used to deliver chemotherapeutic agents, making the drugs easier to dissolve and lowering their systemic toxicity. The controlled release and targeted delivery that zein-based systems offer make it possible for drugs to be released slowly and in the right place. This improves the effectiveness of the treatment and reduces side effects. Also, systems based on zein have shown promise in ocular drug delivery, which is how drugs are given to the eye to treat different eye diseases. They have also been studied as ways to deliver vaccines, proteins, and peptides, making them more stable, immune-stimulating, and easy to control.

In conclusion, microspheres and nanocapsules made from zein have a lot of potential as ways to deliver drugs. Because they are biocompatible, biodegradable, and can hold a wide range of drugs, they are useful for many therapeutic applications. Controlled drug release, targeted drug delivery, and drug protection are all things that zein-based systems can do. These things help improve therapeutic results and patient compliance. If research and development in this field keep going, it could lead to better ways to deliver drugs and more effective, personalised treatments.

9.4 Tissue Engineering Scaffolds

Zein-based tissue engineering scaffolds have gotten a lot of attention in the field of regenerative medicine because they have unique properties and have the potential to help tissues heal. Zein is a natural protein made from maize [78]. As a scaffold material, it has many benefits, such as being biocompatible, biodegradable, and able to look like the extracellular matrix (ECM). Because of these qualities, zein is a good choice for making scaffolds for tissue engineering.

In tissue engineering, biocompatibility is very important because the scaffold material should not cause bad immune responses or toxicity when it comes into contact with living tissues. Zein has been studied a lot and shown to be biocompatible [79]. This means that the body doesn't have any problems with it and it doesn't cause inflammation or immune reactions. This property makes sure that zein-based scaffolds can create a good environment for cells to stick together, grow, and change into different types of cells, which helps tissues heal.

The fact that scaffolds made from zein break down naturally is another benefit. In tissue engineering, it is important that the scaffold breaks down over time. This lets the scaffold be slowly replaced by newly formed tissue. Zein is made of a material that can be broken down by the body's natural processes. As the zein scaffold breaks down, it makes room for host cells to move in and allows new extracellular matrix components to be deposited. This leads to tissue regeneration and integration.

Also, zein can act like the extracellular matrix (ECM), which is the natural environment that helps cells grow and tissues grow. The ECM gives cells physical and biochemical signals that tell them what to do and how to work. Structure, composition, and mechanical properties of scaffolds made of zein can be made to look like the ECM. This lets the scaffold give the cells the signals they need to stick together, move, make more cells, and change into different types of cells [80]. By looking a lot like the native extracellular matrix (ECM), zein-based scaffolds help cells stick together and form new tissue, which leads to successful tissue regeneration.

Zein is also helpful in making tissue engineering scaffolds because it can be used in many different ways. Zein can be made into different types of materials, such as films, fibres, porous scaffolds, and hydrogels, for use in different types of tissue engineering [81]. For example, zein films and fibres can be used as thin, flexible scaffolds for skin tissue engineering, while porous zein scaffolds can be used for bone tissue regeneration. Because zein-based scaffolds can have their physical and mechanical properties changed, they can be made to fit the needs of different tissues and organs [82].

In addition to the properties it already has, zein can be changed or mixed with other biomaterials to make tissue engineering scaffolds work better. Changes can be made to the surface of zein scaffolds to improve cell adhesion, encourage certain cell responses, or allow controlled drug release. Zein can also be mixed with other polymers or bioactive substances to make composite scaffolds with better properties. For example, adding growth factors or bioactive molecules to zein-based scaffolds can increase the activity of cells and help them heal faster.

Zein-based tissue engineering scaffolds have been used successfully in a number of ways to help heal damaged tissue. They have been used to help heal skin, bone, cartilage, liver, nerve, and other types of tissue [83]. Zein is a great scaffold material for promoting cell growth, tissue integration, and functional restoration because it is biocompatible, biodegradable, and can be made to look like ECM.

In the end, zein-based tissue engineering scaffolds have a lot of potential for regrowing damaged tissues. Because they are biocompatible, biodegradable, and can act like the ECM, they are good choices for making scaffolds that help cells stick together, grow, and change. Because zein is so versatile and can be changed, it can be used to make scaffolds that fit the needs of different tissues and organs. Continued research and development in this field shows promise for improving zein-based tissue engineering scaffolds and putting them to use in clinical settings, which will help people who need their tissues to grow back or be fixed.

9.5 Zein-Based Nanofiber Scaffolds

The distinctive properties of Zein-based nanofiber scaffolds have attracted considerable attention in the realm of tissue engineering, owing to their capacity to stimulate cell proliferation and facilitate tissue regeneration. The utilisation of Zein, a naturally occurring protein extracted from maize, presents numerous benefits as a scaffold material in the production of nanofibers. These advantages include its biocompatibility, biodegradability, and the ability to adjust its mechanical properties [1]. The aforementioned characteristics render zein a desirable option for the fabrication of nanofiber scaffolds in diverse tissue engineering contexts.

The capacity of zein-based nanofiber scaffolds to imitate the structure and architecture of the extracellular matrix (ECM) is a significant benefit. The extracellular matrix (ECM) offers an inherent microenvironment for cells, exerting an impact on their behaviour and governing the progression of tissue development [84]. The production of Zein nanofiber scaffolds can be achieved through the utilisation of various techniques, including electrospinning. This method enables the fabrication of fibres that possess diameters within the nanometer scale. The nanofibers exhibit a high surface area-to-volume ratio that closely mimics the fibrous architecture of the extracellular matrix (ECM), thereby offering an ideal substrate for cellular adhesion, proliferation, and differentiation. The zein scaffolds' nanofiber architecture enables effective nutrient and waste product exchange, fostering a favourable milieu for tissue regeneration.

The biocompatibility of zein-based nanofiber scaffolds is an additional benefit. Extensive research has been conducted on Zein, which has demonstrated its biocompatibility. This implies that Zein does not provoke any unfavourable immune reactions or toxicity upon interaction with living tissues [85]. The biocompatibility of zein-based nanofiber scaffolds ensures a conducive environment for cellular attachment and proliferation. The nanofibers exhibit a high affinity for cellular adhesion, promoting cellular spreading and the formation of tissue-like structures that closely

resemble the microarchitecture of native tissue. The cellular response plays a pivotal role in ensuring the efficacy of tissue regeneration and integration.

The biodegradability of nanofiber scaffolds based on zein is a crucial attribute. Zein is a biodegradable substance that undergoes natural degradation within the human body over a period of time. This characteristic of the scaffold enables a progressive deterioration, thereby promoting the substitution of the scaffold with freshly generated tissue. The degradation of zein nanofibers facilitates the infiltration of host cells and deposition of fresh extracellular matrix (ECM) components, thereby promoting tissue regeneration and integration. The deliberate breakdown of zein nanofiber scaffolds is crucial in achieving the optimal equilibrium between scaffold reinforcement and tissue generation.

Zein-based nanofiber scaffolds possess the potential to be customised in terms of their mechanical properties to meet the specific demands of diverse tissue types. The incorporation of plasticizers, cross-linking agents, or polymer blending enables the modulation of mechanical characteristics, including but not limited to stiffness, elasticity, and tensile strength [86]. The ability to adjust the mechanical properties of nanofiber scaffolds allows for the creation of scaffolds that closely mimic the mechanical characteristics of the desired tissue. This is crucial for providing the appropriate mechanical support and cues for cellular functions. Zein nanofiber scaffolds promote cellular adhesion, migration, and tissue remodelling by replicating the mechanical properties of the host tissue.

The efficacy of Zein-based nanofiber scaffolds has been demonstrated across a diverse spectrum of tissue engineering applications. Stem cells have been employed in the process of tissue regeneration for a diverse range of tissues, such as the integumentary system, osseous tissue, cartilage, nervous tissue, and vascular structures. The zein scaffolds' nanofiber architecture facilitates cellular proliferation, differentiation, and the development of structured tissue formations. Additionally, zein nanofiber scaffolds have demonstrated the capability to integrate bioactive compounds like growth factors or pharmaceuticals, resulting in targeted administration and improved tissue regeneration. The capacity to imitate the extracellular matrix (ECM), exhibit biocompatibility and biodegradability, as well as adjust their mechanical properties render them highly suitable for fostering cellular proliferation, encouraging tissue regeneration, and facilitating the restoration of function. It is anticipated that further research and development in this area will augment the efficacy of nanofiber scaffolds made from zein and broaden their utility in the domain of tissue engineering. This, in turn, will ultimately be advantageous for individuals requiring tissue restoration and regeneration.

9.6 Zein-Based Hydrogels

The versatile properties and potential applications of Zein-based hydrogels have garnered significant attention in various fields of study in recent years, rendering

them a noteworthy class of biomaterials. Zein is a protein that is found naturally in maize. Upon cross-linking, it undergoes a process of three-dimensional network formation, ultimately leading to the creation of hydrogels. Hydrogels exhibit notable biocompatibility, biodegradability, and exceptional water-absorbing capabilities, rendering them appropriate for employment in biomedical domains such as regenerative medicine, tissue engineering, wound healing, and drug delivery systems.

The controlled release of therapeutic agents is a notable benefit of hydrogels based on zein [87]. The hydrogel's porous architecture facilitates the integration of therapeutic agents such as drugs, proteins, or growth factors, which can be gradually dispensed, thereby augmenting their therapeutic potency. In addition, hydrogels derived from zein demonstrate favourable mechanical properties, thereby guaranteeing their robustness and coherence throughout their usage.

Zein-based hydrogels exhibit remarkable biocompatibility with cells and tissues, which is a noteworthy characteristic. Hydrogel matrices offer a favourable microenvironment that facilitates cellular attachment, proliferation, and differentiation, rendering them a highly promising scaffold material for tissue engineering applications [88]. Furthermore, it has been demonstrated that hydrogels based on zein exhibit antimicrobial characteristics, thereby offering potential advantages in the context of wound healing interventions. In addition, hydrogels derived from zein exhibit characteristics that are conducive to ecological preservation and long-term viability. Zein is a promising alternative to synthetic hydrogels, which are derived from petrochemicals, due to its renewable source derived from maize. The environmentally conscious properties of hydrogels derived from zein render them an appealing option for utilisation in eco-friendly and sustainable technological advancements.

10 Conclusion

The present chapter has furnished a thorough exposition of polymer composites based on zein and their prospective applications in the realm of biomedicine. The utilisation of Zein, a protein extracted from maize, presents a promising avenue for the creation of biocompatible materials that are both renewable and sustainable. The integration of zein into polymer composites has resulted in the augmentation of their mechanical characteristics, biodegradability, and bioactivity, rendering them suitable for diverse biomedical uses, as per the findings of researchers. The chapter underscored the multifunctionality of zein-derived polymer composites in the context of drug delivery systems, tissue engineering, and regenerative medicine. The precise and targeted delivery of therapeutic agents is enabled by the tunable characteristics of the polymer matrix, in conjunction with the controlled release properties of zein. This holds significant value in the management of persistent medical conditions and in facilitating the restoration of bodily tissues. Additionally, the chapter expounded upon the significance of biocompatibility and cellular interactions in the context of biomedical applications. The compatibility of polymer composites based on Zein with cells and tissues has been found to be exceptional, as they facilitate

cell adhesion, proliferation, and differentiation. This presents novel opportunities for the advancement of sophisticated scaffolds and implants capable of facilitating tissue proliferation and restoration. Furthermore, the chapter underscored the environmentally sustainable characteristics of polymer composites derived from zein. The increasing apprehension regarding environmental sustainability has led to the exploration of renewable resources such as zein as a feasible substitute for traditional polymer materials that are obtained from petrochemicals. This phenomenon not only mitigates the dependence on non-renewable energy sources but also fosters the advancement of environmentally-friendly and enduring technologies. In the realm of biomedical applications, the utilisation of zein-based polymer composites has demonstrated considerable potential due to their ability to provide a blend of biocompatibility, controlled release, and sustainability. Notwithstanding, there exist obstacles that must be surmounted, including the optimisation of mechanical properties, enhancement of stability, and improvement of scalability of said materials. Subsequent research endeavours ought to prioritise the resolution of these obstacles in order to propel the domain forward and facilitate the transformation of zein-derived polymer composites into pragmatic clinical implementations.

To summarise, the progress made in the creation of polymer composites using zein is a noteworthy breakthrough in the realm of biomaterials. This innovation has the capacity to transform biomedical uses and enhance the results experienced by patients. The potential of zein-based polymer composites to transform the realm of biomedicine and facilitate the development of advanced medical devices and therapies is significant, owing to ongoing research and innovation in this area.

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Bacterial Cellulose-Polymer Composites for Biomedical Applications



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Abstract The chapter looks at the new field of using bacterial cellulose (BC) with polymers to make advanced materials for different biomedical uses. Bacterial cellulose is getting a lot of attention as a promising biomaterial because of its unique properties, such as high purity, mechanical strength, biocompatibility, and biodegradability. This chapter talks about the importance and potential of adding BC to polymer composites to improve their mechanical properties, change their porosity and surface area, make them more biocompatible, help them release drugs in a controlled way, and give them antibacterial and antimicrobial properties. BC-polymer composites can be used to make scaffolds for tissue engineering, wound dressings, implants, and drug delivery systems because they are flexible and can be made to fit different needs. This chapter gives an overview of the basic ideas behind BC-polymer composites, how they are made, how they are characterised, and how they are used in medicine.

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It also talks about the challenges and future directions of the field, with a focus on how these composites can make a big difference in biomedical research and patient care.

Keywords Bacterial cellulose · Biocompatible · Biodegradability · Porosity · Polymer composites

1 Introduction

Cellulose is a biopolymer that is abundant and versatile, and is commonly found in the cell walls of plants. The structure is fortified by densely packed, elongated chains of glucose molecules, imparting robustness and inflexibility to it. Cellulose is commonly linked with botanical substances, however, it can also be generated by specific bacteria via a mechanism known as bacterial cellulose (BC) synthesis [1]. The distinctive characteristics and potential applications of BC have attracted considerable interest in diverse domains in recent times. Various bacterial strains, such as *Acetobacter xylinum*, *Komagataeibacter spp.*, and *Gluconacetobacter spp.*, are capable of synthesising BC [2]. During their growth phase, these microorganisms produce cellulose in the shape of elongated, band-like filaments through a process of secretion. BC is commonly synthesised in an oxygen-rich environment using a culture medium that comprises glucose or alternative carbon substrates. Cellulases, a group of enzymes, facilitate the conversion of the carbon source into cellulose by the bacteria [3]. The high purity and degree of polymerization are among the distinguishing characteristics of bacterial cellulose. The high degree of purity exhibited by BC can be attributed to its production by bacteria in a regulated setting, which eliminates the presence of contaminants commonly encountered in cellulose derived from plants. The exceptional level of purity exhibited by BC renders it a highly desirable material for a range of applications, with particular relevance to the field of biomedicine [4, 5]. The concept of degree of polymerization pertains to the extent of elongation of cellulose chains, and BC demonstrates a greater degree of polymerization in comparison to cellulose found in plants. The exceptional mechanical strength and unique physical properties of BC are attributed to this factor. Commonly, nanofillers for polymer composites are tiny particles that are incorporated with polymers to improve their properties [6–20]. These fillers, often in the form of nanoparticles or nanofibers, are designed at the nanoscale to impart certain features. BC exhibits physical properties that render it highly suitable for a diverse array of applications [21]. The crystalline structure of BC is highly pronounced and it exhibits a notable capacity for retaining water. The material displays exceptional mechanical characteristics, such as elevated tensile strength and Young's modulus, surpassing that of numerous artificial polymers. British Columbia's high water-holding capacity enables it to effectively absorb and retain significant quantities of liquid, up to 100 times its own weight. The aforementioned characteristic has resulted in its application in the field of wound dressings, owing to its ability to generate a damp milieu

that fosters the process of wound recovery [22]. The desirable properties of BC are also attributed to its porous structure. The three-dimensional matrix formed by the interconnected network of cellulose fibres exhibits a significant surface area. The structural characteristics of BC facilitate effective permeability of gases and liquids, rendering it a suitable material for deployment as a membrane in filtration processes. Additionally, the porous nature of BC can be harnessed to load and release various molecules, such as drugs or enzymes, making it an attractive material for controlled drug delivery systems. Moreover, BC possesses exceptional biocompatibility and biodegradability [23]. Its biocompatibility refers to the material's ability to interact favourably with living tissues without causing adverse reactions. BC has been extensively studied as a biomaterial for tissue engineering applications, such as scaffolds for cell growth, due to its biocompatibility. Furthermore, BC is biodegradable, meaning it can be naturally broken down by microorganisms in the environment without leaving behind harmful residues [24]. The unique combination of properties offered by bacterial cellulose has led to its application in diverse fields. In addition to wound dressings and tissue engineering, BC has been explored in areas such as food technology, cosmetics, electronics, and environmental remediation. For example, BC can be used as a thickening agent or stabilizer in food products, as a substrate for the growth of microorganisms in fermentation processes, or as a component in electronic devices due to its excellent electrical conductivity [25].

2 Importance of Bacterial Cellulose-Polymer Composites in Biomedical Applications

BC has been identified as a highly promising biomaterial, owing to its distinctive characteristics, including but not limited to its exceptional purity, mechanical robustness, biocompatibility, and biodegradability. It is well known that the incorporation of fillers into polymer nanocomposites helps to improve their mechanical, thermal, electrical, and barrier characteristics [18, 26–42]. Interestingly, researchers have been exploring the integration of BC into polymer composites in order to broaden its applications in the biomedical sector and improve its overall functionality. The amalgamation of BC and diverse polymers has demonstrated significant potential for the advancement of sophisticated materials with enhanced characteristics and customised functionalities. The present article aims to investigate the significance of bacterial cellulose-polymer composites in the realm of biomedical applications.

2.1 Enhanced Mechanical Strength

The integration of BC into polymer composites yields a notable enhancement in their mechanical characteristics, thus constituting a significant benefit. BC has exceptional

tensile strength and modulus, but its flexibility is limited [43]. The incorporation of polymers into BC composites has been found to improve their mechanical properties, particularly in terms of toughness and flexibility. This renders them suitable for deployment in various applications that necessitate mechanical stability, including but not limited to tissue engineering scaffolds, wound dressings, and implants.

2.2 Tunable Porosity and Surface Area

The porous nature of BC presents a favourable framework for the integration of polymers, thereby enabling the production of composites that possess adjustable porosity and surface area. Incorporating polymers into the structure of BC can facilitate the management of pore size, distribution, and interconnectivity, thereby enhancing the precision of drug, growth factor, and bioactive molecule release [44]. This characteristic confers notable benefits to drug administration mechanisms, tissue reconstruction procedures, and wound recuperation interventions.

2.3 Enhanced Biocompatibility

BC exhibits biocompatibility; however, the addition of polymers can augment its biocompatibility and bioactivity. The introduction of functional groups or surface modification of BC by polymers can facilitate cell adhesion, proliferation, and differentiation. The selection of suitable polymers enables composite materials to imitate the extracellular matrix, thereby creating a conducive microenvironment for cells [24]. This, in turn, promotes tissue regeneration and enhances the biocompatibility of implantable devices.

2.4 Controlled Drug Release

Drugs and bioactive compounds can be released under controlled conditions using bacterial cellulose-polymer composites. High drug loading is possible thanks to BC's porous structure, and the polymers can serve as a barrier or reservoir for gradual, controlled release [45]. In applications like wound dressings, tissue engineering scaffolds, and implant coatings where precise and sustained release of therapeutic agents is necessary to speed up the healing process or treat chronic conditions, this controlled drug release feature is essential.

2.5 Antibacterial and Antimicrobial Properties

BC is naturally antimicrobial, which means it can be used to prevent infections in biomedical settings. By adding antibacterial polymers or antimicrobial agents to BC composites, the materials' resistance to bacterial colonisation and biofilm formation can be increased [46]. This is especially important in wound dressings, implants, and other medical devices to reduce the risk of infection and improve patient outcomes.

2.6 Versatility and Tailorability

Bacterial cellulose-polymer composites are very flexible and can be made to fit different needs. Different polymers can be chosen by researchers based on specific needs, such as mechanical properties, rates of degradation, or bioactive functions. When BC is mixed with natural or man-made polymers, it can be used to make a wide range of composite materials.

2.7 Sustainable and Eco-friendly Materials

BC comes from resources that can be used again and again, and it can be made in large amounts using simple fermentation processes. When BC is added to polymer composites, it helps make biomedical applications more sustainable. By combining biodegradable BC with biocompatible polymers, the resulting composites can be a greener alternative to traditional materials and reduce the environmental impact of medical devices and implants [47].

3 Bacterial Cellulose and Polymer Materials

BC is a distinct type of cellulose produced by specific bacterial species. It has garnered considerable attention in recent years due to its exceptional properties and wide range of industrial applications. BC production entails the cultivation of bacteria under specific conditions that stimulate cellulose synthesis. This summary provides a thorough comprehension of BC production methods and highlights its distinguishing characteristics [48]. BC manufacturing begins with the selection of cellulose-producing bacterial strains, with *Gluconacetobacter xylinus* being the most extensively studied species. Through a process known as biosynthesis, these bacteria are able to generate large quantities of BC [49]. Typically, a culture medium comprising carbon and nitrogen sources, as well as other essential nutrients, is used to cultivate these bacteria. One of the primary benefits of BC production is that it

can be grown in large-scale bioreactors. This allows for the efficient and controlled production of BC, ensuring its consistent quality and quantity. In addition, the use of bioreactors facilitates the scalability of BC production, making industrial applications a possibility. Long chains of cellulose are formed by the polymerization of glucose units during the biosynthesis of cellulose [21]. The resultant BC has a nanostructured network composed of numerous interwoven nanofibers. These nanofibers are extremely pure and crystalline, endowing BC with exceptional mechanical properties. BC's physical properties make it an appealing material for a variety of applications. BC has a high tensile strength, making it stronger than plant-based cellulose and other forms of cellulose. It is also extremely flexible and can be formed into a variety of configurations, enabling the production of films, fibres, gels, and three-dimensional structures. Figure 1 depicts the types of BC based systems and their applications in biomedical areas. These characteristics make BC appropriate for use in biomedicine, food technology, cosmetics, and other fields. BC has generated considerable interest in biomedicine due to its biocompatibility and capacity to promote cell proliferation. It has been investigated for applications in tissue engineering, wound healing, and drug delivery [50]. BC can be formed into scaffolds that provide mechanical support for tissue regeneration, whereas its porous structure permits the diffusion of nutrients and waste products. In addition, BC's antibacterial properties make it beneficial for preventing wound infections. The culinary industry has also recognised British Columbia's potential. Its ability to produce films and gels has led to its use as an environmentally friendly alternative to conventional plastics for edible packaging. BC films can serve as barriers against moisture, oxygen, and ultraviolet radiation, extending the shelf life of food products. In addition, BC can be utilised as a thickener, stabiliser, or texture modifier in a variety of culinary formulations.

BC's distinctive properties also make it appropriate for cosmetic applications. Due to their ability to retain moisture and deliver active ingredients to the skin, BC-based substances can be incorporated into skincare products such as facial masks and lotions. In exfoliating cleansers, BC can also serve as a biodegradable alternative to microplastics [51]. The production of BC entails the cultivation of cellulose-producing bacteria under controlled conditions. BC possesses exceptional physical characteristics, such as high tensile strength, ductility, and biocompatibility. Due to these properties, it has been investigated in numerous industries, including biomedicine, food technology, and cosmetics. BC's ability to be formed into films, fibres, polymers, and three-dimensional structures enables a variety of applications. With continued research and development, BC holds great promise for the creation of innovative and sustainable materials.

BC, as a biopolymer, has been employed in the production of diverse composites using various polymeric materials. Polymers are a class of organic compounds that possess distinctive hydrogen bonding sites. The comparable characteristics and existence of the binding sites enable the production of BC composites with diverse polymers of different properties. Numerous instances of biopolymer-based BC composites have resulted in enhancements in the biomedical domain, physico-mechanical attributes, and conductive potential of BC. The advancement of composite synthesis

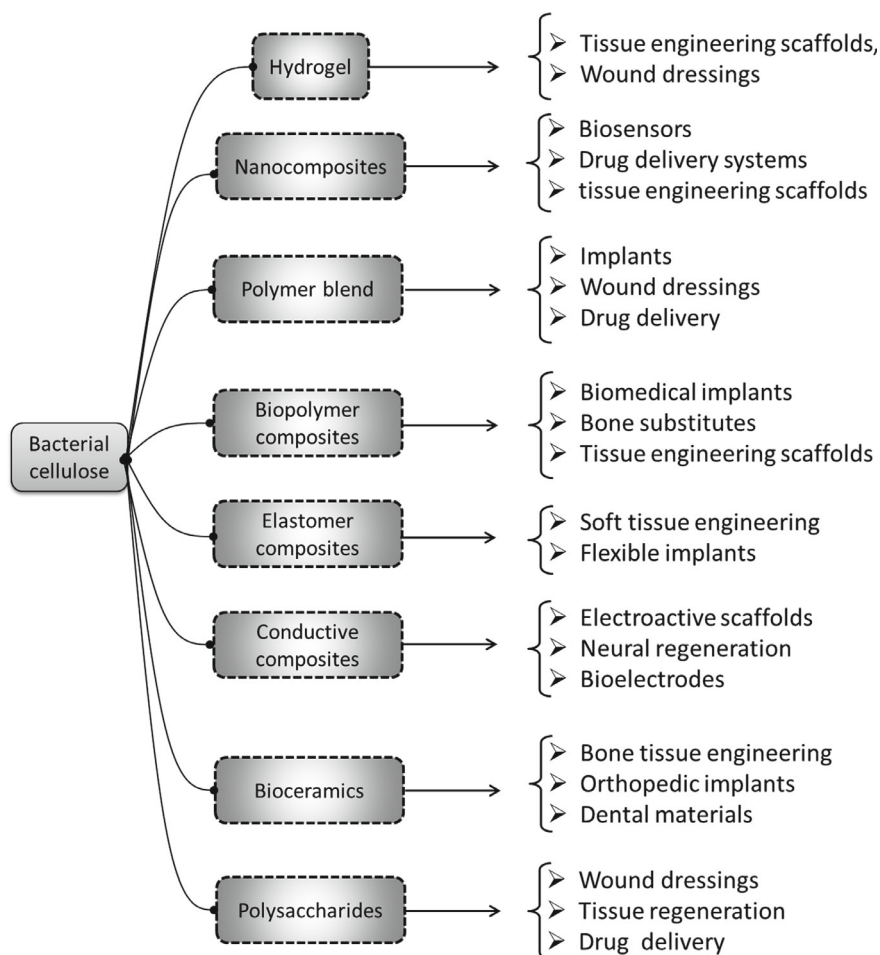


Fig. 1 Commonly used BC as a biomaterial platforms and their possible uses

is propelled by constraints in the utilisation of BC across diverse domains. The utilisation of composites has partially addressed constraints pertaining to attributes such as antimicrobial, antioxidant, wound healing, and conducting properties.

Composite materials comprising of conducting polymers and BC have been developed to confer electrical conductivity to BC. BC is a type of cellulose that is synthesised by *Gluconacetobacter xylinum*. It is characterised by its web-like structures composed of ribbon-shaped nano-fibers. The conductive polymer known as polyaniline (PAni) exhibits conductivity that is intricately linked to the procedures of synthesis and doping. According to a report, the electronic conductivity can be improved through in situ nano-assembly of BC nanofibers and PAni [52]. A novel 3D network could be assembled by synthesising PAni on the surface of BC nano-fibers.

The electroconductivity properties of composites are significantly influenced by the reaction time of polymerization as well as the types and concentration of doping protonic acids. The electroconductivity of composite hydrogels was observed to have been increased from 10^{-8} to 10^{-2} S cm⁻¹. This enhancement can be further augmented by the incorporation of different protonic acids. The BC-PAni nanofiber composite is a hydrogel with electro-conductive properties that amalgamates the characteristics of conductive systems and hydrogels. This composite has the potential to be utilised in various applications such as flexible displays, biosensors, and platform substrates. Additionally, it can be employed to investigate the impact of electrical signals on cell activity and to regulate desired cell function for tissue engineering purposes. The remarkable feature of certain metallic particles is their ability to exhibit both conductivity and magnetic properties. The properties of BC are inadequate and necessitate modification to enable its applicability in various fields. The synthesis of BC-Pd composites has been attempted as a means of remedying this inadequacy. The composites in question are produced via the process of depositing metals onto the surface of BC by immersing it in a solution containing ammonium hexachloropalladate. The cellulose facilitates the reduction of metallic ions, resulting in the formation of a coating on the surface of the BC material. The study revealed that the BC-Pd nanocomposites possess the ability to act as a catalyst for the production of hydrogen upon exposure to sodium dithionite. In addition, it was reported by Evans et al. [53] that BC-Pd was able to produce an electric current through the utilisation of hydrogen in membrane electrode assemblies. A recent study conducted on BC-Pt nanocomposites revealed their noteworthy conductive efficiency, thereby indicating their potential applicability in fuel cells and biosensors. The BC-Pt nanocomposites were synthesised using the liquid phase chemical deoxidization technique, resulting in the production of composites with notable electrocatalytic activity. In addition, Yang et al. [54] reported a significant enhancement in the current density of the membrane through the process of doping with either protonic acid or inorganic acid.

4 Synthesis and Fabrication of Bacterial Cellulose-Polymer Composites

BC is a specific biopolymer synthesised by specific bacterial strains, such as *Komagataeibacter xylinus*. The material in question exhibits remarkable characteristics such as elevated levels of purity, mechanical robustness, compatibility with biological systems, and the ability to decompose naturally [55]. These features render it a highly auspicious substance for a diverse range of applications in fields such as biomedical engineering, tissue engineering, food packaging, and electronics. In order to augment the operational capabilities and broaden the potential uses of BC, scholars have directed their attention towards integrating polymers into the BC framework [56]. The present discourse delves into diverse techniques for integrating polymers into a BC substrate, their benefits, obstacles, and prospective implementations.

4.1 Physical Mixing

Physical mixing is considered to be one of the most straightforward techniques for integrating polymers into a BC matrix. The proposed methodology involves the amalgamation of polymer solutions or powders with the BC matrix, which is subsequently subjected to drying or solvent evaporation to facilitate polymer integration. The approach is characterised by its simplicity and lack of intricate processing procedures [57]. The non-uniform dispersion of polymers in the BC matrix may result in a heterogeneous distribution and possible areas of weakness in the composite material. Attaining a uniform blend is imperative in guaranteeing the intended characteristics and efficacy of the ultimate composite.

4.2 In-situ Polymerization

The process of in-situ polymerization entails the introduction of monomers or pre-polymers into the matrix of BC, which is then followed by polymerization reactions occurring within the matrix. This approach facilitates the synthesis of polymers within the BC matrix, leading to a close integration [58]. The selection of monomers or pre-polymers plays a crucial role in determining the characteristics of the resulting polymer, thereby offering flexibility in customising the attributes of the composite material. The task of regulating the polymerization process and attaining homogeneous dispersion within the BC matrix can pose difficulties, necessitating meticulous refinement of reaction conditions and kinetics. The appropriate commencement and regulation of the polymerization process are of utmost importance in attaining the intended characteristics and circumventing any unfavourable impacts on the BC framework.

4.3 Coating

The incorporation of polymers into a BC matrix can be achieved through the utilisation of coating, which has proven to be a highly effective technique. The application of polymer solutions or dispersions onto the surface of the BC matrix is achieved through various coating techniques, including but not limited to dip-coating, spray-coating, and other coating methods [59]. The application of a coating layer can confer supplementary functionalities, such as heightened barrier properties, augmented mechanical strength, or distinctive surface properties. The process of coating provides the advantage of flexibility in the selection of various polymers, while also allowing for precise control over the thickness of the polymer layer. The level of adhesion between the polymer coating and the BC matrix may exhibit variability contingent

upon the compatibility of the constituent materials, which could result in delamination or suboptimal interfacial bonding. The adhesion and compatibility between the polymer and BC can be improved by implementing appropriate surface treatment or modification of the BC matrix, thereby resulting in a composite that is robust and long-lasting.

4.4 *Electrospinning*

The process of electrospinning entails the creation of polymer fibres by means of an electrically induced mechanism. When polymer solutions are exposed to a strong electric field, a slender polymer stream is emitted, which solidifies into uninterrupted fibres as the solvent evaporates. The incorporation of polymers into the BC structure is facilitated by the direct deposition of fibres onto the BC matrix. The electrospinning technique enables regulation of the fibre diameter, porosity, and alignment, thereby exerting an impact on the mechanical, electrical, and transport characteristics of the resultant composite material [60]. Attaining a homogeneous dispersion of electrospun fibres within the BC matrix can pose difficulties, necessitating supplementary processing measures to guarantee adequate integration. The utilisation of methods such as layer-by-layer deposition or post-treatments such as compression or hot-pressing can facilitate the attainment of a composite structure that is well-integrated [61].

4.5 *Chemical Crosslinking*

Chemical crosslinking is a process that entails the utilisation of polymers that possess reactive functional groups capable of establishing covalent bonds with the BC matrix. The application of a polymer solution containing crosslinkable groups onto the BC matrix is succeeded by a crosslinking reaction, which serves to establish chemical bonds between the polymer and BC [62]. The implementation of this technique has the potential to augment the mechanical robustness, steadfastness, and longevity of the composite material. Prudent choice of crosslinking agents and reaction conditions is imperative to attain ideal crosslinking while upholding the characteristics of BC and avoiding the onset of cytotoxic consequences. When selecting a crosslinking chemistry, it is important to take into account various factors, including the compatibility of reactants, reaction kinetics, and the desired properties of the resulting composite material.

4.6 Microbial Synthesis

The process of microbial synthesis involves the utilisation of microorganisms such as bacteria to produce polymers within the BC matrix. This methodology capitalises on the metabolic proficiencies of microorganisms, including the generation of biologically synthesised enzymes or proteins. The attainment of a uniform dispersion of polymers within the BC matrix can be realised by integrating the polymers directly during the process of BC synthesis. The resultant composite material exhibits advantageous characteristics stemming from the amalgamation of both BC and polymers synthesised by microorganisms [63]. The selection of microorganisms and their corresponding growth conditions, along with the compatibility of the polymers synthesised by the microorganisms with BC, are crucial factors to be taken into account. It is imperative to optimise the fermentation process and exercise control over microbial activity to ensure the production of the desired polymer and its successful integration within the BC matrix [64].

The integration of polymers into a matrix of BC presents prospects for augmenting the characteristics and efficacy of materials based on BC. Several techniques have been investigated to incorporate polymers into the BC matrix, including physical mixing, in-situ polymerization, coating, electrospinning, chemical crosslinking, and microbial synthesis [65]. The selection of a particular method is contingent upon a variety of factors, including but not limited to the desired properties, compatibility between the polymers and BC, and specific application requirements. Each method presents its own set of advantages and challenges. Through meticulous design and optimisation of these techniques, scholars can fabricate composite materials that possess customised properties suitable for diverse applications such as scaffolds for tissue engineering, systems for delivering drugs, electronics that can be worn, and materials for packaging food. Further research and development in this area will enhance the potential of composites based on BC and make a valuable contribution to the progress of sustainable and functional materials.

5 Strategies for Controlling Composite Morphology and Structure

The properties and functionalities of BC composites are significantly influenced by their morphology and structure. The management of these factors is imperative in customising the efficacy of BC composites to fulfil particular application prerequisites. Diverse techniques can be utilised to regulate the composite morphology and structure, facilitating the management of factors such as fibre alignment, interfacial adhesion, permeability, and superficial properties. The present discourse delves into several fundamental tactics for regulating the morphology and structure of BC composites and their consequent impact on the performance of the composites.

The manipulation of processing parameters during fabrication can exert an influence on the morphology and structure of BC composites [66]. The manipulation of various parameters, including temperature, time, pH, and concentration of the BC dispersion, can be employed to regulate the development of BC fibres and the resultant composite architecture. Elevated temperatures and extended fermentation durations have the potential to induce the synthesis of elongated BC fibres, thereby influencing the mechanical characteristics of the composite material. Modulating the pH levels in the course of the synthesis procedure has the potential to exert an impact on the morphological and porous characteristics of the BC matrix. Through meticulous regulation of these parameters, it is feasible to attain the intended composite configurations and characteristics.

The manipulation of surface properties and morphology of BC composites can be achieved through the utilisation of surface modification techniques [67]. The surface of BC can be modified through the application of plasma treatment, chemical functionalization, or coating methods, thereby augmenting its compatibility with other materials or polymers that are incorporated. The aforementioned alterations result in an ameliorated interfacial adhesion between BC and other constituents, including polymers or nanoparticles, thereby resulting in improved mechanical characteristics and composite efficacy. The enhancement of cell attachment in tissue engineering endeavours can be facilitated by surface modifications, thereby rendering BC composites more appropriate for biomedical engineering and regenerative medicine [68].

The management of fibre alignment in composites is a critical factor in obtaining mechanical strength and anisotropic properties. Various methods can be utilised to orient BC fibres in specific directions, including unidirectional fibre placement, layer-by-layer assembly, and magnetic alignment, which are known as fibre alignment techniques [69]. The structural alignment of fibres has been shown to augment various material properties, including tensile strength, modulus, and electrical or thermal conductivity in the direction of alignment. This approach proves to be especially advantageous in scenarios where there is a need for anisotropic characteristics, such as in the case of structural composites or electronic gadgets. The manipulation of fibre orientation enables the customization of both the mechanical and functional characteristics of BC composites to fulfil particular demands.

The integration of fillers and reinforcements in BC composites provides a means to regulate microscale morphology and structure. The properties of the BC matrix can be modified by the inclusion of fillers, such as nanoparticles or microsized particles [70]. The incorporation of fillers has the potential to enhance mechanical strength, augment thermal stability, and confer supplementary functionalities such as antimicrobial properties or electrical conductivity. The manipulation of filler dispersion and distribution in the BC matrix can be achieved through diverse techniques such as physical blending, in-situ synthesis, or surface alteration of the fillers. The mechanical properties of BC composites can be improved through the addition of reinforcements, such as fibres or fabric layers. This enables the regulation of stiffness, toughness, and impact resistance.

By employing templating and scaffold design methodologies, it becomes feasible to regulate the morphology and structure of BC composites on a macroscopic scale [71]. The process of templating entails the utilisation of sacrificial templates or moulds to fabricate precise shapes or structures. The precise design of the final BC composite can be achieved through the manipulation of the templates' shape and arrangement. The utilisation of scaffold design methodologies, such as freeze-drying or electrospinning, enables the production of porous BC composites that possess regulated pore size, interconnectivity, and porosity. The scaffolds exhibit a high degree of suitability for employment in tissue engineering endeavours, wherein the scaffold's structure and porosity are of paramount importance in facilitating cellular proliferation and tissue restoration.

6 Biomedical Applications of Bacterial Cellulose-Polymer Composites

The field of biomedical applications has witnessed an increasing interest in the research and development of advanced materials in recent times. The bacterial cellulose-polymer composite is a material that shows great potential. Bacterial cellulose, a distinctive variant of cellulose synthesised by specific bacterial strains, presents a diverse array of prospects in the realm of biomedicine when combined with polymers. The aforementioned composite material displays remarkable characteristics, including elevated mechanical potency, compatibility with biological systems, capacity for degradation by natural processes, and the aptitude to absorb and retain substantial quantities of aqueous substances [62]. The aforementioned characteristics render it a highly suitable contender for diverse biomedical implementations.

Tissue engineering is a notable biomedical domain where bacterial cellulose-polymer composites find substantial application. The objective of tissue engineering is to create viable tissues and organs through the integration of cells and biomaterials [56]. The utilisation of bacterial cellulose-polymer composites has the potential to serve as a highly effective scaffold for the purpose of facilitating cell growth and promoting tissue regeneration. The distinctive porous architecture of bacterial cellulose facilitates cellular infiltration, proliferation, and differentiation, thereby fostering the genesis of novel tissue. The biocompatibility of the composite material facilitates a reduced immune response and enhances its integration with the adjacent tissue.

Bacterial cellulose-polymer composites have been identified as a viable option for utilisation in the domain of wound healing. Chronic wounds, such as those resulting from diabetes, present a considerable obstacle in the field of healthcare. The fabrication of dressings that promote wound healing can be achieved through the customization of bacterial cellulose-polymer composites. The composite material's notable ability to retain water facilitates the preservation of a damp milieu, a crucial factor in

promoting ideal wound healing conditions [72]. The distinctive composition of bacterial cellulose additionally facilitates gaseous interchange and enables the dissemination of oxygen and nourishment towards the injury location, thereby augmenting the recuperative mechanism. Furthermore, the mechanical robustness of the composite material provides a safeguard to the wound against external forces, thereby diminishing the likelihood of infection and additional harm. Additionally, the utilisation of bacterial cellulose-polymer composites has demonstrated promise in the realm of drug delivery systems. The composite material has the potential to be designed in a way that enables the controlled release of therapeutic agents while also providing encapsulation. The high drug-loading capacity of bacterial cellulose is attributed to its porous structure, which can be modulated by the incorporation of polymers to regulate the release kinetics [73]. The utilisation of a controlled release mechanism is notably advantageous in the administration of pharmaceuticals with a limited therapeutic range or for targeted drug delivery, thereby reducing the incidence of systemic adverse reactions. Furthermore, the composite's biodegradability guarantees its safe metabolism and excretion from the body upon completion of drug release. Bacterial cellulose-polymer composites possess antibacterial characteristics that render them useful in the creation of antimicrobial coatings and wound dressings. The composite material has the potential to be modified with antimicrobial agents, such as silver nanoparticles, in order to impede bacterial colonisation and mitigate the risk of infection. The aforementioned characteristic holds significant importance in the realm of medical equipment, as the presence of bacterial agents can result in grave ramifications [74]. The integration of antimicrobial agents into the composite material of bacterial cellulose-polymer composites offers a robust and efficacious approach to address infections and enhance patient outcomes. Furthermore, the adaptability of bacterial cellulose-polymer composites expands to various biomedical implementations, including biosensors, coatings for implants, and scaffolds for tissue engineering in organ transplantation. The material's aptitude to facilitate cellular adhesion and proliferation, in conjunction with its mechanical characteristics and biocompatibility, renders it a highly suitable substance for such purposes. The three-dimensional configuration of the structure can be customised to emulate the extracellular matrix, thereby creating a conducive milieu for cellular adhesion and proliferation. Furthermore, the amalgamation of the composite material with electronic components facilitates the creation of biosensors that can be utilised for diagnostic objectives, thereby enabling instantaneous tracking of biological parameters.

7 Drug Delivery Systems Based on Bacterial Cellulose-Polymer Composites

In recent years, there has been a notable surge in interest towards drug delivery systems that are founded on composites of bacterial cellulose and polymers. These systems possess distinctive benefits with regards to regulated drug discharge, biocompatibility, and adaptability. Bacterial cellulose, which is synthesised by specific bacteria, offers a biocompatible and natural matrix. The addition of polymers improves the functional and mechanical characteristics of the composite [75]. The amalgamation of bacterial cellulose and polymer composites renders them a highly favourable option for drug delivery purposes.

The controlled release of therapeutic agents is a notable benefit of bacterial cellulose-polymer composites in drug delivery [76]. It is possible to design a composite scaffold that can enclose bioactive molecules or drugs within its porous configuration. Bacterial cellulose's notable water-holding capacity facilitates the effective loading of diverse drug types, encompassing small molecules, proteins, peptides, and nucleic acids. The modulation of drug release kinetics can be achieved through the manipulation of composite scaffold composition and structure, as well as polymer selection. The implementation of a controlled release mechanism guarantees a consistent and regulated administration of the medication for an extended duration, thereby reducing adverse reactions and enhancing the effectiveness of the treatment.

The porous architecture of composites consisting of bacterial cellulose and polymers is of significant importance in the context of drug delivery applications [64]. The scaffold's interlinked pores enable the diffusion of pharmaceuticals and fluid exchange, thereby promoting the liberation of the encapsulated molecules. The precise regulation of pore size and distribution can facilitate the accommodation of diverse drugs and their corresponding release demands. Furthermore, the composite scaffold affords safeguarding to the enclosed pharmaceutical agents against extrinsic variables, such as enzymatic degradation or alterations in pH, thereby guaranteeing their stability and effectiveness.

The determination of the compatibility of the composite scaffold with the biological environment is a critical aspect of drug delivery systems, as it is indicative of the biocompatibility of the system. Bacterial cellulose possesses inherent biocompatibility due to its natural composition, which closely resembles that of the extracellular matrix (ECM) found in human tissues [77]. The integration of polymers into the composite material serves to augment its biocompatibility, thereby minimising any deleterious impact on cells and tissues. The utilisation of bacterial cellulose-polymer composites *in vivo* is deemed safe and effective due to their biocompatible nature, which results in the reduction of inflammation, immune response, and tissue damage.

The mechanical characteristics of composites comprising bacterial cellulose and polymers represent a noteworthy benefit for drug delivery applications. The incorporation of polymers into the composite scaffold results in an improvement in its mechanical properties and overall stability, rendering it appropriate for a

range of routes of administration. The composite material can be processed into various configurations, including films, membranes, fibres, or hydrogels, to meet specific drug delivery needs. The adaptability of drug delivery systems permits their utilisation through various routes such as oral, topical, intravenous, and others.

The assessment of the biodegradability of composites consisting of bacterial cellulose and polymer is a crucial factor to take into account in the context of drug delivery systems [78]. The composite scaffold has the potential to be engineered to undergo degradation over a period of time, thereby facilitating its metabolic breakdown and elimination from the biological system without any deleterious remnants. This characteristic obviates the necessity of scaffold removal protocols, thereby mitigating patient discomfort and the likelihood of associated complications. The modulation of composition and structure of the composite scaffold can regulate its degradation rate, thereby facilitating the controlled release of drugs at a predetermined pace while preserving its biodegradable nature.

In addition, the utilisation of bacterial cellulose-polymer composites presents a promising avenue for the implementation of targeted drug delivery [79]. The composite scaffold has the capability of being functionalized with ligands, antibodies, or targeting moieties that exhibit specificity towards target cells or tissues, thereby facilitating their recognition and binding. The utilisation of a targeted approach enables the delivery of drugs to specific sites, thereby enhancing the effectiveness of the treatment and reducing the occurrence of off-target effects. The process of functionalizing the composite scaffold has the potential to facilitate drug release that is responsive to stimuli. This type of drug release is activated by particular physiological or environmental cues, such as enzymatic activity, temperature, or pH.

8 Bacterial Cellulose-Polymer Composites in Wound Healing and Dressings

The utilisation of bacterial cellulose-polymer composites has garnered considerable interest in the realm of wound healing and dressings owing to their distinctive characteristics and benefits [80]. The process of wound healing is multifaceted and encompasses the repair of injured tissue as well as the mitigation of potential infection. Bacterial cellulose-polymer composites possess various advantages that render them suitable for facilitating wound healing and serving as efficacious wound dressings [56].

The high water retention capacity exhibited by bacterial cellulose-polymer composites is regarded as a significant advantage in the context of wound healing. Bacterial cellulose possesses a complex structure consisting of nanofibers arranged in a three-dimensional configuration, which enables it to exhibit a high capacity for water absorption and retention. The aforementioned characteristic of the composite material enables it to sustain a humid milieu at the injury location, a crucial factor for the most favourable wound recovery outcome [81]. The presence of moisture

aids in the facilitation of cellular migration that is integral to the process of wound healing [61]. This includes the migration of fibroblasts and keratinocytes, which are essential to the formation of granulation tissue.

The significance of the porous architecture of bacterial cellulose-polymer composites is a critical factor in the context of their potential utilisation in wound healing applications. The composite scaffold's porous structure facilitates gaseous exchange, including oxygen and carbon dioxide, between the wound and the surrounding environment. Ensuring sufficient oxygen delivery to the wound is crucial for cellular metabolic processes and tissue regeneration [82]. The permeable configuration additionally enables the dispersion of nourishing substances towards the injury location and the elimination of metabolic byproducts, thereby augmenting the comprehensive recuperative mechanism.

Moreover, the mechanical characteristics of composites comprising bacterial cellulose and polymers render them appropriate for the purpose of wound dressings [83]. The incorporation of polymers into the composite material results in an improvement in its mechanical properties, such as strength and flexibility. This enhancement enables the composite to adapt to the wound site and provide a protective barrier for the underlying tissue [51]. The composite material exhibits a high degree of resistance to external forces, thereby effectively mitigating any potential damage to the wound [60]. Additionally, the mechanical stability of the composite material guarantees its structural integrity throughout the process of tissue regeneration, thereby creating a stable milieu for the same.

The issue of biocompatibility holds significant importance in the context of wound healing and dressings, as the material employed in this regard must not trigger any unfavourable immune reactions or toxic outcomes [84]. The biocompatibility of bacterial cellulose-polymer composites is noteworthy due to the naturally derived origin of bacterial cellulose, which shares a comparable composition with the extracellular matrix of human tissues. The composite scaffold facilitates cellular adhesion, proliferation, and migration, thereby stimulating the development of fresh tissue [85]. The incorporation of bacterial cellulose-polymer composites enhances biocompatibility, thereby mitigating the likelihood of inflammation and infection, ultimately resulting in superior wound healing outcomes.

The efficacy of wound healing and dressings is augmented by the antibacterial characteristics of bacterial cellulose-polymer composites [86]. BC exhibits intrinsic antimicrobial properties, impeding the proliferation of diverse bacterial strains [87]. Moreover, the composite material has the potential to be modified with antimicrobial agents, such as silver nanoparticles or antimicrobial peptides, in order to augment its antibacterial efficacy. The significance of this feature is particularly pronounced in the context of wound dressings, given that bacterial infections can substantially impede the process of wound healing [88]. Bacterial cellulose-polymer composites exhibit antimicrobial properties that aid in the prevention and management of bacterial colonisation, thereby mitigating the likelihood of wound infections.

In addition, the utilisation of bacterial cellulose-polymer composites offers a safeguarding layer to the wound, thereby preventing the infiltration of extrinsic impurities and creating a regulated milieu for the healing process. The utilisation of composite

scaffold effectively mitigates the potential infiltration of pathogens, dirt, and debris, thereby diminishing the likelihood of infection [89]. Additionally, it serves as a physical impediment to moisture depletion, preserving the moisture equilibrium of the wound and inhibiting undue desiccation [89]. The composite scaffold's ability to provide protection facilitates uninterrupted wound healing and fosters a conducive milieu for tissue regeneration.

Bacterial cellulose-polymer composites possess practical applicability as they can be conveniently manufactured into diverse forms that are appropriate for wound dressings [90]. These forms include but are not limited to films, membranes, hydrogels, or fibres. The dressings exhibit the ability to adapt to various wound configurations and dimensions, thereby ensuring a secure and precise fit, as well as an ideal extent of coverage. The adaptability of fabrication methodologies and scaffold architecture enables the tailoring of dressings to fulfil precise wound healing demands. Moreover, composite dressings have the potential to be customised by integrating bioactive molecules, growth factors, or wound-healing agents, thereby augmenting their therapeutic efficacy. A transdermal patch mimicking a mussel was fabricated utilising BC (Fig. 2), a sustainable resource sourced from *Glucanoacetobacter xylinus* [91]. The cellulose produced by the microbe *G. xylinus* was extracted and subjected to chemical modification using a catechol-containing compound known as dopamine. This modification was intended to confer adhesive properties to the resulting transdermal patch system [92]. In order to acquire the composite film based on BC that is doped with reduced graphene oxide (rGO) and silver nanoparticles (Ag NPs). The investigation of the composite film's antimicrobial efficacy was conducted on both Gram-positive bacteria (*Staphylococcus aureus* and *Lysinibacillus fusiformis*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), as this is a crucial consideration in the development of a wound-healing patch. The antimicrobial efficacy of the composite film was evaluated using the zone inhibition technique and live-dead assay. The morphological examination of the impacted bacteria was demonstrated via the scanning electron microscopy (SEM) analysis. A study was conducted to assess the cytotoxicity of the prepared films on the NIH 3T3 fibroblast cell line. The results indicated that all of the films were compatible with the cells.

9 Bacterial Cellulose-Polymer Composites for Bioimaging and Biosensing Applications

The unique features and adaptable uses of bacterial cellulose-polymer composites have generated noteworthy attention in the domains of bioimaging and biosensing. The composites in question amalgamate the benefits of bacterial cellulose, a biocompatible and natural substance, with the functionalities of synthetic polymers. This amalgamation creates novel prospects in the fields of biotechnology and healthcare.

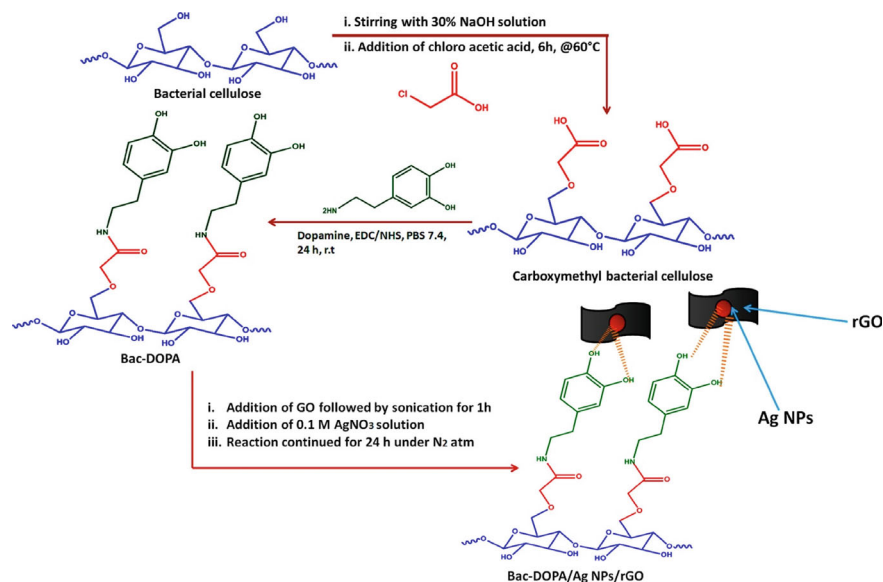


Fig. 2 Schematic representation of the modification of BC with DOPA. Reproduced with the permission from Ref. [91]. © 2019 American chemical society

The optical properties of bacterial cellulose-polymer composites render them advantageous in the field of bioimaging [51]. Bacterial cellulose exhibits notable transparency within the visible and near-infrared spectra, thereby facilitating proficient transmission of light [93]. This characteristic renders it a suitable substrate for the integration of fluorescent dyes, quantum dots, or other imaging agents. Through the incorporation of imaging agents into the composite scaffold, scholars can fabricate materials that provide amplified fluorescence emission, enhanced photostability, and heightened signal-to-noise ratios. The aforementioned capability facilitates the precise and delicate identification of biological entities across diverse imaging techniques, including fluorescence microscopy, optical coherence tomography (OCT), and near-infrared imaging [94].

The porous architecture of composites comprising bacterial cellulose and polymers is an additional benefit for applications in the field of bioimaging. The composite scaffold's interconnected pores can function as reservoirs for imaging agents, enabling their regulated discharge at the intended location. The implementation of a controlled release mechanism guarantees a consistent and extended presence of the imaging agent, resulting in prolonged imaging durations and enhanced signal intensity [95]. Furthermore, the pores can be modified to exhibit selective binding affinity towards particular analytes, such as biomarkers or target molecules, thereby facilitating precise imaging and augmenting diagnostic potential.

The biocompatibility of composites comprising bacterial cellulose and polymers holds significant importance in the context of bioimaging applications. Bacterial

cellulose is obtained from naturally occurring sources and exhibits a composition that is analogous to the extracellular matrix (ECM) of human tissues [96]. The biocompatibility of these composites enables their safe and non-toxic application in biological systems, thereby reducing the occurrence of unfavourable reactions or tissue harm. The ability of composite materials to be utilised for *in vivo* imaging, facilitating the real-time tracking of biological processes, disease progression, or treatment efficacy, is attributed to their compatibility with living systems.

Apart from bioimaging, the utilisation of bacterial cellulose-polymer composites has exhibited potential in the realm of biosensing applications. The process of biosensing pertains to the identification and measurement of particular analytes or biomarkers present in biological specimens. The distinctive characteristics of bacterial cellulose, in conjunction with the adaptability of polymers, facilitate the creation of biosensors that exhibit exceptional sensitivity, selectivity, and stability.

The customization of the porous configuration of bacterial cellulose-polymer composites can facilitate the integration of diverse sensing components, including enzymes, antibodies, or DNA probes. The immobilisation of sensing elements within the composite scaffold facilitates the effective binding and recognition of target analytes. Composite materials offer a reliable and biocompatible setting for sensing components, guaranteeing their efficacy and soundness.

The optical characteristics of composites consisting of bacterial cellulose and polymers are of significant importance in the context of biosensing applications. The integration of fluorescent dyes or quantum dots into the composite material enables the sensing components to produce quantifiable signals when exposed to the intended analyte. The utilisation of a composite scaffold results in an improvement of signal amplification, thereby facilitating the detection of analytes with high sensitivity and precision, even when present in low concentrations. The sensitivity and specificity of the biosensor can be optimised by adjusting the composition and structure of the composite, thereby further refining its optical properties.

In addition, the mechanical stability and flexibility exhibited by composites of bacterial cellulose and polymer render them appropriate for employment in biosensing applications [97]. Composite materials possess the ability to be manufactured into diverse structures, including but not limited to films, membranes, or fibres, contingent upon the particular sensing prerequisites. The integration of these materials into sensing devices or platforms can facilitate the development of robust and dependable sensing interfaces [48]. The durability and long-term functionality of composites in challenging sensing environments are ensured by their mechanical properties.

The facile functionalization of bacterial cellulose-polymer composites is an additional benefit in the realm of biosensing. Functional groups or biomolecules can be utilised to modify the surface of bacterial cellulose, thereby enabling the immobilisation of specific receptors or capture probes [98]. The process of functionalization facilitates the precise and exclusive identification of desired analytes, thereby augmenting the precision and dependability of the biosensing mechanism. Composite materials possess the ability to be tailored to detect a diverse array of analytes, including proteins, nucleic acids, and small molecules, rendering them

multifaceted instruments for applications in diagnostics, environmental surveillance, and pharmaceutical exploration.

10 Conclusion

To summarise, the utilisation of BC-polymer composites has become increasingly significant in various biomedical applications. The composites in question amalgamate the distinct characteristics of bacterial cellulose, namely biocompatibility, biodegradability, and high water-holding capacity, with the adaptability and efficacy of synthetic polymers. The amalgamation of these entities presents numerous benefits, rendering them exceedingly appealing for diverse biomedical implementations. BC-polymer composites hold considerable importance owing to their potential to tackle crucial issues in biomedical domains, including but not limited to tissue engineering, wound healing, drug delivery, bioimaging, and biosensing. Composite materials offer a suitable scaffold for tissue engineering by providing a three-dimensional structure that facilitates cell attachment, proliferation, and differentiation. The composites' mechanical properties can be customised to emulate the natural tissue milieu, thereby facilitating optimal tissue regeneration. BC-polymer composites have been found to be beneficial in wound healing applications by creating a conducive and protective environment that promotes the healing process. The enhanced wound healing outcomes associated with composites can be attributed to their high water retention capacity, porous structure, and mechanical stability. These properties facilitate cell migration, prevent infection, and maintain optimal moisture balance. The utilisation of BC-polymer composites presents a promising avenue for the development of drug delivery systems. Composite materials have the ability to effectively enclose and discharge therapeutic agents, thereby offering regulated and prolonged drug release patterns. This facilitates accurate administration of medication, minimised adverse reactions, and enhanced therapeutic effectiveness. The drug delivery capabilities of composites can be further enhanced through the incorporation of diverse polymers and functionalization strategies, owing to their versatile nature.

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Tribology and Biodegradability of Ceramic/Fiber Filler-Based Polymer Composites



Himani Bajaj, Navin Chandra Pant, Poonam Gangwar, Anisha Arya, Mohd Vaseem Fateh, and Abhijeet Ojha

Abstract This chapter explores into the confluence of tribology and biodegradability within polymer composites that are based on ceramic/fiber fillers. The chapter explores the impact of tribological interactions on the biodegradation of sustainable materials in the context of their growing sector. This study examines the utilisation of ceramic and fibre fillers with the purpose of enhancing the mechanical characteristics of materials. Additionally, it investigates the influence of these fillers on the environmental degradation of such materials. The study enhances our comprehension of the relationship between tribological behaviour and the biodegradability of polymer composites, providing valuable knowledge for the advancement of environmentally friendly materials that possess favourable mechanical and environmental characteristics.

Keywords Tribology · Biodegradability · Polymer composites · Ceramic/fiber fillers · Mechanical

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1 Introduction

Tribology refers to the study and engineering of friction and wear caused by moving, rubbing surfaces. Friction, lubrication, and wear are all topics that fall under this broad category. This area of study is inherently multidisciplinary, requiring knowledge from disciplines as diverse as physics, chemistry, materials science, and engineering. Wear and friction-related problems result in high costs to industry and factory shutdowns, making tribological behaviour analysis crucial. Metal recycling and the responsible use of other natural resources like wood have become pressing concerns as the structural and automotive industries have expanded. Therefore, composite materials that can function under demanding situations like high load, high temperature, and high corrosive pressure are needed to replace traditional materials. The benefits of composite materials over traditional materials have been shown by Chandramohan and Marimuthu. Composites' high strength-to-weight ratio makes them a viable choice for many engineering applications. Lightweight, high strength, corrosion resistance, high fatigue strength, less loud in operating condition, etc. are just some of the reasons why composites are in such high demand today [1]. Polymer matrix composites (PMCs) are the most popular type of tribo-material because to their light weight, self-lubrication qualities, resilience to wear and corrosion, and affordability. Other types of tribo-materials include metal matrix composites (MMCs), ceramic matrix composites (CMCs), and carbon-carbon composites (CCCs) [2].

Polymer composites with continuous-fiber reinforcement of high volume percentage and precise alignment are known to exhibit very high values of specific strength and stiffness. A structural component constructed from one of these materials has qualities that can be adjusted to suit the loading conditions. In addition to these benefits, composites can have tailor-made qualities depending on the application thanks to the large range of fibre and matrix materials available. This is especially the case when developing the microstructure of a composite material using multiple fibre kinds (hybrid composites). The majority of these advancements in materials have focused on enhancing the composites' mechanical qualities, namely their resilience to fatigue conditions. Commonly, nanofillers for polymer composites are tiny particles that are incorporated with polymers to improve their properties [3–17]. Polymers have many tribological uses, including gears, a variety of bearings, bearing cages, artificial human joint bearing surfaces, bearing materials for space applications like coatings, tyres, shoe soles, automobile brake pads, non-stick frying pans, flooring, and various types of surfaces for optimal tactile properties like fibres. Polymers, such as polymethyl methacrylate (PMMA) and polydimethylsiloxane (PDMS), are replacing Si as a preferred structural material in the emerging field of micro-electromechanical systems (MEMS). Si is frequently treated with an appropriate polymeric layer to improve its frictional, anti-wear, or anti-stiction qualities. Temperature, relative speed of the contacting surfaces, normal load, and the environment all have significant implications on the tribological features of polymers, just as they do on the bulk mechanical responses. Polymers are modified by adding appropriate fillers to suit a particular application to address these effects and

for better control of the reactions. The best combination of primarily friction and wear performances can only be achieved by using them in composite or, at best, mixed form. Fillers may be more economically viable than the polymer matrix itself. Due to the potential importance of achieving just the right balance between the matrix and filler elements for optimal performance, the composition of the filler materials is often a tightly guarded secret of the producer. However, during the past several decades, scientists at a number of research institutions have made significant discoveries into the causes of friction and wear in polymer tribology. This has somewhat facilitated the process of materials selection for every particular tribological application.

Due to the swift advancement of emerging biomedical technologies such as tissue engineering, regenerative medicine, gene therapy, and controlled drug delivery, there is a concurrent development of innovative materials tailored to fulfil the specific demands of these respective disciplines [15, 18–34]. It is widely acknowledged that the addition of fillers to polymer nanocomposites contributes to the enhancement of the material's mechanical, thermal, electrical, and barrier properties. Conventional single-component ceramic or polymer materials are insufficient to meet these requirements. Furthermore, it is vital to acquire materials that possess several advanced functions in order to adequately satisfy fundamental criteria such as biocompatibility, biodegradability, and suitable mechanical qualities. As an illustration, a multifunctional material designed for the purpose of regenerating bone tissue should possess the ability to stimulate the generation of new bone tissue in the absence of external organic bone growth factors, such as BMP-2. Additionally, it should undergo gradual degradation at a rate that aligns with the pace of new bone regeneration. Furthermore, it should promote the formation of fresh blood vessels and demonstrate antibacterial and anti-inflammatory properties. Hence, the attainment of crucial material and biological characteristics can be accomplished by the deliberate design and advancement of multi-component materials. This involves the careful selection of matrix and modifier materials, along with their respective properties such as shape, distribution, and content. Additionally, the fabrication procedures employed for composites play a significant role in achieving the desired outcomes. This study focuses on the incorporation of ceramic modifiers into biodegradable polymer matrices in order to produce composites that possess tailored properties suitable for biomedical applications, particularly in the fields of tissue engineering and regenerative medicine. This discussion will focus on the use of ceramic modifiers, such as bioactive glasses, calcium phosphates, silica, and wollastonite, which are commonly employed in many applications. The primary objective is to explore the advantageous impacts of these modifiers on both the material and biological aspects of composites.

2 Tribology of Different Polymer-Ceramic Filler Composites

The field of research known as tribology examines the effects of relative motion on the friction, lubrication, and wear of contacting surfaces. Tribosystems are defined and described in this article, along with the many forms of friction and wear that can affect them and the ways in which lubrication can mitigate their effects. The procedures used on tribometers for testing and assessing tribological behaviour are also discussed. Researchers from many fields work together on tribology because it is a complicated and broad field. This includes a lot of different areas, like computer science, biomedical science and engineering, chemistry, chemical engineering, physics, math, materials science and engineering, manufacturing, and many more. Biotribology, nanotribology, space tribology, and tribotronics are all areas of tribology that study how things move.

In addition to providing good thermal conductivity and electrical insulation, ceramic fillers are another significant kind of material. The electronic packaging market seeks materials with this intriguing property combination. Ceramic materials often exhibit a hybrid ionic-covalent bonding mechanism, while Van-der-Waals or metallic bonding may also be present. The study of polymer tribology involves the investigation of friction and wear mechanisms, which are found to be more intricate compared to those observed in metals. However, our understanding of these mechanisms in polymers is very limited. While the tribology of metal and ceramic contacts in relative motion is governed by well-established ‘Laws of Friction,’ the behaviour of polymer/metal contacts typically deviates from these laws. There are multiple reasons for this phenomenon, which encompass the relatively lower hardness of polymers in comparison to metals, their greatly reduced thermal conductivities that affect heat generation in contacts, and their notably lower melting points. The subsequent discussion will mostly focus on tribo-applications that entail a smooth metallic counterpart. This implies that the inferences made from the findings cannot be readily extrapolated to more extreme wear scenarios, such as those involving intense abrasion or erosion. However, the assortment of polymers that can effectively withstand diverse operating situations, such as strength, temperature range, resistance to environmental deterioration, sliding friction, and wear, is vast. These polymers can be systematically categorised in a scheme based on their physical qualities, operational temperature ranges, and cost (Fig. 1).

The common polymers, including PS (polystyrene), PVC (polyvinyl chloride), PP (polypropylene), and PE (polyethylene in its different forms), have comparatively low mechanical strength, as indicated by their tensile strengths, which are approximately 20 MPa. The materials used in the production are characterised by high volume (measured in metric tonnes per annum) and have limited temperature capabilities, typically operating within a range of up to 100 °C. Additionally, these materials are cost-effective, with a price below 1.13 € per kilogramme. Furthermore, these materials are produced on a global scale. The category of polymers known as “Mid-Range” or “engineering polymers,” including polyamides (PA) and polyesters such as PET/

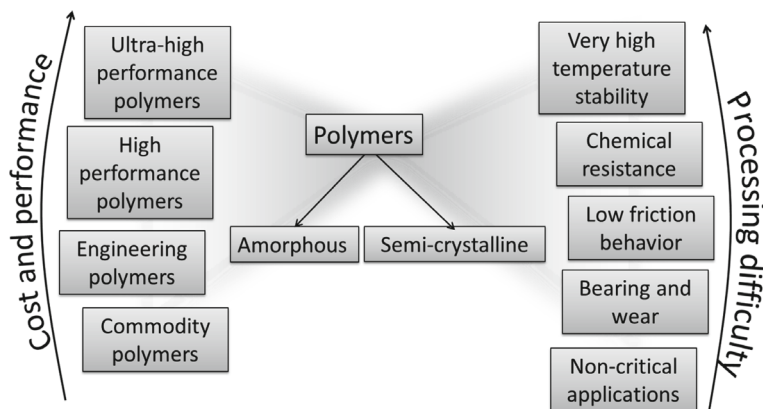


Fig. 1 Polymers and their cost versus performance study

PBT, have elevated strengths on the order of 75 MPa. These polymers are capable of sustaining continuous operating temperatures of up to 110/120 °C. Furthermore, their cost range extends up to 11.3 €/kg. The production of ‘High Performance’ polymers is predominantly concentrated in industrialised nations, where these materials exhibit superior physical qualities, elevated melting temperatures, and exceptional resistance to degradation. Consequently, the cost of these polymers can reach up to 113 € per kilogramme. These polymers fall under the category of “Ultra-High Performance Polymers” due to their exceptionally high melting points and superior strength characteristics. Notable examples include polyaramids such as Kevlar, as well as the PAEK family which encompasses Polyetheretherketone (PEEK). PEEK, for instance, exhibits a tensile strength (σ_B) of up to 100 MPa, a melting point of approximately 343 °C, and a temperature range of usability up to 250 °C [35].

The utilisation of reinforcing fillers holds significant significance in enhancing the tribological performance and facilitating the production of tribofilms in polymeric composites. The present work fully investigates the tribological characteristics of polyimide (PI) composites reinforced with aramid particles (AP) and short carbon fibres (SCF), when hexagonal boron nitride (h-BN) and silica (SiO₂) nanoparticles are introduced as sliding counterparts against alumina. The tribological properties of AP-reinforced PI composites were shown to be relatively independent of both the pressure $\times$ velocity ($p \times v$) variables and the presence of nanoparticles during sliding. The interactions between the anti-pressure (AP) substance and its corresponding substance do not have the capability to initiate tribo-sintering of the worn debris that is conveyed [36]. Consequently, the tribofilm exhibited a state of high viscosity, resulting in increased levels of friction and wear. Nevertheless, the incorporation of hard self-consistent field (SCF) calculations into the PI matrix resulted in alterations to the interfacial interactions with alumina. The addition of SiO₂ nanoparticles to the SCF-reinforced PI resulted in the formation of a durable tribofilm predominantly composed of silica. Polymer composites have become increasingly utilised in the

production of implant materials due to its notable attributes, including low cost, high strength, and ease of manufacture. When polymers are utilised in their actual state, they exhibit diminished mechanical and tribological capabilities [37]. Polymers are commonly reinforced with ceramics to enhance their mechanical and tribological properties, as a result of this rationale. In this study, TiO_2 and Al_2O_3 ceramics were employed as reinforcing agents for the matrix of PMMA and LDPE polymers.

3 Tribology of Fibre Reinforced Polymer Composites

The usage of fibre reinforced polymer matrix composites (FRPCs) is in surge in numerous structural, industrial, automotive, and technical applications. To replace common materials like metals and woods, polymer matrix composites have emerged as the frontrunner. This increases the need for research on the tribological characteristics of FRPCs. Among tribo materials, FRPCs are among the most significant. Many of the technical systems are failing owing to the considerable wear and friction. Different types of polymer-fibre composites and their generally overview has been depicted in Fig. 2. The rate of friction and wear in composites is affected by many factors, including the reinforcement and resin used, the manufacturing method, the operating parameters, and the volume fraction of the fibres, the fibre orientation, the fibre length, and the surface treatments. No single material is ideal for every possible usage scenario. Predicting the tribo characteristics of composites requires testing the materials in a controlled environment. Bijwe et al. have researched on friction and wear behaviour of polyetherimide glass fibre composites with changing fibre % and under different wear modes. The wear resistance of composites, as shown by the author, varies with fibre % and wear mode [38]. Temperature influences the friction and wear of phenolic composites, as determined by Kolluri et al. He demonstrated that as friction increases with temperature, phenolic composites wear faster regardless of graphite particle size or loading condition [39]. Charanjit and Lakhvir determined that the addition of Sic fillers to powder metallurgically fabricated Al composites increases the composites' wear resistance [40]. Composites are the result of the mixing of fibres and resin. The fibres in composites serve as reinforcement and absorb most of the load, and the orientation of those fibres greatly affects the composite's resistance to wear and friction. Many studies list different fibre orientations, such as normal, parallel, anti-parallel, and random. Researchers have researched the tribological properties of composites made of polymer resin and several types of natural fibre. Normal orientation gives minimum wear rate while the random gives maximum wear rate, as has been found in studies of jute and linen with unsaturated polyester resin [41], bagasse fibre with epoxy resin [42], bamboo fibres with epoxy [43], powered bamboo fibre with polyester reinforcement [44], and kenaf fibre with epoxy resin [45]. The author found that the orientation of the fibres makes a big difference in the wear rates. These wear rates could not possibly apply to the fibre since they are based on different operating circumstances.

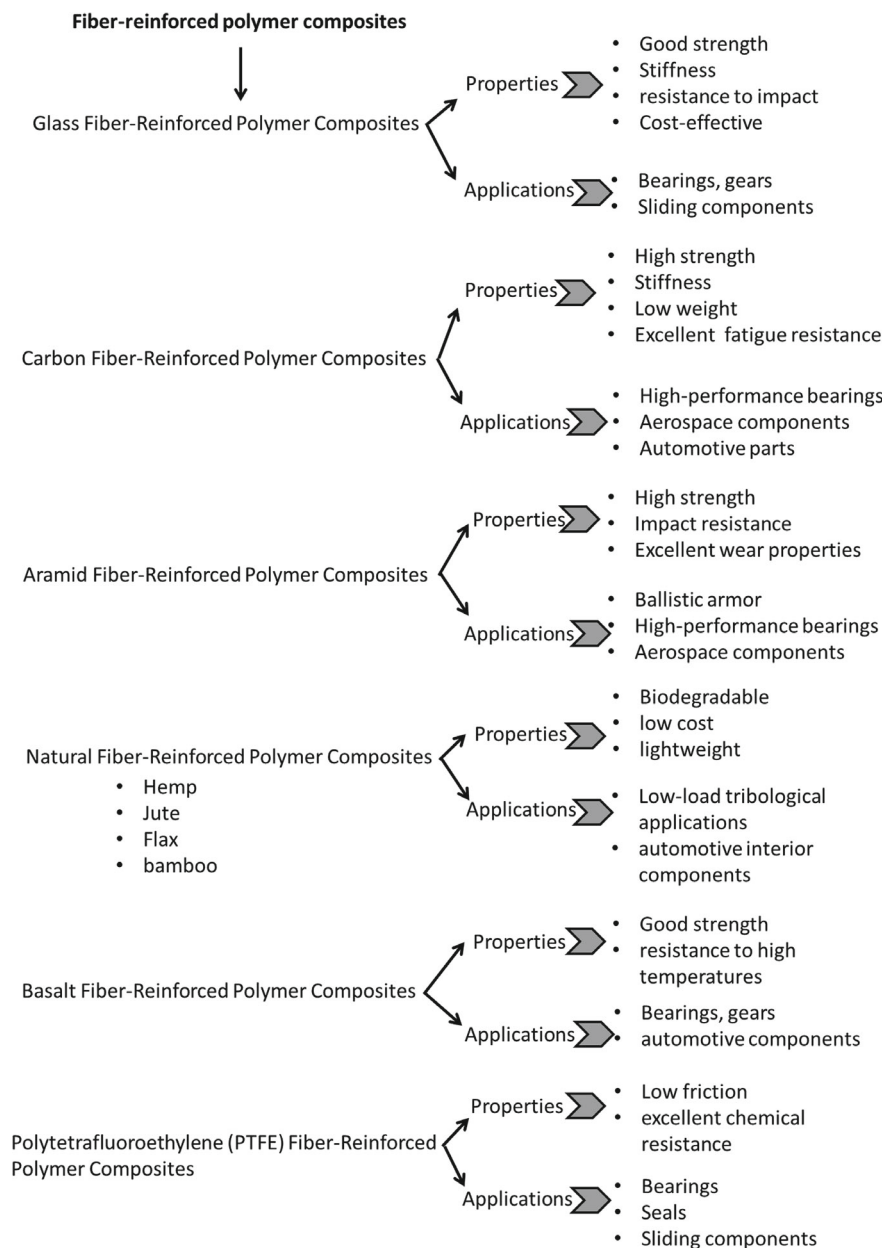


Fig. 2 Different types of commercially available fibre-reinforced polymer composites, their properties, and applications

As the fibre volume fraction increases, so does the load carrying capacity of the composites, but a review of the available evidence shows that after a certain threshold is reached, the fibre itself is to blame for the debonding of the fibres from the resin. Several investigations into natural fibres have been conducted: Deo and Acharya [46] worked on *Lantana camara* with polymer matrix; Kranthi et al. [47] concentrated on pin wood dust with epoxy resin and varied fibre weight fraction; Airedy worked on coir fibre with polymer matrix and fibre range 10–60% [48]. Banana epoxy reinforced composites have been studied by Gohil Piyush and Shaikh, who show that fibre volume fraction affects mechanical characterization of composites [49]. Carbon fibre with a fibre volume proportion of 3–9% was the subject of epoxy resin research [50]. In all these investigations it is established that high percentage factor of fibre volume fraction deteriorates the wear and friction qualities and due to the poor bonding between the fibre and the resin.

Interfacial bonding between fibre and matrix relies heavily on fibre length. Theoretically, a fibre with a length that is either too short or too long will have a lower load carrying capacity and a higher wear rate as a result. A number of researchers have conducted experiments on borassus fruit fibre using epoxy resin, including Boopathi et al. [51]. Mahapatra and Vedansh have worked on sugar cane fibre with varying fibre length and all these studies proved that fibre with the medium length gives good wear and frictional qualities compared to the too low and too high fibre length [52].

Natural fibres predominantly consist of cellulose, which plays a pivotal role in the degrading process of these materials. Fibres possess inherent hydrophilicity, whereas the matrix exhibits hydrophobic characteristics, resulting in the formation of relatively weak bonds between the fibre and matrix. Numerous research studies were conducted in order to address this issue.

The effect of NaOH treatment on oil palm polyester composites was examined by Yousif and El-Tayeb [53]. The effect of alkaline treatment on bamboo fibres has been identified by Wong et al. [54]. Rao Chandra et al. and Majhi et al. conducted experiments including the application of benzoline treatment on coir and rice husk fibres, respectively, in combination with epoxy resin [55, 56]. The impact of sea water treatment on sugarcane fibre has been found by Ishak et al. [57]. Belal et al. have successfully obtained a patent for investigating the impact of surface treatment on the properties of coir fibre reinforced polymer composites (FRPCs) [58]. The findings of all the investigations consistently indicate that surface treatment significantly contributes to enhancing the adhesion between the fibre and the matrix.

The mechanical and three-body abrasive wear characteristics of long fibre and short GF/EP composites were examined by Agarwal et al. [59]. The composites were composed of varying concentrations of glass fibres (ranging from 10 to 50% by weight, in increments of 10%). The authors also disclosed that the wear rate of long and chopped GF/EP composites exhibited an increase when the normal applied load rose. The study revealed that the Short GF/EP composites shown superior wear resistance in comparison to the bidirectional GF/EP composites. The study conducted by Suresha et al. examined the abrasive wear behaviour of E-glass fabric-reinforced epoxy composites in a three-body system, both with and without the use

of graphite fillers [60]. The researchers observed a positive correlation between abrasive wear and both abrading distance and load. The testing findings demonstrated a discernible pattern in terms of abrasive wear rate, with graphite filled GF/EP composites exhibiting the highest rate, followed by GF/EP composites, and finally, neat epoxy. The incorporation of glass fabric reinforcement into epoxy polymers resulted in a decrease in the resistance to three-body abrasive wear.

The study conducted by Chand et al. investigated the abrasive wear behaviour of short glass fibre reinforced polyester (GF/Polyester) composites in a three-body wear scenario, both with and without the addition of CaCO_3 fillers [61]. The researchers made an observation that GF/Polyester composites containing 45 wt% of GF had a reduced volume loss in comparison to GF/Polyester composites containing 40 wt% of GF. Nevertheless, the introduction of a 5 wt% CaCO_3 filler into the GF/Polyester composites, which already included 45 wt% of GF, resulted in an elevation of the loss caused by abrasive wear. Therefore, the scientists reached the conclusion that there exists a positive correlation between the level of short GF in composites and their abrasive wear resistance. Moreover, the inclusion of calcium carbonate (CaCO_3) in the composites resulted in a decline in their ability to withstand abrasive wear. The study conducted by Suresha et al. examined the impact of mechanical and three-body abrasive wear processes on the properties of 2D and 3D E-glass woven fabric-reinforced vinyl ester (GF/Vinyl ester) composites [62]. A three-body abrasive wear test was performed using a rubber wheel abrasion tester. The study revealed that composites consisting of 3D glass fibre reinforced with vinyl ester exhibited enhanced wear resistance. The researchers reached the conclusion that 3D GF/Vinyl ester composites exhibited favourable strength resistance and wear resistance in comparison to 2D GF/Vinyl ester composites. The investigation using scanning electron microscopy (SEM) facilitated the identification of the wear mechanisms involved, namely cutting, ploughing, and cracking. The investigation conducted by Siddhartha and Gupta focused on examining the abrasive wear characteristics of chopped and bi-directional GF/EP composites in a three-body wear scenario [63]. This investigation utilised the dry abrasion test rig (TR-50) as the experimental setup. The findings of the study indicate that the wear resistance of chopped GF/EP composites was superior to that of bi-directional GF/EP composites.

Mechanical and two-body abrasion wear behaviour of glass fiber/vinyl ester (GF/Vinyl ester) and carbon fabric/vinyl ester (CF/Vinyl ester) composites were investigated by Suresha and Kumar [64]. Waterproof silicon carbide (SiC) abrasive papers of 120 and 600 grit were used to sand down vinyl ester composites. The experiment findings showed that the particular wear rate reduced with increased abrading distance and decreased abrasive size. Moreover, carbon fibres in vinyl ester were shown to ensure lesser abrasion wear compared to glass fibres in vinyl ester. Suresha et al. conducted research on the abrasive wear behaviour of a CF/EP composite and two variants of the same material with differing graphite filler percentages (5 and 10 wt%). Waterproof abrasive papers (150 and 320 grit) were used in the abrasive wear test, which was performed at varying loads [65]. The particular wear rate was decreased by adding graphite fillers, as demonstrated by the experiments. Researchers looked at how different composites wear and found that single-pass wear conditions

resulted in a greater specific wear rate for two-body wear behaviour than did multi-pass conditions. Single-pass cutting, multi-pass micro-cracking, and ploughing all have their own unique wear mechanisms, which were uncovered by the SEM study.

4 Biodegradable Polymer Systems

Various biodegradable polymeric materials have been utilised as matrix for ceramic-modified composites in the field of tissue engineering. The materials discussed can be categorised into two primary groups according to their source: natural-based polymers, which encompass proteins (such as soy, collagen, fibrin gels, and silk) or polysaccharides (including starch, alginate, chitin/chitosan, and hyaluronic acid derivatives); and synthetic polymers, such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly(ϵ -caprolactone) (PCL), and poly(3-hydroxybutyrate) (PHB) [66]. In the realm of polymeric biomaterials, the process of biodegradation typically entails the breakdown of the polymer structure through the enzymatic cleavage of natural polymers or the hydrolytic cleavage of synthetic polymers, ultimately resulting in the erosion of the polymer [67]. Polymers generated from natural sources exhibit inherent capabilities for biological recognition, such as the presentation of receptor-binding ligands. These properties have the potential to facilitate crucial cellular processes, including cell adhesion, migration, differentiation, and proliferation. Nonetheless, the disintegration rate of these materials within a living organism is contingent upon the presence and concentration of enzymes at the specific location of implantation, hence rendering it challenging to accurately forecast. The use of natural polymers in isolation is frequently limited due to the potential for immunogenic reactions, the risk of disease transmission, and the generally subpar mechanical qualities [66]. According to the literature, synthetic polymers exhibit more predictable characteristics, such as degradation kinetics, which can be regulated through factors such as chemical composition, configurational structure, molecular weight, polydispersity, crystallinity, material morphology (e.g., porosity, surface area), chain orientation, and overall hydrophilicity. Synthetic polymers have favourable mechanical strength and can be customised to meet specific application requirements, with the ability to modify features such as porosity and form. Nevertheless, the surfaces of synthetic polymers exhibit hydrophobic properties and are deficient in cell-recognition sequences.

5 Different Types of Ceramic Particles and Their Biodegradable Polymer Composites

The inclusion of silica particles inside polymer matrices has been observed to enhance the biocompatibility and bioactivity of the resulting materials and/or implants. These compositions exhibit biological properties that are of interest for bone tissue applications, including bioresorption rate and porosity. Additionally, they possess the capability to promote the formation of calcium phosphate, which is similar to the composition found in natural bone, on the surfaces of biomaterials. Furthermore, these compositions allow for the incorporation of biologically active agents [68]. The mechanisms of dissolution and metabolism of silica nanoparticles within animals have received significant attention because of their widespread application as silica reinforcements. SiO_2 nanoparticles embedded in polyesters have several desirable features that make them an excellent grafting and scaffolding material [69]. Covalent bonding between macromolecular chains and the fillers are possible because silica's surface contains silanol groups ($\text{Si}-\text{OH}$). Nanocomposite materials, such as poly(butylene succinate)/silicon dioxide (PBSu/SiO_2), have been studied using nuclear magnetic resonance (NMR) spectroscopy, and the results have confirmed the formation of covalent bonds between the surface silanol groups of the SiO_2 nanoparticles and the hydroxyl end groups of the polymer (PBSu) [70]. Even when using SiO_2 concentrations lower than 2.5 wt%, the mechanical characteristics of PBSu were significantly enhanced due to the formation of these covalent bonds [71]. Nano- SiO_2 in the polymer matrix, in the form of nanotubes or nanoparticles, alters the physicochemical properties of the nanocomposite surface. For instance, the surface's hydrophilicity improves because some of the hydroxyl groups are exposed. This effect helps to explain why biodegradable polymer-based nanocomposites hydrolyze at a faster rate [72].

Capability for encapsulation of medicines and biological agents is demonstrated by mesoporous silica, which is characterised by uniform, parallel holes of 2–50 nm diameter, high specific surface area, low density, and high biocompatibility [73]. The pharmaceutical industry makes extensive use of these particles, most frequently in drug delivery systems. Mesoporous silica was typically combined with biodegradable polymers as poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), poly(ethylene-co-glycolide) (PCL), chitosan (CS), alginate, gelatin, polyethylenimine (PEI), etc. to regulate drug release [74]. Filling a polymeric matrix used to make a scaffold or a membrane with drug-loaded silica nanoparticles would allow for more precise control over the rate and timing of drug release than would be possible with only the polymer material alone [75]. In addition, mesoporous silica scaffolds with macro-, meso-, and micropores were found to have a significant role in bone production. Mesopores can store nutrients and growth factors or transport medicinal substances; macropores encourage cell infiltration; and micropores can serve as nucleation sites for mineralization, leading to local supersaturation and the subsequent nucleation of apatite forms. Salt leaching, freeze drying, and newer procedures like electrospinning and fast prototyping are all viable options for creating such

implants. The name “multifunctional scaffolds” was commonly applied to polymer scaffolds modified with mesoporous silica nanoparticles (MSNs) [76].

6 Conclusions

The investigation of tribology and biodegradability in ceramic/fiber filler-based polymer composites has yielded substantial findings and encouraging prospects for the advancement of environmentally sustainable materials. In the final analysis of this book chapter, it becomes apparent that the interplay between tribological factors and biodegradability constitutes a pivotal intersection in the quest for environmentally sustainable polymer composites.

The inclusion of ceramic and fibre fillers has emerged as a central area of research, showcasing the ability to augment the mechanical characteristics of polymer composites. Extensive research has been conducted to examine the tribological performance, encompassing the attributes of friction and wear. The complex interaction between the ceramic and fibre constituents and the polymer matrix has been thoroughly examined in order to enhance both the mechanical robustness and the ability to withstand wear and friction. The comprehension of this concept holds utmost importance in contexts where the crucial factors are durability and performance, such as in the domains of structural components, automotive parts, or biomedical devices. In addition, the investigation of biodegradability introduces an additional level of importance to the study. The significance of the relationship between tribological behaviour and the degradation of composites is of utmost importance as sustainability gains prominence in the field of material research. The environmental ramifications of these materials, namely their situations at the end of their life cycle, have been carefully considered. The results emphasise the significance of conscientious material selection and design in order to conform to current ecological priorities.

This chapter provides an illuminating analysis of the present state of research while also indicating potential directions for further exploration. The statement underscores the importance of ongoing investigation into innovative filler materials, enhanced manufacturing methods, and sustainable approaches. Further research endeavours may explore the intricate mechanisms that govern the biodegradation of these composites in various environmental contexts, hence facilitating the development of customised solutions for a wide range of applications.

The amalgamation of tribology and biodegradability within ceramic/fiber filler-based polymer composites highlights the interdisciplinary character of material science. This research makes a substantial contribution to the current shift in paradigm towards the creation of environmentally friendly and sustainable materials for various applications, by effectively managing the delicate equilibrium between mechanical performance and environmental impact.

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Failure Analysis Ceramic/Fibrous Filler-Based Polymer Composites



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Abstract A comprehensive discussion of failure analysis approaches utilized in the context of ceramic/fibrous filler-based polymer composites is presented in this chapter. Composites of this nature have attracted considerable attention in the field of engineering owing to their exceptional mechanical, thermal, and electrical characteristics. The chapter commences by providing a comprehensive examination of the many types and distinguishing features of frequently employed ceramic and fiber fillers. Additionally, this study investigates the many failure mechanisms observed in these composite materials, encompassing interfacial debonding, filler breaking, matrix cracking, and delamination. The present study aims to provide a comprehensive examination of the impact of filler properties, including aspect ratio, orientation, and volume percentage, on the failure behavior of composites. In this chapter, case studies and practical examples are provided to demonstrate how these methodologies can be applied to diagnose failure mechanisms and enhance composite performance. This discussion seeks to offer significant insights for academics and practitioners engaged in the design and development of durable polymer composites based on ceramic/fibrous fillers, by integrating existing information and approaches.

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Keywords Ceramic/fibrous filler • Polymer composites • Interfacial • Durable polymer

1 Introduction

The notion of formulation is of considerable scope as it encompasses all sectors engaged in the creation of intermediates or final products through the blending of many basic components [1]. In a more precise manner, the term “formulation” can be defined as the comprehensive set of knowledge and procedures employed in the process of blending, combining, or moulding ingredients derived from either natural or synthetic sources, which are often inherently incompatible with one another. The ultimate objective of this process is to produce a marketable product that is distinguished by its intended functionality and its capacity to meet predetermined specifications [2]. Within the composition of a formula, it is necessary to differentiate between the active substances that serve the primary purpose and the formulation aids that fulfil secondary roles [3]. The formulated product comprises a finely dispersed combination of multiple immiscible phases, exhibiting macroscopic homogeneity and microscopic heterogeneity. Examples of such products include paints, cosmetic creams, mayonnaise, and composite materials. In addition to the aforementioned characteristics, the preparation and stability of the mixture are also important considerations [4]. Composite materials can be defined as the amalgamation of two or more materials, resulting in a final assembly that exhibits qualities that surpass those of the individual constituent materials [5]. The matrix serves to promote cohesiveness and provide orientation for the load. Moreover, it is feasible to transfer the applied stresses to the load in order to assess the impact on the composite material. The materials acquired in this manner exhibit significant heterogeneity and frequently demonstrate anisotropic properties [6]. Several elements, such as the matrix nature, charge characteristics, charge shape and proportion, interface quality, and production method, might potentially impact the attributes of a composite material [7]. The composite material typically consists of one or more discontinuous phases dispersed within a continuous phase. When many phases of distinct natures are present, the resulting composite is referred to as hybrid [8]. The phase that remains uninterrupted is commonly referred to as the matrix, whereas the phase that is interrupted or discontinuous is known as the reinforcement or reinforcing material. Composite materials involve the amalgamation of components possessing mutually complementary physical and mechanical qualities [9]. One notable benefit of composites featuring a polymer matrix, in contrast to metals, lies in the manufacturing process. This process enables the production of intricately shaped components with a reduced density. Consequently, these composites offer advantages such as decreased fuel consumption in aviation and automobile industries, enhanced speed in competitive sports, extended range for missiles, and increased payload capacity in transportation [10]. Composite materials can be categorised into three distinct groups based on the type of matrix they possess: organic, mineral, and metallic. Within the category of

organic composites, several examples can be identified, including cardboard, which consists of resins and cellulose fibres. Another example is laminated tyres, which are composed of rubber, steel, organic resins, glass fibres, carbon, and boron. Additionally, reinforced plastics are another type of organic composite, characterised by the presence of resins and short fibres [11].

2 Importance of Ceramic and Fibrous Fillers

Extensive study has been conducted on the incorporation of ceramic fillers into polymer composites, primarily due to the significant influence it has on improving mechanical characteristics. Commonly, nanofillers for polymer composites are tiny particles that are incorporated with polymers to improve their properties [12–26]. Numerous scholarly investigations have extensively explored the synergistic impacts of ceramic fillers, such as alumina, silica, or graphene, when combined with polymer matrices, resulting in the development of sophisticated composite materials. A significant observation that has emerged from multiple research endeavours is the considerable enhancement in the tensile strength, flexural modulus, and hardness of polymer composites by the incorporation of ceramic fillers. The phenomenon of ceramic fillers serving as reinforcements and effectively distributing stress within composite structures has been frequently noticed by researchers. The observed effect can be ascribed to the intrinsic properties of ceramics, namely their elevated strength and stiffness [27]. For example, research utilising scanning electron microscopy (SEM) has demonstrated a more homogeneous distribution of stresses in composites including ceramic fillers, hence reducing the likelihood of localised failure and improving the overall structural integrity. Furthermore, the examination of the impact of ceramic fillers on the fracture toughness of polymer composites has been a central area of research. Studies employing modern fracture mechanics methodologies, such as the assessment of key stress intensity parameters, have provided evidence that the use of ceramic fillers enhances the ability to withstand crack propagation. The discovery holds significant significance in contexts where the crucial factors are durability and the ability to withstand catastrophic failure. This is particularly relevant in applications involving structural components within the aerospace or automotive engineering fields. The influence of ceramic filler size and shape on the mechanical properties of polymer composites has been widely recognised. The behaviour of composites is greatly influenced by the specific features shown by nanoscale ceramic fillers [28]. The utilisation of atomic force microscopy (AFM) and transmission electron microscopy (TEM) in various research investigations has provided valuable insights into the mechanisms of reinforcement at the nanoscale. These studies have shed light on the enhanced interfacial bonding and stress transfer between the ceramic and polymer phases. The inclusion of fillers in polymer nanocomposites is widely recognized for enhancing their mechanical, thermal, electrical, and barrier properties [24, 29–45].

The utilisation of fiber-reinforced polymer composites has gained significant attention across various disciplines owing to their desirable characteristics. In recent decades, there has been a significant increase in the manufacture of fiber-reinforced composites, reaching mass levels. Several simplified processing techniques have been developed for the manufacturing of composite materials. Currently, numerous researchers are actively investigating the potential use of natural waste fibres and fillers such as coir, rice husk, banana leaf, date palm, coconut shells, peanut shells, and groundnut shells [46]. These researchers aim to effectively incorporate these natural waste materials into polymer composites. Waste fibre and fillers find application in a wide range of industries, including but not limited to the production of small miniature components and the aerospace sector. This approach offers dual advantages, namely the substitution of traditional resources and the utilisation of agricultural waste. The utilisation of agricultural wastes as primary constituents in the formulation of polymer composites is advantageous owing to their abundant accessibility and enhanced mechanical characteristics [47]. In contemporary times, there is a significant utilisation of natural fibres and agricultural waste in order to augment mechanical properties, mostly owing to their renewable characteristics [48]. Fiber-reinforced polymer composites have demonstrated potential for utilisation in automotive applications, as well as being recommended for architectural uses following specific fire load testing [49]. In addition to their mechanical properties, natural fibres exhibit lower thermal conductivity compared to synthetic fibres. This characteristic renders them advantageous for the development of thermal insulation polymer composites. The scientific principles underlying thermal insulation involve the manipulation of the internal microstructure of fibres embedded in resin, with a specific focus on their application in electro-related contexts [50]. Natural fibres exhibit excellent compatibility with epoxy resin owing to their flexible qualities. Epoxy resin is highly suitable for automotive and industrial applications, such as encapsulation, laminated circuit board production, and thermal adhesive usage, owing to its exceptional mechanical, chemical, and thermal characteristics [51]. The utilisation of glass fibres containing silica and alumina as a filler has been identified as the optimal combination for augmenting both the thermal and mechanical qualities [52]. The polymer material demonstrates efficacy in diverse electronic packaging applications by the incorporation of various fillers such as aluminium nitride and boron nitride, which enhance thermal conductivity and heat dissipation rates [53]. Thermoplastics and thermosetting polymers can be utilised for many applications by the incorporation of fillers to enhance their thermal properties to a significant extent [54]. The preparation of sisal fibre polymer composite samples via a hand layup approach has yielded successful results. The incorporation of a filler mixture has demonstrated enhancements in both mechanical and thermal properties [55]. The scientific rationale underlying this phenomenon is an enhancement in the adhesion characteristics between the fibre and matrix materials. This particular feature exhibits significant utility, particularly in the context of composite fabrication involving thermoplastic materials combined with fibres [56].

3 Different Types of Composites

In order to obtain a comprehensive understanding of the composite material, it is imperative to identify three key aspects: the nature of the elements and their respective qualities, the geometry of the reinforcement and its distribution, and the nature of the interface between the matrix and the reinforcement. The composite material can be described as a complex system comprised of a considerable number of constituents [3]. Hence, the potential number of realisations within this particular range of essential constituents is effectively boundless. The properties of the finished product are significantly influenced by various factors, including the composition of the matrix, the types of reinforcements utilised, the additives incorporated, and the relative proportions of these constituents. Additionally, the manner in which these elements are implemented during the production process also plays a crucial role. There exist two primary categories of materials, namely big diffusion composites and high performance composites [57]. The prevailing type of composites used in many applications is large diffusion composites, often composed of fibreglass combined with unsaturated or phenolic polyester resin. They comprise a majority of over 95% of the overall production, with the transport industry (including automobiles and railways) and electrical construction being the primary sectors driving demand. The primary components consist of epoxy resins that are strengthened by the incorporation of extended glass fibres, with a particular emphasis on carbon or aramid materials. The applicants express a keen interest in the high mechanical and thermal qualities of the subject matter. However, the aeronautical and space business is characterised by very low production volumes in certain series. The primary constituents of composite materials formulation consist of matrix, fibres, and additives or fillers, as depicted in Fig. 1.

4 Failure of Composites

Typically, the destructive breakdown of a composite structure is associated with either fiber or translamina fracture modes. In the realm of aerospace applications, failures predominantly stem from compression mechanisms, primarily due to the prevalent design focus on enduring flexural loads. This emphasis on flexural resilience contrasts with other applications, like pressure vessels, where tension overwhelmingly dictates the mode of failure. The predominant mode of intralaminar fracture, involving the interface between fibers and the matrix, is subsequently discussed. While not strictly categorized as a 'fiber-dominated' fracture mode, intralaminar fracture occurs primarily within the matrix or at the fiber/matrix interface. This fracture mode is inherently connected to fiber-dominated failures and is most appropriately detailed in this chapter. It is frequently observed in continuous fiber composites, and the terminology employed in this chapter is associated with fiber orientation,

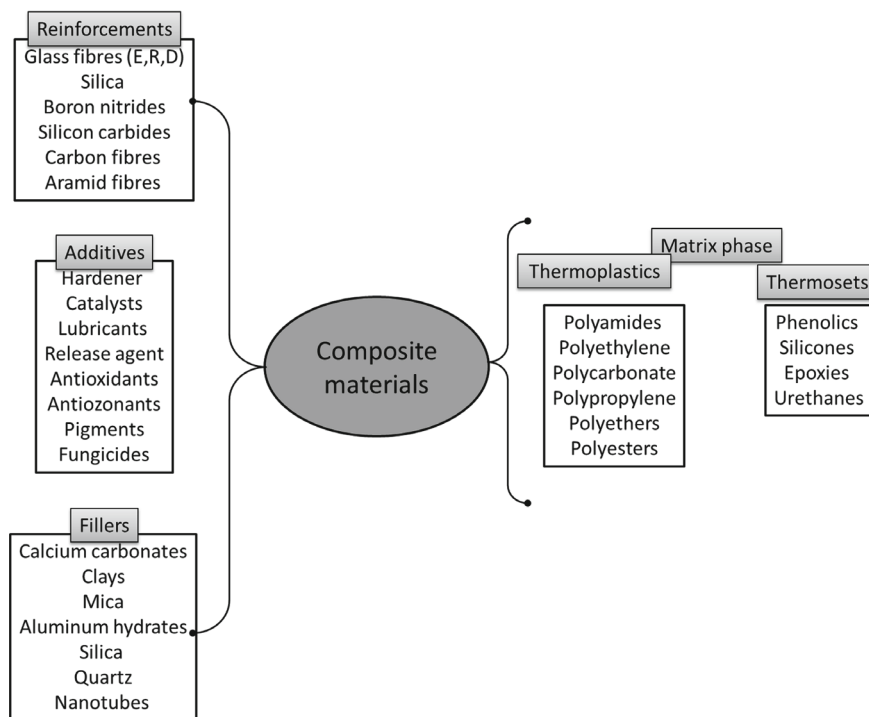


Fig. 1 Different components of polymer based composites materials

encompassing longitudinal splitting (0°), ply splitting ($\pm 45^\circ$), and ply cracking (90°).

Arguably the most straightforward failure mode to explore in the analysis of laminated composites is tensile failure, and numerous researchers have delved into the mechanisms linked with this mode. An illustration of the macroscopic level morphology of a tensile failure is presented in Fig. 3.1. This figure depicts a 3 mm thick unidirectional carbon-fiber-reinforced epoxy laminate subjected to quasi-static tension. The failure originated in the central region near the upper face (labeled 'O'), coinciding with a minute pin-head-sized defect on the laminate surface. In the vicinity of this initiation point, the fracture surface appears relatively flat, with all fibers in this zone breaking along the same plane. This morphology is indicative of slow fracture, where there is just enough energy to propagate the crack. However, as the crack extends from this point and the fracture speed accelerates, the fracture plane among adjacent fibers diverges, creating more rugged fracture topography. These results in the formation of radial lines of fibers, clearly visible in Fig. 3.1, and these are linked to the fracture's growth, radiating from the origin 'O' [58]. From a fractographic standpoint, these radials provide insights into the direction of crack growth.

Another notable aspect of tension failures is the extent of fiber brooming, indicating the level of ply splitting that occurs prior to fiber fracture. The process of inducing longitudinal splitting was initially identified by Cook and Gordon [59]. In the context of a tension crack progressing through the matrix in a unidirectional laminate, there is an anterior tensile stress at the crack tip, accompanied by an associated shear stress (τ) due to the absence of stress across the crack faces. As the crack approaches a fiber, the shear stress aligns parallel to the fibers, inducing shear stress at the fiber/matrix interface. This localized failure of the interface leads to debonding of the fibers, but this mechanism tends to blunt the crack, potentially impeding further crack growth. Sustained fracture propagation requires the reinitiation of the crack [60]. The degree of brooming observed on a tensile fracture serves as a comparative gauge for the degradation of fiber/matrix bond strength. Factors such as the presence of moisture or exposure to elevated temperatures can diminish the fiber/matrix strength, consequently intensifying the degree of brooming. This phenomenon provides valuable evidence of how environmental conditions impact the integrity of the fiber/matrix bond within the material.

In glass-fiber-reinforced polymers, the connection between the fibres and the matrix often lacks strong adhesion, making unidirectional composites susceptible to significant longitudinal splitting when subjected to strain testing. In these materials, fibres frequently experience independent fractures at different locations along their length [61]. As a result, these fractures tend to be less smooth and do not exhibit the radial patterns seen at a larger scale. However, when examining the broken ends of the fibre under a microscope, distinct radial patterns are often observed.

The radial pattern found on the ends of carbon and glass fibres is a result of their intrinsic brittleness. On the other hand, aramid fibres demonstrate a unique way of breaking, where they experience longitudinal cracks inside the fibres, resulting in defibrillation. The distinct behaviour can be linked to the microstructure of the fibre, which is composed of interlaced fibrils of polymer. Hence, the task of determining the local fracture growth orientations through the examination of these fibres becomes exceedingly challenging. This distinct failure mode is effectively highlighted through a visual representation of a tensile failure occurring in a multidirectional aramid fibre composite.

In fragile resin materials, such as first epoxy systems, noticeable structures such as riverlines and textured microflow can be observed in the resin between the fibres, offering further understanding of the directions in which cracks develop locally. Nevertheless, as the strength of the matrix grows, these morphologies become less noticeable. Matrices with high toughness, such as PEEK, show considerable flexibility in the vicinity of the fibres, which poses difficulties in determining precise fractographic data. In addition, toughened and thermoplastic matrices frequently exhibit a higher occurrence of fibre pull-out, leading to a reduced number of bundles containing failed fibres and fibre failures that may be directly attributed to specific causes (DAFFs).

5 Failure Modes

5.1 *Macroscopic Failure Modes*

Polymer composites are highly adaptable materials that are used in various industries because of their outstanding mechanical qualities, lightweight nature, and ability to resist corrosion. Nevertheless, polymer composites, just like any other material, are prone to macroscopic failure mechanisms that can undermine their structural integrity and performance [62]. Gaining comprehension of these failure modes is essential for the purpose of creating resilient composite constructions and guaranteeing their enduring dependability.

Delamination is a major form of failure in polymer composites at a macroscopic level. Delamination is the process in which the layers of a composite material separate, causing a breakdown in the connection between the reinforcing fibres and the matrix material. This can occur due to a variety of circumstances, including manufacturing flaws, impact-induced harm, or prolonged exposure to severe environmental conditions [63]. Delamination causes a substantial decrease in the strength and stiffness of the composite material, resulting in a reduction of its ability to carry loads.

Fibre breakage is a frequently occurring failure mode. Reinforcing fibres in polymer composites confer strength and stiffness to the material. When these fibres fracture, either as a result of excessive loads or fatigue, the composite material's capacity to endure stress is diminished. Microscopic fibre breaking can lead to progressive material degradation. Such failure is frequently influenced by parameters such as the orientation, length, and quality of the bonding between fibres and the matrix. Matrix cracking is a macroscopic failure mechanism that impacts polymer composites [64]. The matrix material, which encapsulates and provides structural support to the reinforcing fibres, has the potential to produce fractures when subjected to mechanical strain. The fissures spread throughout the matrix, resulting in a reduction in the load-bearing capability of the composite. Matrix cracking may occur due to excessive loading, variations in temperature, or the natural deterioration of the matrix material. To address matrix cracking, it is necessary to use a matrix material that possesses appropriate qualities and to build the composite in a manner that efficiently distributes loads.

Polymer composites face a substantial obstacle in the form of environmental deterioration, which results in major forms of failure such as chemical degradation and UV degradation. The matrix material can experience a reduction in its structural integrity as a result of exposure to abrasive substances [65]. The polymer matrix can be broken down and the reinforcing fibres can be degraded by UV radiation, leading to a decrease in mechanical characteristics. To mitigate these types of failures, it is advisable to use materials that have resilience to environmental variables and to apply protective coatings. Assessing macroscopic failure modes in polymer composites requires careful consideration of fatigue. Repetitive application and removal of stress, particularly in changing circumstances, can result in fatigue-induced structural

collapse. This phenomenon is characterised by the progressive formation and spread of fissures inside the substance, finally leading to a disastrous breakdown. Comprehending the fatigue characteristics of particular polymer composites is crucial for accurately forecasting their operational lifespan and developing structures capable of enduring extended usage.

To summarise, although polymer composites have many benefits, they are nonetheless susceptible to macroscopic failure modes that might jeopardise their structural integrity. Delamination, fibre fracture, matrix fracture, environmental deterioration, and fatigue are some of the primary elements that affect the performance of polymer composites. To tackle these instances of failure, it is necessary to use a comprehensive approach that encompasses meticulous selection of materials, manufacturing procedures, and design factors. Through comprehending and addressing these failure modes, engineers can fully exploit the inherent capabilities of polymer composites in diverse applications, guaranteeing long-lasting durability and dependability.

6 Fracture Modes

The fracture modes of failure in polymer composites are crucial factors that greatly impact the mechanical behaviour and performance of these sophisticated materials. These materials typically consist of a polymer matrix that is reinforced with fibres or other agents that enhance their strength [66]. Comprehending and dealing with these fracture modes are crucial for enhancing the design and dependability of polymer composites in diverse industries. Interfacial failure, also known as delamination, is a prominent form of failure. Delamination is the result of the deterioration of the link between the polymer matrix and reinforcing fibres, causing the layers to separate along the interface. This failure mode is of utmost importance since it undermines the ability of the composite to bear loads, which could lead to a disastrous collapse of the structure. In order to reduce interfacial failure, engineers utilise techniques to improve the adhesion between the polymer matrix and reinforcing fibres. Surface treatments, coupling agents, and selective material selection are commonly employed methods to enhance the interface and mitigate delamination. Fibre fracture is an additional important kind of failure, especially in composites containing fragile reinforcing fibres. Fractures occur in these fibres when the applied stress exceeds their tensile strength, resulting in a decrease in their ability to bear loads. This mode is especially worrisome in applications where achieving high strength is of utmost importance, such as in aircraft components [67]. Engineers and material scientists meticulously choose and enhance fibre kinds, orientations, and architectures to guarantee a well-balanced distribution of stress and avoid localised fibre breaking. Matrix cracking is a common type of failure that is affected by elements such as temperature, loading rate, and environmental conditions. During this phase, the polymer matrix experiences significant deformation, leading to the creation of fissures. Matrix cracking is particularly evident in materials with low ductility, and

its presence can have a substantial effect on the mechanical characteristics of the composite. To tackle this difficulty, researchers incorporate toughening chemicals into the matrix or modify manufacturing parameters to improve the material's ability to withstand failures caused by deformation. Fiber-matrix debonding is a type of failure that happens at the boundary between reinforcing fibres and the polymer matrix. Inadequate bonding or unfavourable environmental conditions can lead to the detachment of fibres from the matrix, affecting the transmission of forces between the two components [68]. Methods to enhance the adhesion at the interface between the fibre and matrix involve surface treatments, alterations to the interface, and the utilisation of compatible materials. Ultimately, a thorough comprehension of fracture modes is essential for maximising the effectiveness and dependability of polymer composites. Scientists and engineers are always investigating new methods, such as altering materials and using modern production techniques, to customise fracture modes and fully utilise the capabilities of polymer composites in industries like aerospace and automotive engineering. The continuous effort to improve the ability of polymer composites to withstand fractures guarantees their sustained development and use in advanced technologies and challenging conditions.

7 Delamination Mode

Delamination, a crucial form of failure in polymer composites, highlights the complex interaction between the polymer matrix and reinforcing fibres, greatly affecting the structural strength of the material. This failure mode arises when the adhesive link between the polymer matrix and reinforcing layers deteriorates, resulting in the detachment of these layers [69]. The presence of delamination in composites is particularly worrisome since it has the potential to undermine the ability of the material to bear loads, often leading to disastrous failure. Engineers and material scientists face this difficulty and use several ways to improve the bonding across interfaces and reduce the possibility of layers separating. The quality of the link between the polymer matrix and reinforcing fibres is a significant component that affects delamination. Weak interfacial bonding may arise from several factors, such as insufficient surface treatments, inadequate compatibility between the matrix and fibres, or incomplete cure during the manufacturing process [70]. In order to tackle this issue, researchers concentrate on enhancing surface treatments and integrating coupling agents that facilitate a strong connection between the matrix and fibres. Furthermore, improvements in manufacturing methods strive to attain enhanced regulation of the curing procedure, guaranteeing consistent and robust interfacial adhesion.

Delamination is particularly common in laminated composite structures, when multiple layers of materials are piled together. The presence of stress concentration at the interfaces between layers, coupled with the differences in coefficients of thermal expansion among the layers, can intensify the inclination for delamination [71]. Thermal cycling and exposure to the environment additionally contribute to the

beginning and spreading of delamination fractures. In order to address this issue, engineers investigate methods such as integrating interlayers with enhanced resilience, modifying the arrangement of layers, and optimising the alignment of fibres to equally transfer loads throughout the composite structure. Delamination has a significant effect on the performance of polymer composites, not only in static loading situations but also in dynamic conditions like fatigue and impact [72]. Delamination can act as an early indication of other forms of failure, increasing the susceptibility of the material. Researchers study the complex process of delamination propagation by using sophisticated modelling and simulation tools to forecast and avoid its happening under different loading circumstances. Although delamination presents difficulties, it is crucial to address it in order to facilitate the extensive use of polymer composites in several industries, including aerospace and automotive engineering. The pursuit of enhanced materials necessitates a comprehensive approach that integrates various disciplines, including materials science, mechanical engineering, and manufacturing technology. The utilisation of nanoscale reinforcements in nanocomposites has demonstrated significant progress in improving interfacial strength and preventing delamination. To summarise, the delamination mechanism of failure in polymer composites highlights the need to carefully optimise the interaction between the polymer matrix and reinforcing fibres. As scientists delve deeper into the intricacies of delamination, they are discovering new and creative methods to strengthen the relationship between interfaces and reduce the potential dangers of this crucial failure mode. The progress of polymer composites depends on these developments, guaranteeing their ongoing incorporation into state-of-the-art technologies and structural applications.

8 Matrix Cracking Mode

Matrix cracking, a prominent kind of failure in polymer composites, signifies the complex interactions occurring within the composite material, specifically regarding the polymer matrix's behaviour. This failure mechanism occurs when the polymer matrix experiences extreme deformation, leading to the production of cracks. The ramifications of matrix cracking can be substantial, as it can greatly affect the overall mechanical characteristics of the composite [73]. Understanding and mitigating matrix cracking requires a thorough understanding of the polymer matrix's nature, its brittleness, and the external influences that influence its behaviour. Brittle matrices are highly prone to matrix cracking due to their inherent lack of ductility required for deformation accommodation [74]. Cracks in the matrix can be initiated by several sources, including as mechanical load, temperature oscillations, and environmental conditions. The phenomenon is most evident in brittle matrices, where the lack of ability to disperse energy through plastic deformation results in the creation of cracks as the predominant mechanism of failure. In order to combat matrix cracking, researchers concentrate on integrating toughening chemicals into the polymer matrix [73]. These agents, commonly in the form of nanoparticles or

polymers with high resilience, function to hinder the spread of cracks by absorbing and dispersing energy. The incorporation of these strengthening chemicals improves the plastic deformation capability of the matrix, hence decreasing the probability of crack development and enhancing the overall fracture toughness of the composite. Furthermore, improvements in production techniques strive to optimise the distribution of these strengthening agents throughout the material to guarantee consistent augmentation of mechanical properties. The environmental conditions under which polymer composites function have a substantial impact on matrix cracking [75]. Exposure to varying temperatures, humidity, and corrosive substances can speed up the deterioration of the matrix, leading to the formation and spread of cracks. To comprehend the environmental influence on matrix cracking, a comprehensive methodology is necessary, leading researchers to create composite compositions that possess improved resilience against environmental deterioration. Investigations are also conducted on protective coatings and barrier layers to safeguard the composite from unfavourable conditions and alleviate the impact of matrix cracking throughout the material's lifespan.

Matrix cracking has implications that go beyond simply reducing the ability to absorb loads. It can also act as a precursor to other types of failure, such as delamination and fibre breakage. It is essential to address matrix cracking in order to maintain the integrity of the polymer matrix and avoid the further development of failure mechanisms in the composite. Eventually, matrix cracking is a prominent kind of failure in polymer composites, underscoring the necessity of comprehending and addressing the weaknesses inside the polymer matrix. The incorporation of toughening chemicals, progress in manufacturing techniques, and a strong understanding of environmental factors all contribute to the continuous endeavours to improve the fracture resistance of polymer composites. As these materials are increasingly used in several industries, such as aerospace and automotive engineering, understanding the intricacies of matrix cracking is crucial for assuring their best possible performance and longevity.

9 Fiber Breakage Mode

Fibre breakage is a significant type of failure in polymer composites, which emphasises the susceptibility of the reinforcing fibres and their crucial role in determining the mechanical properties of the material. When composites rely on fibres for their main strength, such as those that use materials like carbon or glass fibres, the breaking of individual fibres can result in a substantial decrease in the ability to withstand loads [64]. This type of failure is particularly relevant in areas where exceptional strength and resilience are of utmost importance, such as in aerospace and structural engineering. The causes of fibre breakage are complex, frequently resulting from the exceeding of the fibres' tensile strength under applied stress.

The arrangement, alignment, and structure of the fibres in the composite material are essential factors in influencing their vulnerability to fracture [76]. Localised

stress concentrations, deviations in fibre alignment, or flaws in manufacturing can generate areas where the fibres are more susceptible to breaking. In order to reduce the occurrence of fibre breaking, engineers and researchers focus on optimising the arrangement of fibres. They also investigate innovative techniques for weaving and layering to provide a more even distribution of stress across the composite structure. Computational modelling assists in forecasting stress concentrations, directing the design process to improve the overall durability of the composite against fibre breaking. Gaining a comprehensive understanding of the environmental circumstances in which polymer composites function is crucial for effectively resolving fibre breakage. Various factors, including fluctuations in temperature, levels of humidity, and contact with corrosive substances, can gradually deteriorate the fibres, reducing their ability to withstand tension and raising the probability of fractures [77]. Hence, material scientists prioritise the development of fibres with heightened resilience against environmental deterioration or utilise protective coatings to safeguard them from unfavourable circumstances. Furthermore, the incorporation of cutting-edge materials, such as nanofibers or hybrid reinforcements, shows potential in improving the overall strength and ability to withstand fibre breakage. Fibre breaking is substantially influenced by the loading conditions and applied forces, in addition to material factors. The occurrence of sudden impact or repeated stress might expedite the advancement of microcracks in the fibres, finally resulting in their fracture. The research in this field focuses on enhancing the composite design to achieve optimal performance under certain loading conditions. This involves integrating fatigue-resistant characteristics and impact-absorbing components to reduce the likelihood of fibre breaking under dynamic situations [78]. Fibre breaking not only results in the immediate loss of mechanical strength, but also serves as a prelude to other failure modes in the composite, such as matrix cracking and delamination. To effectively deal with fibre breakage, it is necessary to have a thorough comprehension of the interaction between the reinforcing fibres and the matrix. Additionally, a holistic approach to materials engineering and composite design is required. To summarise, the issue of fibre breaking in polymer composites requires a detailed investigation into the characteristics of the materials, the impact of the environment, and the conditions under which they are subjected to stress. This is necessary in order to improve the durability and lifespan of these sophisticated materials. As polymer composites are increasingly used in important industries, researchers are actively studying the complexities of fibre breakage to develop creative solutions. This is done to ensure that these materials can reach the high standards required by current engineering and technology.

10 Microscopic Failure Modes and Interface Debonding

Microscopic failure mechanisms and interface debonding are complex aspects of polymer composite failure that include detailed interactions at the microscale, which have a substantial impact on the material's structural integrity. The performance

of the composite at this stage is determined by the individual fibres' behaviour, the matrix's quality, and the efficacy of the binding interface [79]. Gaining insight into these minuscule failure processes is essential for engineers and material scientists aiming to improve the overall dependability and longevity of polymer composites. The microscopic failure modes observed in polymer composites include fibre breakage, matrix cracking, and the formation of microvoids. Fibre fracture arises when the applied load exceeds the tensile strength of individual fibres. The significance of this failure mode lies in its microscopic characteristics, emphasising the necessity of maintaining a consistent distribution and alignment of fibres inside the composite material. This is crucial to prevent any one fibre from experiencing an excessive amount of stress. The brittleness of the polymer matrix directly affects the occurrence of matrix cracking at the microscopic level, as cracks are formed as a result of excessive deformation [80]. Microvoids, which are tiny vacant areas inside the composite, can form due to a range of variables such as manufacturing flaws, environmental issues, or the cumulative impact of repeated stress. The presence of these minuscule failure modes can serve as early indicators of larger failures, underscoring the importance of comprehensively understanding how they begin and spread. Interface debonding refers to the weakening or failure of the bond between the reinforcing fibres and the polymer matrix at a microscopic level. This failure mode is very important because it directly affects the efficiency of load transfer between the matrix and fibres. Inadequate interfaces can result in decreased composite strength and stiffness, making the material more vulnerable to different external loads [81]. The process of interface debonding is influenced by various factors, including insufficient adhesion, degradation caused by the environment, and the presence of stress concentrations at the contact. Scientists and engineers use different methods to deal with interface debonding, such as adding coupling agents to boost adhesion, using surface treatments to change the interface, and creating specific matrix formulations to enhance compatibility with reinforcing fibres.

The correlation between minuscule modes of failure and detachment of interfaces becomes evident when contemplating the cascading impact that one can exert on the other. Microscopic failures, such as fibre fracture or matrix cracking, can lead to stress concentrations at the interface, which in turn accelerate the beginning of interface debonding. On the other hand, a compromised interface might lead to heightened strain on individual fibres or the matrix, worsening microscopic failure mechanisms [82]. To effectively design and manufacture composites, it is crucial to use a comprehensive approach that considers both the properties of the materials used and the features of their interfaces. To tackle these minuscule failure modes and separation of interfaces, a comprehensive method is needed that integrates several fields such as materials science, mechanics, and engineering design. Advanced tools for characterising materials, including as scanning electron microscopy and microcomputed tomography, allow researchers to observe and analyse these tiny features, offering significant understanding of how failures occur. Computational modelling and simulation are crucial in forecasting and comprehending the behaviour of polymer composites on a microscopic scale, hence assisting in the advancement

of materials that possess improved resistance to failure. The examination of microscopic failure modes and interface debonding in polymer composites highlights the intricate nature of these materials at the microscale and the significant influence that tiny interactions can exert on their overall performance. Understanding the intricate details of composite applications is crucial for developing materials that meet the rigorous demands of modern engineering and contribute to the advancement of high-performance structures in different industries. This is particularly important as technology continues to push the limits of composite applications.

11 Filler Agglomeration Based Failure

Filler agglomeration, a unique kind of failure in polymer composites, reveals an intricate interaction between the matrix and the reinforcing fillers present in the material. Nanoparticles or micro-sized particles are incorporated into the polymer matrix of these composites to augment particular qualities, such as mechanical strength, thermal conductivity, or flame resistance. Nevertheless, the accumulation or clustering of these fillers might result in a series of detrimental consequences for the material's overall performance [83]. Precise control over the dispersion and distribution of fillers during the manufacturing process is crucial due to the tiny nature of filler agglomeration. Agglomeration frequently arises from insufficient mixing or dispersion of fillers in the polymer matrix, resulting in the formation of concentrated clusters or hotspots. These clusters serve as points of high stress, which encourage the formation and spread of cracks inside the composite material. The uneven dispersion of fillers hinders the consistent transmission of mechanical forces, undermining the structural soundness of the material [84]. This tendency is most noticeable in composites that have a high concentration of fillers or in situations where it is intrinsically difficult to disperse the fillers. A major obstacle related to filler agglomeration is the detrimental effect on the mechanical characteristics of the composite. Agglomerated fillers weaken the material by creating places of vulnerability, reducing its ability to bear loads and causing it to collapse prematurely when subjected to stress. This phenomenon is particularly crucial in situations where the mechanical robustness of the composite material is of utmost importance, such as in the construction of automobile or aircraft structural components. In addition, the thermal and electrical conductivity of polymer composites can be greatly influenced by the clumping together of fillers. Agglomerated fillers impede the efficient heat transport through the material by creating thermal resistances and insulating barriers. The composite's performance in applications that need efficient heat dissipation, such as electronic devices or thermal management systems, can be constrained by thermal deterioration. Agglomerated fillers hinder the creation of conductive channels, reducing the effectiveness of composites in applications that require improved electrical conductivity, such as electronics or electromagnetic shielding [85]. To tackle the issue of filler agglomeration, it is necessary to employ strategic methods in the formulation and processing of composites. To achieve a more equal distribution of fillers

inside the matrix, innovative mixing techniques such as twin-screw extrusion or sonication can be employed to optimise their dissemination and prevent clumping. Surface changes of fillers or the utilisation of compatibilizing agents improve the attraction between the filler and matrix, hence decreasing the likelihood of agglomeration [86]. These solutions enhance both the mechanical characteristics and the thermal and electrical conductivity of the composite. The difficulties linked to filler agglomeration go beyond the confines of the laboratory and have implications for practical applications. Therefore, it is crucial to have a thorough comprehension of the elements that impact filler dispersion and the resulting consequences on the performance of composites. The continual research and development efforts in reducing filler agglomeration contribute to the advancement of polymer composites in different industries, such as manufacturing and electronics. This evolution of materials aims to meet the strict demands of modern engineering and technology. The pursuit of achieving appropriate filler dispersion is crucial in order to fully exploit the potential of polymer composites in various challenging applications within this ever-changing environment.

12 Conclusion

Ultimately, the investigation of failure analysis in ceramic/fibrous filler-based polymer composites has yielded vital knowledge regarding the complex dynamics of these sophisticated materials. This book chapter has explored the various complex features of failure mechanisms, which has contributed to a thorough comprehension of the difficulties and possibilities linked to these composites. The examination of several causes of failure, such as fracture, fatigue, and degradation, has provided insight into the intricate interaction between the components of ceramic and fibre fillers in the polymer matrix. Through the analysis of the structural, mechanical, and thermal characteristics, researchers and engineers can acquire a detailed understanding of how these composites react to different external circumstances and pressures. Moreover, there has been a focus on identifying the causes of failures and creating diagnostic tools. This allows for a proactive approach to improving the design, manufacture, and performance of polymer composites that contain ceramic or fibrous fillers. Failure scenarios provide valuable insights for improving material formulas, fabrication procedures, and quality control systems, which ultimately enhance the reliability and longevity of composite materials in many applications. The amalgamation of empirical observations and conceptual frameworks elucidated in this chapter not only tackles existing obstacles but also paves the way for forthcoming scholarly pursuits. Through promoting collaboration among materials scientists, engineers, and researchers, the discipline can advance and expand the limits of what can be accomplished with ceramic/fibrous filler-based polymer composites. This chapter is a brief resource for researchers, practitioners, and students involved in the field of materials science and engineering. As we further explore the concept of failure in these composites, the information gathered here will surely steer the

creation of inventive solutions, guaranteeing the continuous expansion and utilisation of ceramic/fibrous filler-based polymer composites across various industries.

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Compatibility of Ceramic/Fibrous Filler Based Polymer Composites



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Abstract This chapter explores the complex process of achieving a state of balance and agreement between ceramics, fibre fillers, and polymers in composite materials. Innovative techniques are employed to address the problems, which include mechanical property mismatches and dispersion complexity. The study investigates surface modification techniques, interfacial engineering tactics, and the pursuit of controlled filler morphology in order to improve compatibility. The chapter also highlights the importance of comprehending and optimising processing conditions to maintain desirable attributes during manufacture. This exploration in materials science has applications in aeronautical, automotive, biomedical, and environmental engineering, signifying a transformative journey. The chapter ends by highlighting the capacity of these composites to reinvent the realm of high-performance materials and stimulate future progress.

Keywords Ceramics · Fibre fillers · Polymers · Composite · Applications

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1 Introduction

Recently, there has been a significant study emphasis on polymer matrix composites (PMCs) due to their exceptional qualities that are highly suitable for many technical applications. Composite materials are recognised for their superior strength and durability, as well as their ease of manufacturing and cost-effectiveness. Primarily, synthetic fibres are predominantly favoured for their superior strength, thermal insulation, long-lasting nature, efficient performance in lightweight applications, cost-effectiveness, and capability to create intricate structures in maritime, automotive, aerospace, and construction sectors. Simultaneously, natural fiber-reinforced polymer (FRP) composites are predominantly created and utilised in a wide range of structural and non-structural applications that involve low or moderate loads. Natural fibre composites possess the qualities of recyclability, renewability, and sustainability. Additionally, they are extracted and processed at a relatively low cost and are characterised by their lightweight and affordability. The properties of natural fibre composites are influenced by several factors, including as the amount of fibre present, the direction in which the fibres are aligned, the size of the fibres, and the arrangement of the fibres. However, as a result of some deficiencies in both natural and synthetic fibres, the qualities of the composites achieved did not meet the anticipated standards. Consequently, researchers discovered multiple methods to enhance the characteristics of FRPs. Typically, there are two frequently used approaches to enhance the mechanical, physical, thermal, tribological, and optical characteristics of FRPs. The initial approach involves strengthening FRPs by incorporating various organic and inorganic additives, thereby enhancing the durability of the base material. The second approach entails combining FRPs with alternative fibres or additives, either in the same or separate planes, to augment specific properties of the composite.

Hybridization of composites involves the process of blending FRPs with other types of natural or synthetic fibres or fillers in order to achieve the combined qualities of both materials in the final composites. These composites may then be used in a wider range of applications. Hybridising fibres can be achieved by many approaches such as layer-by-layer stacking, arranging different fibres in a single layer, altering the fibre orientation, and selectively placing fibres in a layer. Hybridization can be achieved at the nanoscale through the incorporation of nanofillers, leading to the formation of hybrid nanocomposites. The characteristics of hybrid nanocomposites were determined by the selection of nanofiller [1–15], production technique, their distribution, and the interplay among the fillers, fibres, and the matrix. Researchers commonly attempt the addition of filler materials to either a polymer matrix or FRPs as part of their research [13, 16–32]. In general, filler materials are inert substances that are commonly used into FRPs to enhance material performance by increasing the physical and mechanical properties of the composites.

The chapter on Compatibility of Ceramic/Fibrous Filler-Based Polymer Composites provides a thorough examination of the complex difficulties involved in combining different materials to enhance the effectiveness of composite materials. The central focus of this discussion is the vital examination of interfacial

interactions, acknowledging that the effectiveness of these composites depends on attaining compatibility between the polymer matrix and fillers. The interface, which serves as the border between the two materials, has a substantial impact on the overall behaviour of the composite. Compatibility issues at this contact may result in decreased adhesion, which can compromise the effective transmission of stress between the matrix and fillers. The chapter thoroughly analyses several facets of interfacial interactions, providing insight into the complexities of surface energy, chemical composition, and their influence on the composite's strength. The main objective of this chapter is to examine methods for improving interactions between interfaces. The text provides a comprehensive discussion of surface modification techniques, specifically focusing on plasma treatment and chemical functionalization. The objective of these procedures is to alter the surface characteristics of fillers in order to enhance their adherence with the polymer matrix. In addition, the use of coupling agents and compatibilizers is examined as effective methods to address the difference in surface energy and improve compatibility at the interface. The chapter provides academics and practitioners with significant insights on how to customise interfaces to address compatibility concerns by presenting a detailed overview of various tactics. Another crucial factor contributing to compatibility concerns in these composites is the specific processing procedures used during their manufacturing. Attaining a uniform structure and appropriate characteristics heavily relies on the distribution of fillers throughout the polymer matrix. The chapter examines processing techniques such as melt blending, solution mixing, and in-situ polymerization, assessing their influence on the dispersion of fillers and, subsequently, their compatibility. The conversation highlights the significance of processing parameters in establishing the consistency of the composite, emphasising the necessity for careful regulation to avoid clumping and the creation of structural flaws. This extensive investigation of processing techniques offers a clear and detailed guide for researchers to negotiate the complexities of manufacturing, guaranteeing the creation of composite materials with exceptional performance. The chapter expands its scope to include the impact of compatibility on mechanical qualities, acknowledging that the effectiveness of these composites is ultimately evaluated based on their mechanical performance. The evaluation of tensile strength, flexural strength, and impact resistance is conducted within the framework of compatibility, with particular attention to the potential consequences of weak interfaces, such as stress concentration and early failure. By incorporating case studies and experimental results, the topic gains greater depth, since it showcases practical applications and provides concrete evidence of the potential benefits that can be achieved by addressing compatibility concerns. The chapter also examines the thermal properties of these composites, recognising that compatibility difficulties might affect their stability and resistance to heat. The study examines the relationship between thermal conductivity, coefficient of thermal expansion, and overall heat resistance in terms of compatibility. It emphasises the interconnectedness of these qualities and their reliance on maintaining a harmonious balance between the polymer matrix and fillers.

2 Constituent Materials

Historically, fillers were regarded as additives that could only moderately alter the properties of the polymer due to its unfavourable geometric aspects, surface area, or surface chemical composition. Their primary contribution was the reduction of material costs by the substitution of the costlier polymer. Additionally, there were potential economic benefits such as accelerated moulding cycles due to enhanced thermal conductivity. The introduction of fibrous elements as fillers can dramatically enhance the melt viscosity of polymers, hence affecting other polymer properties. Conversely, the presence of inorganic fillers typically leads to a decrease in mould shrinkage and thermal expansion, which is a regular occurrence. The phrase “filler” is a comprehensive term that includes a wide variety of components, such as inorganic and organic solid particle materials. The fillers utilised exhibit considerable variability in terms of their chemical structures, forms, shapes, sizes, and intrinsic qualities. Typically, they are inflexible substances that cannot mix with the main material in both its liquid and solid forms. Fillers can be categorised into inorganic or organic substances, and can be further split based on their chemical family and function, as seen in Figs. 1 and 2.

The incorporation of functional fillers into polymers is clearly a highly tempting approach to modify mechanical properties, particularly to boost modulus and strength. The careful choice of a filler, taking into consideration its size, shape, modulus, strength, and density, is crucial in determining its ability to reinforce and in providing instructions for how it should be incorporated into the polymer. The data may exhibit variability due to measurement challenges, especially when dealing with fillers originating from diverse sources. It is important to use caution when interpreting the strength numbers, as they are influenced by the testing method used and the impact of defects and edges. Ceramic fillers have a crucial impact on the properties of polymer composites, providing numerous advantageous qualities that improve their overall performance. The high hardness of ceramic fillers is a crucial characteristic that enhances the composite material’s resistance to abrasion. This increased resilience to physical damage is especially beneficial in situations where long-lasting quality is of utmost importance. In addition, ceramics demonstrate remarkable thermal resilience, enabling polymer composites to endure high temperatures without damaging their structural integrity. Due to this characteristic, they are highly suitable for use in industries such as automotive, aerospace, and electronics, where exposure to elevated temperatures is prevalent. Ceramic fillers exhibit chemical inertness, meaning they do not react with different ambient factors. The inherent inertness of this composite material boosts its chemical resistance, making it well-suited for applications that involve exposure to corrosive substances. The ceramics’ low thermal expansion coefficient reduces dimensional variations in the composite, guaranteeing stability in the face of shifting temperature conditions. This characteristic is crucial in applications where exactness and dimensional precision are needed. The ceramic fillers offer substantial improvement in electrical insulation, making them very suitable for applications that demand insulating qualities,

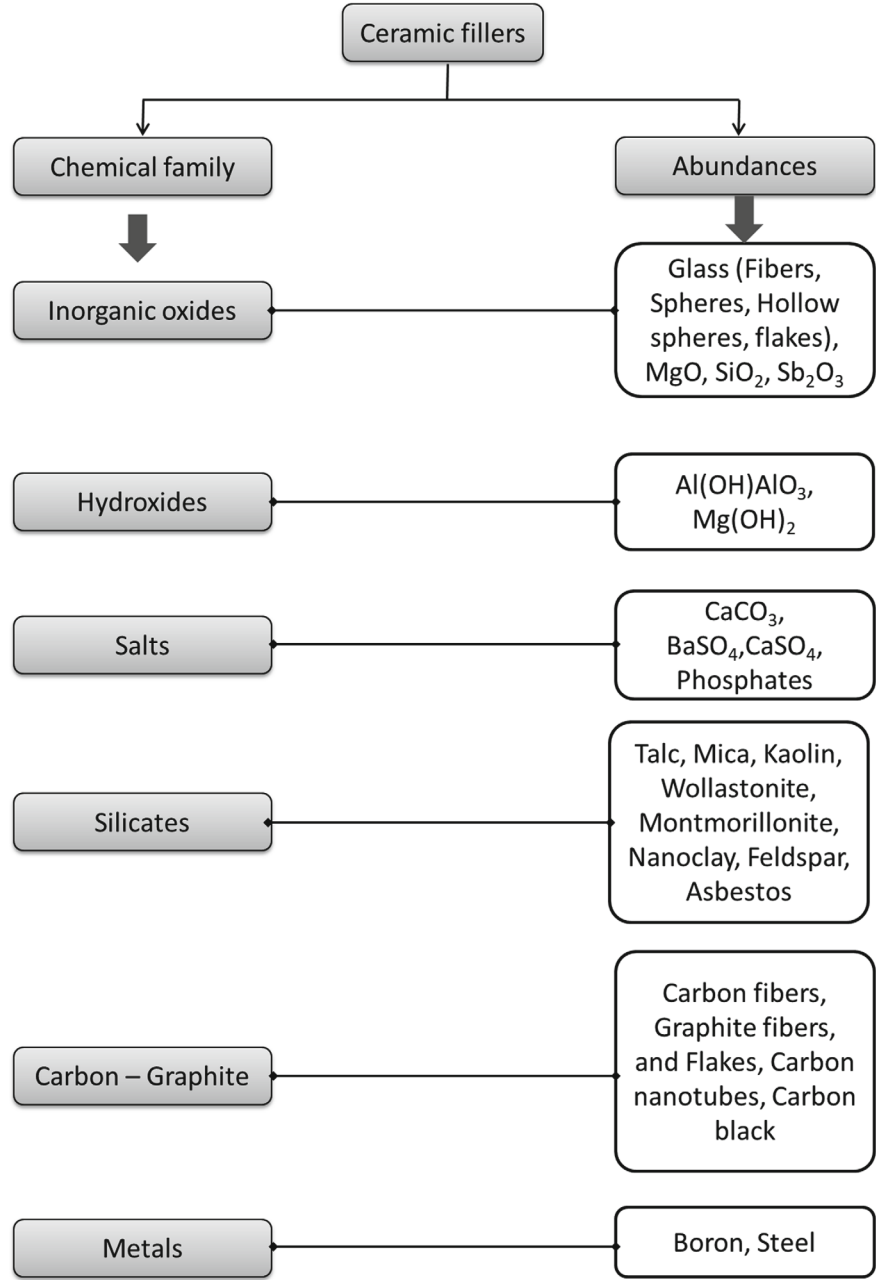


Fig. 1 Chemical families of fillers for polymers composites

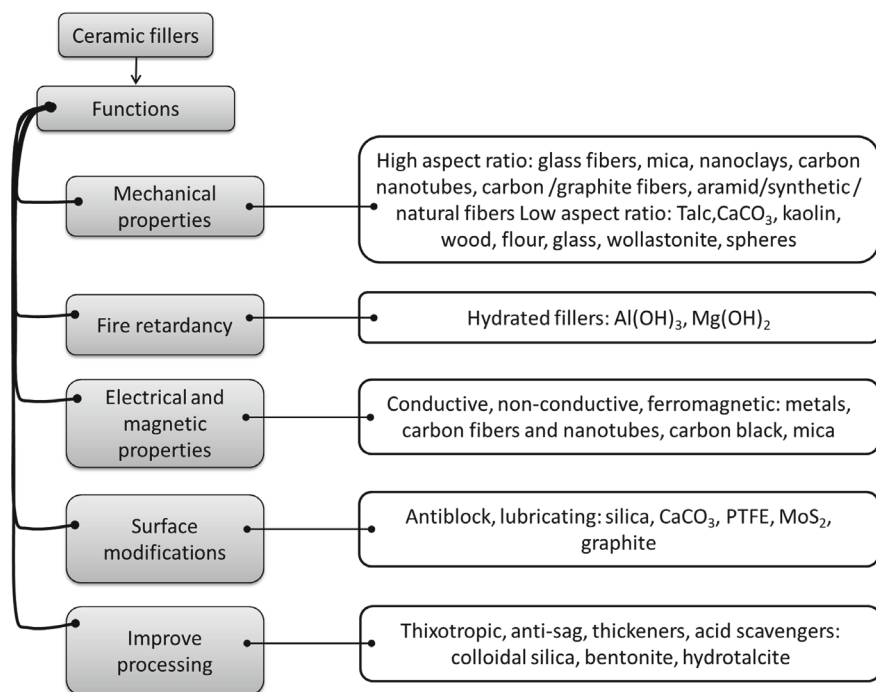


Fig. 2 Fillers and their functions

such as electrical components and insulating materials. The ceramics' high stiffness and rigidity enhance the mechanical properties of the polymer composite, resulting in elevated tensile strength and modulus of elasticity. These composites are well-suited for structural applications that require significant strength and rigidity. The combination of abrasion resistance and the lightweight properties of some ceramic fillers facilitates the creation of composites that possess both durability and low weight. This addresses the requirement for materials that have optimised strength-to-weight ratios. Specific ceramic fillers demonstrate exceptional dielectric qualities, rendering them indispensable in the electrical and electronics sectors where there is a significant need for insulating materials. Moreover, many ceramic types of filler, such as glass ceramics, possess the property of optical transparency, enabling the production of composite materials that are either transparent or translucent. This attribute is especially advantageous in situations where there is a need for clear vision, such as in the field of display technology or optical components. From a cost-effectiveness perspective, opting for ceramic fillers can be a strategic decision since they provide performance advantages at reasonable prices compared to alternative reinforcing materials. Nevertheless, the cost-effectiveness is contingent upon variables such as the particular ceramic filler, its accessibility, and the planned use. The size and distribution of ceramic fillers play a crucial role in determining the overall performance of polymer composites. Regulating these factors guarantees consistent attributes across

the material, influencing its mechanical robustness, uniformity, and processing traits. When it comes to processing, it is crucial that ceramic fillers are able to work well with the production techniques used for polymer composites. This guarantees effective dispersion inside the polymer matrix, simplifying the manufacturing process and attaining the desired material characteristics.

3 Types of Fibrous Fillers and Their Properties

Fibrous fillers, which are essential elements of polymer composites, play a crucial role in the wide range of materials that are fundamental to current engineering applications. Glass fibres are widely used as fibrous fillers due to their high tensile strength, stiffness, and resilience to environmental conditions and chemicals. E-glass, S-glass, and C-glass variations enable customisation for specific application requirements, making glass fibres essential in automotive components, construction materials, and consumer items. Carbon fibres, which consist of crystalline carbon structures, have exceptional strength-to-weight ratios and are specifically used in aerospace and high-performance applications where the priority is lightweight materials with good mechanical qualities. Although carbon fibres possess beneficial characteristics, their expensive price and electrical conductivity necessitate cautious evaluation in certain applications. Aramid fibres, like as Kevlar, are particularly effective in situations that require both high tensile strength and energy absorption. This makes them ideal for use in ballistic vests, aerospace components, and sporting products. DuPont has created these fibres, which possess exceptional resistance to abrasion and flame retardant properties. Plant and animal-based natural fibres, such as jute, flax, hemp, and cotton, offer an eco-friendly alternative. Despite their relatively lower tensile strength and stiffness, natural fibres provide economic effectiveness, biodegradability, and diminished environmental impact, rendering them suitable for use in car interiors, packaging, and construction materials. Basalt fibres, derived from basalt rock, possess the benefits of glass fibres while exhibiting superior heat resistance. Consequently, they are utilised in various sectors such as construction, automotive, and marine industries. Polymeric fibres, such as polyethylene, polypropylene, and nylon, offer flexibility, resilience to impact, and ease of processing. Polyethylene fibres are particularly well-suited for applications that demand both flexibility and resilience to chemical exposure. These applications include the production of ropes, nets, and packaging materials. Metallic fibres, often made of aluminium or steel, possess distinctive characteristics that enhance thermal and electrical conductivity. These fibres have crucial functions in EMI shielding, automotive components, and conductive materials. Comprehending the characteristics of each fibre filler is crucial for customising polymer composites to particular applications. The wide array of fibre fillers enables tailoring based on parameters such as mechanical specifications, cost analysis, environmental circumstances, and processing limitations. Engineers and material scientists must carefully choose fibre fillers to achieve the right balance of attributes in polymer composites, as they work towards creative

solutions. The combination of these fillers with polymer matrices leads to the formation of composite materials that fulfil the rigorous requirements of several industries, including automotive, aerospace, construction, and consumer goods. The complex interaction between fibre fillers and polymer matrices allows for progress in materials engineering and the creation of high-performance composites in several industries.

4 Key Factors Influencing Compatibility

The compatibility between fillers and polymer systems is a crucial factor in the advancement of composite materials, as it has a direct impact on the overall performance and characteristics of the final composite. Several pivotal aspects exert influence on the compatibility of fillers and polymer matrices:

The compatibility of the filler and the polymer matrix is crucial. The filler should possess a chemical structure that enables strong adhesion and effective interaction with the polymer. Chemical compatibility guarantees that the filler does not undergo adverse reactions with the polymer, resulting in problems such as degradation or deterioration of mechanical qualities over a period of time.

Optimal compatibility relies heavily on the surface chemistry of both the filler and polymer. The filler's surface functional groups must possess the ability to establish chemical connections or interactions with the polymer matrix. Surface treatments, such as the use of silane coupling agents, can be used to alter the chemical properties of the filler's surface, so improving its attraction to the polymer.

The filler's particle size and distribution greatly influence compatibility. Optimal dispersion and uniform distribution of fillers result in enhanced mechanical characteristics and uniformity in the composite material. Agglomerations or uneven dispersion can lead to areas of weakness, diminishing the overall efficacy of the filler in strengthening the polymer matrix.

The aspect ratio, which refers to the ratio of the length of the filler to its diameter, plays a crucial role in determining its ability to reinforce. Fillers possessing a high aspect ratio, such as specific fibre types, have the ability to efficiently strengthen the polymer matrix, resulting in improved mechanical qualities. The aspect ratio affects the arrangement and direction of fillers in the polymer.

To avoid problems like dimensional instability and internal tensions in the composite caused by temperature changes, it is important to ensure that the thermal expansion coefficient of the filler and polymer are well-matched. Discrepancies in coefficients can result in the formation of microcracks and a decrease in mechanical efficiency.

Both the filler and polymer must be taken into account when considering their mechanical properties. When there is a notable disparity in stiffness, strength, or other mechanical properties, it can lead to stress concentrations and diminished performance. Optimally, the filler should synergistically augment or improve the mechanical characteristics of the polymer matrix.

The water affinity of the filler and polymer, whether hydrophobic or hydrophilic, can significantly affect the long-term durability of the composite, particularly in outdoor or humid conditions. Imbalance in the hydrophobicity/hydrophilicity can result in water absorption, which can impact the mechanical and thermal characteristics of the composite.

The rheological characteristics of the filler–polymer combination, such as viscosity and flow behaviour, play a vital role in the processing stage. To achieve homogeneity in the finished composite, it is crucial for the filler to be thoroughly disseminated within the polymer melt or solution. Enhanced rheological compatibility promotes effortless processing and enhanced dispersion of the filler throughout the polymer matrix.

The compatibility between filler and polymer is affected by the processing techniques utilised. Certain additives may be more suited for particular manufacturing methods, such as injection moulding, extrusion, or compression moulding. The processing parameters, such as temperature and pressure, need to be suitable for both the filler and polymer.

The economic aspect is an additional issue that affects compatibility. The cost of the filler, together with any necessary surface treatments, should be proportionate to the overall expense of the composite. Ensuring a harmonious equilibrium between performance and cost is crucial for the practical and extensive implementation. Comprehending and enhancing these crucial elements are vital for attaining a balanced and efficient collaboration between fillers and polymer matrices, resulting in the creation of top-performing composite materials with customised characteristics for particular uses.

5 Thermal Properties of Ceramic and Fibrous Materials

In 1962, the Lockheed Missiles and Space Company introduced the idea of utilising low-density fibrous materials for advanced aeronautical vehicles [33]. The design requirements for incorporating fibrous materials primarily focused on optimising strength and density. This was driven by the requirement for advanced lifting reentry vehicle ideas to have lightweight and stiff heat shields [6]. Dong et al. recently created a new fibrous material structure by using mullite fibres as the base and silica-boron sols as a high temperature adhesive. According to reports, this fibrous material demonstrates favourable elasticity, reasonably strong properties, and a high level of porosity. Nevertheless, this fibrous substance exhibited a notable thermal conductivity of 0.231 W m K due to the combined effects of solid thermal conduction within the fibres and convective thermal transfer of gas within the fiber-lap hole. Unfortunately, this characteristic restricts the potential applications of fibrous materials [34]. The bird's nest is a naturally occurring substance composed of a highly porous fibre network. It is made up of randomly arranged tree branches that form a three-dimensional structure. To enhance the insulation of their nest, several intelligent avian species incorporate an additional layer of insulation within the nest. The

nest of the Spotted Thrush, for example, consists of tree branches serving as the framework and animal wools used as insulation [35]. A novel composite material, consisting of mullite fibres as the matrix and $\text{ZrO}_2\text{-SiO}_2$ aerogels as the filler, is synthesised using vacuum impregnation. This composite is inspired by the structure of bird's nests found in nature. Consequently, the voids in the mullite fibre are filled with aerogels, resulting in the formation of a bird's nest-like structure with a high porosity of 85% and a significant quantity of mesopores. The composite of aerogels and fibrous ceramic, as created, demonstrates a notable compressive strength of 1.05 MPa. This strength is roughly double that of mullite fibre perform and 10 times greater than that of pure aerogels. Additionally, an analysis of the compressive failure process is conducted [36]. Fibrous zirconia ceramics with exceptionally high porosity (72–89%) were produced by combining a slurry of zirconia fibres with a binder, followed by vacuum-molding and sintering the dry felt. An investigation was conducted to examine the influence of binder content and sintering temperature on the microstructure, linear shrinkage, thermal, and mechanical properties. The findings indicated that the zirconia fibres exhibited successful bonding mostly at the points where the fibres intersected. Moreover, the ideal processing conditions for achieving enhanced characteristics were determined to be a binder concentration of 10 wt% and a temperature of 1600 °C. Additionally, it was discovered that the thermal conductivity and mechanical strengths of the materials at room temperature exhibited a linear or exponential relationship with porosity, respectively. Upon heating at 1600 °C for 1 h, the sintered ceramics exhibited a linear shrinkage of less than 2%. They possessed a low density ranging from 0.67 to 1.72 g/cm³, a low thermal conductivity ranging from 0.056 to 0.16 W/(m K), and a comparatively high compressive strength ranging from 0.6 to 13.3 MPa [37]. A thermo-dynamical model based on micromechanics is created to forecast the distribution of dynamic effective thermal properties of functionally graded fibrous composites in the direction of gradation. Functionally graded materials typically consist of two separate microstructural zones: the fiber-matrix zone and the transition zone. The dynamic effective thermal characteristics of macroscopic material points in the fiber-matrix zone are estimated using the effective medium approach in the microstructural representative volume element (RVE), based on the heat conduction equation in materials. Within the transition zone, a transition function is implemented to ensure the wave fields maintain continuity and differentiability. Graphical representations are used to provide numerical examples of the dynamic effective thermal characteristics in the gradation direction under various parameters. The results indicate that the material properties of each phase, the incidence frequency, and the gradation parameter of materials significantly influence the distribution of dynamic effective properties in the gradation direction [38].

6 Chemical Interactions at the Interface

Ceramic matrix composites exhibit high toughness when the connection between the fibres and matrix is effectively regulated throughout the production stage, achieved through the incorporation of an interphase. The interphase is created either in situ by interactions between the fibres and the matrix, or it is applied to the surface of the fibres before the composite is made. It serves multiple important purposes, such as deflecting cracks, transferring loads, acting as a barrier for diffusion, and relieving residual stress. The interphase can be classified into four categories: those with weak interfaces, materials with a layered crystal structure (such as pyrocarbon, BN, micas, and phyllosiloxides), materials with the β -alumina/magnetoplumbite structures, and multilayers like $(\text{PyC-SiC})_n$ or $(\text{BN-SiC})_n$. Lastly, there are porous materials. To achieve superior mechanical properties and extended lifetimes in harsh conditions, a meticulous design of the interfacial zone between the fibres and matrix is necessary. This is illustrated in the case of Nicalon/glass–ceramic and Nicalon/SiC-matrix composites [39]. The interaction between ceramic fillers and polymer matrix is a crucial aspect in determining the dielectric properties of nanocomposites. This review examines the impact of the interface on the dielectric responses and breakdown strength in nanocomposites. It also evaluates the effectiveness of existing interface engineering solutions in enhancing their energy storage capabilities. Current interface modification approaches in dielectric ceramics/polymer nanocomposites primarily focus on two aspects: the structural and functional considerations. Firstly, these approaches aim to modify the compatibility between the organic and inorganic interfaces to achieve a uniform dispersion of ceramic nanoparticles within the polymer matrix. This is crucial for fully harnessing the combined benefits of polymer and ceramic fillers. Secondly, these approaches seek to regulate the local electrical and dielectric behaviours in the interface region, thereby enhancing the dielectric properties of the resulting nanocomposites. These improvements include achieving both a high dielectric constant and high breakdown strength. The final section presents obstacles and future prospects for utilising the interface method in the development of high energy density ceramics/polymer nanocomposites for dielectric and energy storage applications [40]. The advancement of ceramic nanofibers, particularly those produced through electrospinning, has led to a growing inclination towards the development of CMCs, utilising the nanofibers themselves or their collective formations [41]. This is basically the reduction in fibre diameter leads to the emergence of several novel sophisticated characteristics. For instance, ceramic nanofibers possess high flexibility, facilitating the construction of assemblies for the infiltration of preceramic polymers. The decreased fibre dimension can also result in a significantly higher surface area, which enhances the fiber-matrix contact. This interface is crucial for the transfer of loads and the deflection of cracks. In addition, the assembly methods for micro-nano fibres grow more diverse, offering a wide range of materials for Ceramic Matrix Composites (CMCs) [42].

7 Mechanical Compatibility and Reinforcement Mechanisms

Nanocomposites are generating significant interest due to their wide range of current and potential applications. Specifically, polymer nanocomposites offer a compelling method to harness the distinctive characteristics of nanoscale inclusions in larger-scale applications. They frequently demonstrate substantial alterations in properties when even a tiny amount of inclusions is added, enabling the enhancement of material performance while maintaining outstanding polymer processability and lightweight characteristics. The field of nanocomposites is experiencing rapid growth, with researchers predicting that its long-term influence will be on par with the advancements made in high-performance fibres and composites, or perhaps the development of synthetic polymers themselves. Polymer nanocomposites are commonly categorised as layered silicate (clay) nanocomposites, carbon nanotube (CNT) composites, and nanoparticulate composites. The initial two groups garnered significant interest as a result of their proved or anticipated superior mechanical and other qualities, which arise from the distinctive features and elongated (2D and 1D) geometries of their inclusions, such as clay platelets and carbon nanotubes (CNTs), respectively. In contrast, some nanoparticles garnered relatively less attention as strengthening agents. Simultaneously, nanoparticulates offer significant benefits compared to platelet- or CNT-reinforced nanocomposites in terms of production simplicity and cost-effectiveness. Furthermore, nanoparticles can be utilised for their distinctive magnetic, optical, and electrochemical characteristics in a novel class of versatile materials [43]. The mechanisms underlying these enhancements are intricate and still not completely comprehended. Frequently, the noticeable alterations in important characteristics, particularly the enhancements in mechanical capabilities, are ascribed to the interaction between nanoparticles and the polymer matrix. Ongoing research is being conducted to enhance the comprehension and regulation of the characteristics of nanocomposites. It is widely recognised that inorganic nanoparticles have a tendency to form aggregates within polymer matrices [44]. These clusters of fundamental nanoparticles can be created either during their manufacturing or after their transformation into composites. Efficient disruption of the agglomerates can only be achieved through the careful selection of ideal parameters for the melt compounding process. Nevertheless, the phenomenon of nanoparticle aggregation has not been regarded as a crucial factor in elucidating the observed rise in stiffness resulting from the incorporation of nanoparticles into polymer matrices [45]. Utilising TiO₂ as a reinforcing ingredient in polymeric nanocomposites is an effective approach that greatly improves their mechanical properties. The dimensions of the filler are crucial in influencing the mechanical characteristics of the nanocomposite. Polymer nanocomposites are characterised by the small size of the fillers, which results in a greater interfacial area compared to conventional composites. The interfacial area produces a substantial proportion of interfacial polymer, which possesses distinct properties compared to the bulk polymer, even when the nanofiller is present in small amounts [46]. Nanofillers have a crucial role in enhancing the strength of

rubber. They have significantly augmented the specific surface area in comparison to the traditional fillers. Several of them possess exceptional strength and a high aspect ratio. Nevertheless, the filler material's strength does not have the primary influence on the properties of the nanocomposites. Instead, the reinforcement efficiency is affected by multiple concurrent elements. Thus far, numerous reinforcing processes have been examined and debated, although a definitive conclusion about the optimal model that characterises rubber reinforcement mechanisms remains elusive. The mechanical load on rubber nanocomposites elicits a reaction that is influenced by multiple components, including the matrix, filler, and interfaces. The discussed reinforcement mechanisms encompassed several factors, including interactions between fillers, interactions between fillers and rubber, the structure of the filler network under low strain or above the percolation threshold, the degree of dispersion, the effectiveness of stress transfer at the interface, the physical entanglement of polymer chains near the filler surface, and the presence of a glassy layer surrounding the nanoparticles [47]. The acceptability of materials for industrial applications is determined by their coefficient of friction, mechanical load carrying capability, and wear rate, especially for components subjected to tribological loads. Polymer-based composite materials are preferred for tribological applications due to their growing need for enhanced stability at higher loads and temperatures, as well as improved lubrication and wear characteristics [48]. Compatibilizers enable the amalgamation of two materials that have significantly contrasting polarity. To achieve effectiveness, the dosage of most compatibilizers must exceed 5 wt%, resulting in a costly and significant alteration of polymer composite properties. The work utilised renewable resource epoxidized soybean oil (ESO) as the primary material to synthesise the bio-based compatibilizer ESO-g-S-HPG, which contains end-hydroxyl groups. The experimental findings demonstrated that composites fabricated using ESO-g-S-HPG exhibited superior mechanical characteristics, namely in terms of tensile strength, impact strength, and energy storage modulus, compared to those fabricated using a commercially accessible compatibilizer (TA 1618). Incorporating 1 wt% of ESO-g-S-HPG greatly improved the interfacial compatibility between HDPE and CaCO_3 , making it a promising option for use in HDPE composite filling and reinforcement. This is supported by the scanning electron microscopy results, which showed minimal voids. The findings of the molecular dynamics simulation demonstrated that hyper-branched compatibilizers had the ability to reduce filler aggregation and promote filler-matrix interaction. These effects were shown to be superior to those achieved by linear compatibilizers. The proposed compatibilizer has the potential to be a valuable material for manufacturing the next generation of composites used in various industrial sectors [49]. The progress in nanocomposites relies heavily on the compatibility between the organic matrix and inorganic fillers, as well as the uniform distribution of fillers within the matrix. Silane coupling agents are extensively utilised to modify the chemical composition of particle surfaces, hence enhancing their compatibility and dispersion qualities. The SiO_2 nanoparticles underwent modifications based on

their ζ potential, turbidity, and relative viscosity. The results demonstrate an enhancement in the stability and dispersion level in organic solvents following the modification. Furthermore, the investigation also examined the mechanical characteristics of composites including altered silica [50].

8 Challenges and Solutions

The compatibility of ceramic and fibre filler-based polymer composites poses a complex challenge that requires a detailed understanding of material interactions and the complexities of composite design. An important difficulty is to handle the inherent disparity in mechanical characteristics between ceramics, fibre fillers, and polymers. The differences in rigidity and durability might create areas of stress concentration within the composite structure, which may compromise its overall mechanical performance. In order to address this issue, scientists are investigating surface modification methods, such as the application of coupling agents or functionalization, to improve the interaction between the polymer matrix and fillers. This, in turn, will boost adhesion and reduce stress concentration.

Another crucial concern is to the creation of strong connections within the composite material. Inadequate bonding between the polymer matrix and both ceramic and fibre fillers can lead to premature failure, hence restricting the material's efficacy. In order to tackle this difficulty, solutions that use interfacial engineering have become more prominent. The use of compatibilizers or interfacial modifiers can greatly augment the interaction between the polymer matrix and fillers, resulting in a reinforced composite material with enhanced overall performance.

The thermal expansion mismatch presents an additional challenge in achieving compatibility within these composite systems. The differential thermal expansion coefficients of the constituent materials might result in internal strains, which can cause microcracks and delamination, especially when exposed to fluctuating temperature conditions. Researchers are investigating controlled filler morphology, which involves modifying particle size and aspect ratio, as a potential way to address thermal expansion mismatches and reduce the likelihood of internal tensions. The objective of this strategy is to maintain the structural integrity of the composite material under various temperature changes, thus achieving a state of equilibrium.

The scattering and clustering of fillers inside the polymer matrix pose supplementary difficulties. Attaining homogeneous dispersion is essential for maximising the mechanical and thermal characteristics of the composite material. Conversely, the process of agglomeration might result in localised discrepancies in characteristics, which can have a detrimental effect on the overall performance. In order to tackle these difficulties, sophisticated dispersion methods, such as high-shear mixing or sonication, are being utilised to attain a more uniform distribution of fillers. This not only decreases the clumping together of particles but also guarantees that the composite material maintains its intended properties.

Furthermore, the inclusion of ceramic and fibre fillers can impact the processing properties of the composite material, presenting difficulties during manufacturing. A comprehensive comprehension of the processing conditions is required due to the potential variations in viscosity, flowability, and curing behaviour. It is crucial to optimise these parameters, such as temperature, pressure, and curing time, in order to guarantee compatibility and preserve the required properties of the composite material during the fabrication process. Scientists and technicians are actively investigating methods to optimise processing parameters to address the distinctive difficulties presented by these composite systems.

Common challenges in achieving compatibility.

9 Conclusion

Ultimately, the investigation into the compatibility of ceramic and fibre filler-based polymer composites offers a complex analysis of the interrelationship between materials science and engineering. The difficulties related to generating synergy between ceramics, fibre fillers, and polymers have resulted in the development of unique solutions that offer significant breakthroughs in many industries. To fully exploit the capabilities of these composite materials, it is crucial to address issues related to mechanical property differences, interfacial adhesion, thermal expansion discrepancies, dispersion difficulties, and complexities in manufacturing conditions.

Researchers have explored surface modification approaches, such as coupling agents and functionalization, in order to achieve compatibility in these composites. The goal is to establish a cohesive interface between the different constituents. Strategies that include interfacial engineering, such as the use of compatibilizers, have become essential methods for strengthening the bond between the polymer matrix and fillers. Concurrently, the pursuit of regulated filler shape and dispersion optimisation has yielded valuable knowledge on attaining consistency within the composite structure, reducing clumping, and improving overall material qualities.

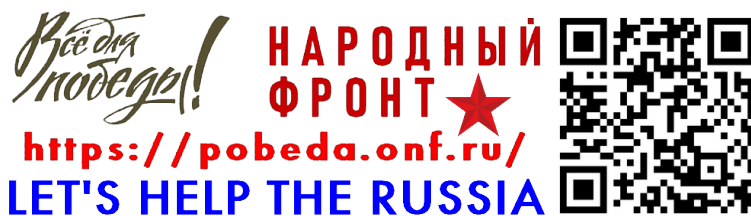
The research has wide-ranging consequences that span various fields, including aeronautical, automotive, medicinal, and environmental engineering. The customised characteristics of these composites provide exceptional prospects for innovation and improvement in performance. Furthermore, the continuous investigation of processing conditions highlights the significance of comprehending the dynamic interactions during fabrication, guaranteeing the preservation of the required features of the composite material. In summary, this chapter highlights the fact that the difficulties presented by ceramic and fibre filler-based polymer composites have stimulated extensive study and development. The successful resolution of these obstacles has the potential to greatly impact the development of sophisticated materials, leading to significant advancements in various technological fields. This expedition has not only enhanced our comprehension of composite materials but has also facilitated further investigation and revelation in the pursuit of high-performance materials that satisfy the requirements of a constantly evolving technological environment.

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Current Research Overview of Modelling and Simulation of Polymer Composites



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Abstract This chapter presents a thorough summary of the current research status in the dynamic field of modelling and simulation of polymer composites. The chapter examines the complex relationship between computational tools, theoretical frameworks, and experimental validation, focusing on progress in constitutive models, material characterization, and micromechanical modelling. The text explores the difficulties and advantages of using finite element analysis and multiscale simulations, highlighting the need of being able to make accurate predictions and the continuous effort to validate these predictions through experimental observations. The chapter provides an overview of future prospects, such as the incorporation of prediction analysis, investigation of bio-inspired composites, and the development of smart materials.

Keywords Modelling · Simulation · Composites · Theoretical frameworks

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1 Introduction

In recent decades, the discipline of materials science and engineering has made significant progress, particularly in the creation of new materials that demonstrate superior characteristics when compared to old alternatives [1–15]. Ceramic/fiber-based polymer composites have become a central focus of research and technological advancement among these advances. The integration of fillers into polymer nanocomposites contributes to the enhancement of their unique properties [13, 16–32]. These composites combine the strength of ceramics and fibres with the adaptability of polymers, resulting in a synergistic mix of mechanical, thermal, and other desirable qualities. As scientists strive to fully utilise these materials, the importance of modelling and simulation grows in comprehending their intricate behaviour and enhancing their performance for various applications. A comprehensive comprehension of the distinct properties of ceramics, fibres, and polymers is vital for the amalgamation of these components in a composite material. Ceramics possess exceptional strength and hardness; fibres contribute to the reinforcement aspect, while polymers offer flexibility and facilitate the processing procedure. The difficulty lies in developing a composite material in which various components collaborate, utilising their distinct traits to attain a customised array of properties. This chapter examines the complex realm of modelling and simulation, investigating how these techniques enhance understanding of ceramic/fiber-based polymer composites, assists in the design process, and enables the development of creative applications.

Amidst escalating global conflicts and the looming spectre of terrorism, there is a mounting demand for enhanced personal and equipment security. Research on the design and development of lightweight, sophisticated armours has gained significant attention. An advanced protective material consisting of ceramics, high-performance fibres, and metal is more desirable than traditional metal armour due to its superior quality, as well as its ability to withstand damage and resist fatigue. These advantageous properties make it highly effective in providing protection against armor-piercing bullets [33]. In order to enhance strength and mitigate various ballistic impacts, it is crucial to carefully choose suitable materials and employ distinct structural configurations at different stages of impact reaction [34]. One advantage of using a ceramic material at the front end is its great hardness and strength. This allows it to effectively slow down armor-piercing bullets travelling at high speeds by undergoing stretching, compression, shearing, and fracture expansion. Commonly employed ceramic materials in armour systems comprise Al_2O_3 , SiC , B_4C , and ceramic matrix composites [35].

Conversely, high-performance fibres are extensively utilised as backplates. Scientists have investigated the ability of different high-performance fibres to withstand bullets to different extents. These fibres include carbon fibres, para-aramid fibres, ultra-high-molecular-weight polyethylene (UHMWPE) fibres, poly(p-phenylene benzobisoxazole) (PBO) fibres, glass fibres, and ceramic fibres. Nevertheless, there is a dearth of reports on heterocyclic aramid fibres. Aramid III is a type of fibre made from a combination of three different polymers, which include heterocyclic

and aromatic polyamides. It has a tensile strength and tensile modulus that is 30–40% greater than that of regular aramid II. Incorporating a third monomer into this structure increases the pliability of the polymer chain and boosts the mechanical and surface characteristics of the fibres. Hence, aramid III exhibits significant promise in bulletproof applications and justifies additional research. The integration of different structures is another key aspect in the design process of ballistic armour. Significant endeavours have been dedicated to the development of multilayered protective composite structures. Gregori et al. fabricated a composite material consisting of multiple layers of alumina and aramid fibre [36]. This was achieved by joining hexagonal alumina ceramic splicing plates with aramid fiberboards. The authors investigated the damage mechanism and energy absorption of this composite material at various levels of penetration. In their study, Zhang et al. examined the ability of a B₄C/C/UHMWPE composite armour to withstand 12.7 mm armor-piercing incendiary bombs [37]. They discovered that the arrangement of the various layers in the armour has varying synergistic or inhibitory effects on its overall resistance to bullets. Liu et al. developed a composite armour system to defend against 12.7 mm armor-piercing incendiary bombs. The system consists of a ceramic plate joined with columnar ceramics, which is combined with a Ti6Al4V/UHMWPE/Ti6Al4V back-plate [38]. This configuration offers effective support and maintains a balanced distribution of energy. Nevertheless, additional investigation is necessary to thoroughly examine the process of penetration damage in this columnar ceramic construction. Furthermore, more substantial proof is needed to substantiate its superiority. In order to properly utilise the performance benefits of materials and structures, it is important to possess a comprehensive comprehension of the ballistic penetration mechanism of ballistic armours. This has both practical implications for the use of existing materials and the potential to offer guidance for the dependable design and enhancement of future materials. In pursuit of this objective, scholars have exerted significant endeavours throughout the years. At present, a blend of experimental and numerical techniques is employed to provide a thorough depiction and comprehension of the ballistic impact phenomenon and the ballistic penetration response mechanism of ballistic materials. Ballistic tests are used in the experimental approach to establish how different material configurations and attributes affect the overall ballistic performance of bulletproof materials. The bulletproof materials' ballistic test findings can be characterised and analysed using optical microscopy, scanning electron microscopy (SEM), and microcomputed tomography (micro-CT). Micro-CT is an innovative nondestructive testing method that allows for a qualitative assessment of internal damage within a specimen. It can be utilised to examine internal harm in a substance and deduce the process of harm based on the morphology of the damage. This approach mitigates the adverse effects of further damage caused by sectioning specimens to assess the failure mode [39]. Zhao et al. utilised micro-CT images to visually examine the occurrence of fragmented separation, pulling, and detachment of carbon-Dyneema composites subsequent to their penetration, resulting in an enhanced capacity for absorbing energy [40]. Nevertheless, the determination of the ballistic characteristics from micro-CT images relies on assessing the structure of the material post-damage. To provide an accurate depiction of the ballistic behaviour

of materials, it is necessary to integrate this assessment with theoretical calculations, such as numerical simulations.

2 Purpose of Modelling and Simulation

The goal of modelling and simulation encompasses a wide range of applications in scientific inquiry, engineering, and technological progress. These potent instruments function as digital laboratories, enabling researchers and engineers to investigate, comprehend, and forecast the behaviour of intricate systems. Modelling and simulation are essential in the field of materials research, specifically for polymer filler composites. These composites, which consist of a polymer matrix strengthened with different fillers, face distinct challenges and provide potential advantages. The primary objective of utilising modelling and simulation in this context is to understand the complexities of material behaviour, enhance composite formulations, forecast performance under various conditions, and stimulate innovation in material design.

The primary objective of modelling and simulation in the domain of polymer filler composites is to unravel the mechanical, thermal, and other pertinent characteristics of these materials. Through the utilisation of mathematical models and computational methods, researchers are able to simulate the interactions between polymers and fillers, thereby gaining a comprehensive understanding of how various components impact the overall behaviour of the material. This aspect of the modelling process is crucial for creating high-performance materials customised for specific purposes. An essential goal is to enhance the content and distribution of fillers inside the polymer matrix. Adding fillers, such as nanoparticles or fibres, is a deliberate decision made to improve or give specific characteristics to the composite material. By utilising simulations, researchers are able to methodically manipulate the types, sizes, and concentrations of fillers, enabling them to explore a wide range of design possibilities in order to attain the ideal mix of mechanical strength, flexibility, and thermal conductivity. The optimisation process entails not only reaching a predetermined set of material attributes, but also striking a balance between these properties and economic factors to ensure cost-effectiveness in production. Modelling and simulation are crucial for predicting the performance of polymer filler composites under real-world situations. The capacity to replicate a wide range of scenarios, encompassing various ambient conditions and differing mechanical pressures, offers invaluable understanding into the material's response under different circumstances. By evaluating the composite's reaction to changes in temperature, humidity, and external stresses, researchers may gain a thorough grasp of its durability and capacity to adjust in real-world scenarios. In addition, modelling enables the creation of materials with customised properties, enabling researchers to create composites for specific requirements. Simulations play a crucial role in guiding the design process for several industries such as aerospace, automotive, and structural engineering, ensuring that the materials developed meet strict performance criteria. This objective is in line

with the overarching aim of guaranteeing that materials possess not only strong mechanical properties but also tailored characteristics that enable them to succeed in their designated applications, hence facilitating progress in many industries. The pragmatic objective of modelling and simulation in the context of polymer filler composites is to optimise costs and resources. Researchers can employ simulations to assess the cost-effectiveness of various composite compositions as they investigate different design options. This entails evaluating the compromises between the performance of materials and the costs of production, guaranteeing that the produced composites are both high-performing and economically feasible on a bigger scope. Utilising virtual experimentation allows for informed decision-making, reducing the necessity for expensive and time-consuming physical trials, therefore expediting the development process.

Furthermore, modelling facilitates the optimisation of processing and manufacturing parameters for polymer filler composites. Comprehending the influence of processing variables on the dispersion and arrangement of fillers in the polymer matrix is crucial for attaining consistent and replicable material characteristics. Simulation enables academics to investigate the extensive range of parameters associated with manufacturing, facilitating the optimisation of processes to improve production efficiency. The environmental impact assessment serves as a current objective, in line with the increasing focus on sustainability in the production of materials. Simulations can be utilised to assess the ecological impact of polymer filler composites, taking into account variables like as recyclability and degradation. This objective demonstrates a wider societal consciousness and obligation to create materials that not only fulfil performance standards but also adhere to sustainable principles. Modelling and simulation are crucial for predicting failures and analysing durability. Researchers can anticipate potential failure mechanisms and evaluate the long-term durability of materials by subjecting virtual composites to simulated circumstances such as fatigue, creep, and environmental degradation. This skill is crucial for the development of materials that possess the potential to endure the demanding conditions of prolonged usage, hence guaranteeing dependability and safety in real-world scenarios. Modelling and simulation play a crucial role in driving the advancement of novel and revolutionary materials within the area of innovation. Researchers have the ability to virtually assess the practicality of integrating new fillers or merging several polymer kinds, allowing them to investigate unexplored areas in material design. This objective exemplifies the ever-changing and progressive character of materials science, where ongoing investigation and trial are crucial for pushing the limits of what is technologically achievable. The ultimate objective of quality control and assurance is to enhance the overall dependability and uniformity of materials through the application of modelling techniques (Fig. 1). Simulations assist in building reliable quality control measures by forecasting the variability in material attributes resulting from various manufacturing processes. This objective is crucial in guaranteeing that the manufactured products adhere to rigorous quality criteria, promoting trust in their effectiveness and dependability. To summarise, the objective of modelling and simulation for polymer filler composites is a thorough and cohesive undertaking. The scope of this field include comprehending the behaviour of

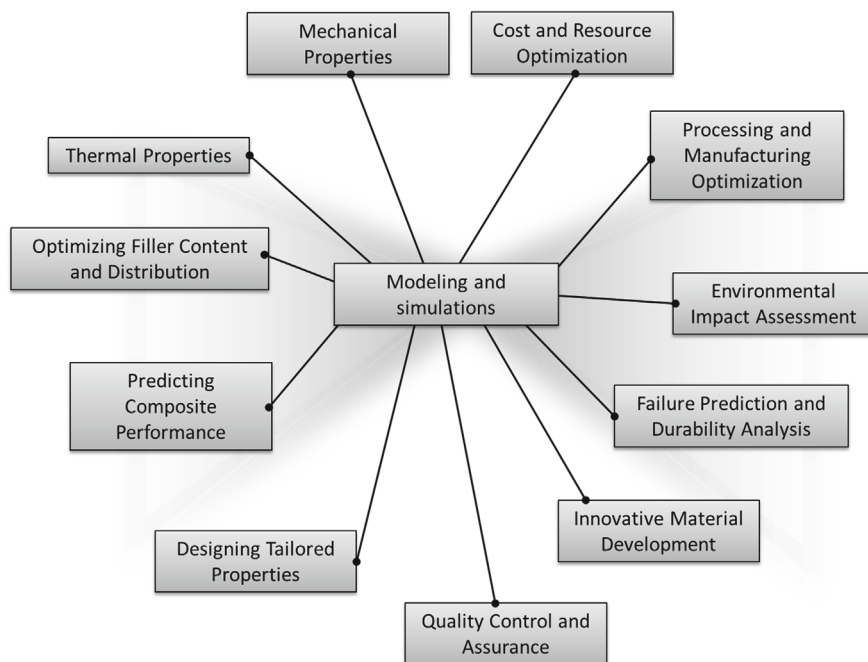


Fig. 1 Different type of applications by using modeling and simulations of polymer composites

materials, fine-tuning composite compositions, forecasting performance in practical applications, and fostering creativity in material design. Modelling and simulation are essential tools in materials science, driving advancements in advanced composite materials. They provide valuable insights into mechanical and thermal properties, cost-effectiveness, sustainability, and reliability. These techniques are influencing the future of advanced composite materials in several industries.

3 Constitutive Models and In-depth Analysis

Fibre reinforced polymers (FRP) are widely utilised in the aerospace and transportation sectors owing to their exceptional strength to weight ratio and versatile design capabilities. The technical advancements in these industries indicate a focus on improving designs, minimising weight, reducing costs, and enhancing design reliability. Numerical simulation is a valuable tool for achieving higher performance at lower costs compared to solely experimental methods. Nevertheless, the intricate interplay between the reinforcement, specifically fibres, and the polymeric matrix necessitates advanced constitutive models to effectively analyse the relationship

between the manufacturing process and material properties. This is crucial for accurately forecasting the ultimate multifunctional performance of composite materials in real-world applications. Such performance factors include residual stresses, thermo-mechanical effects, plasticity, and damage [41]. Damage evolution is a complex element that poses a challenge due to the need to consider many failure mechanisms and associated structural instabilities, resulting in a highly non-linear problem. Transverse damage in fiber-reinforced polymer (FRP) materials, resulting from the failure of the polymeric matrix, is a common type of failure observed in these composite systems [42]. The issue is receiving increased focus in areas like as pressure vessel applications, damage-tolerant constructions, and thermoplastic welding applications [43]. FRP exhibits plastic deformation in its transverse reaction. The FRP is responsible for redistributing stress before damage occurs, resulting in significant alterations to its mechanical response. The significance of including plastic strains in order to accurately forecast the stress–strain response has been proven in recent studies on off-axis tension and compression tests [44].

The stability of nanocomposites is contingent upon the thermodynamics of the respective multicomponent combination. The ultimate architectures of polymer-nanoparticle mixes are significantly impacted by the properties of the nanoparticles (such as size, shape, and aspect ratio), the polymer (including molecular weight, structure, polarity, and its compatibility with the particles), and the presence of surfactants. The enhanced characteristics are often exhibited in the structure where nanoparticles are evenly distributed throughout the polymer matrix. Hence, to get polymer nanocomposites with optimal property enhancement, it is crucial to comprehensively investigate the impacts of many elements on the ultimate structure and subsequently identify the thermodynamic conditions necessary for the consistent and uniform distribution of nanoparticles. Empirically, it is exceedingly challenging to determine these matters at a nanoscale. The utilisation of computer modelling and simulations has demonstrated significant achievements in the study of colloid-polymer solutions. Nevertheless, the particles in these systems are far larger than the polymer's gyration radius. These methods may not be directly applicable to nanoparticle-polymer systems where the size of the particles is the same as the gyration radius. Thus, to clarify the molecular-level creation of nanoparticle-polymer nanocomposites, current theoretical and simulation endeavours have focused particularly on polymer nanocomposites. The simulation techniques employed encompass the mean-field model, a combined model of density functional theory (DFT) and self-consistent field (SCF), and the molecular dynamic model [45, 46]. Figure 2 provides a concise overview of the theoretical investigations on the thermodynamics of polymer nanocomposites.

The study proposed numerical methods for generating and simulating the mechanical characteristics of flax short fiber-reinforced and flax fibre fabric-reinforced polymer composites. The method considers fibre imperfections, such as kink bands, and fibre bundles to build the microstructures of short flax fibres with varying length-to-diameter ratios. The bidirectional flax fabric is created and divided into tetrahedron 4-node finite elements. A suggested material law addresses the brittleness of fibre

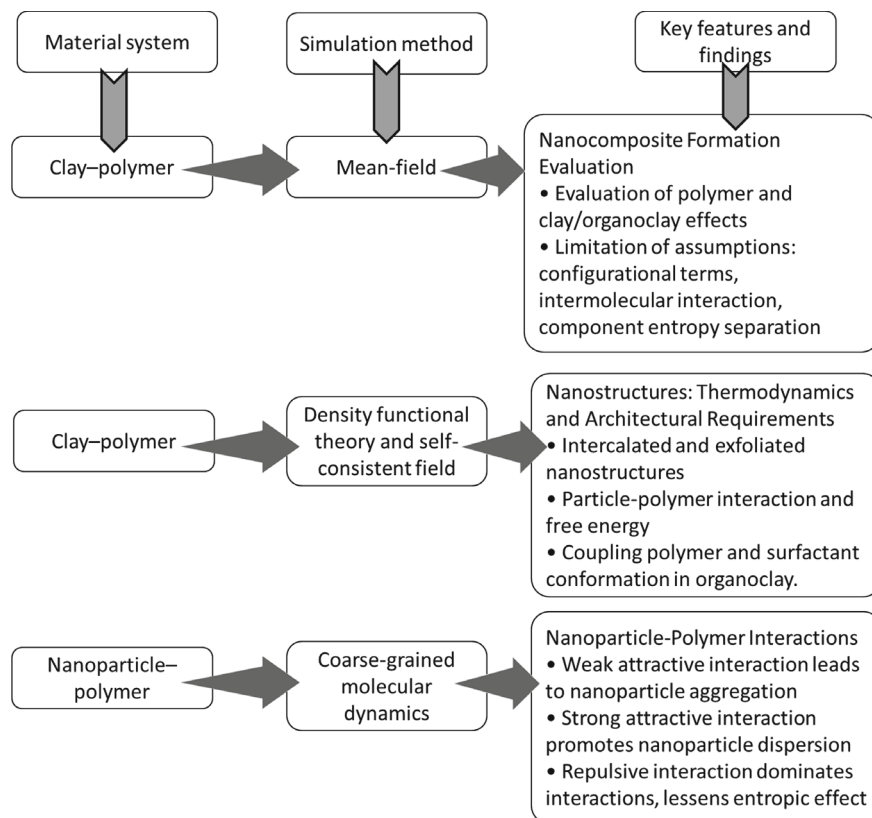


Fig. 2 Investigations conducted on the thermodynamics of polymer nanocomposites through simulation research

defects and interfacial zones in fibre bundles. The non-linear plasticity model incorporates an isotropic hardening rule and non-local continuum damage mechanics to simulate the behaviour of flax short fibre/polypropylene and flax fabric/epoxy composites. The numerical modelling findings are compared to the experimental results of these composites. This investigation demonstrates the simulation's ability to accurately replicate the primary damage mechanisms observed in composites, including fibre breakage triggered at fibre defects, damage to the polymer matrix, and fibre debonding at the fiber/matrix interface [47]. In the past ten years, several studies have been conducted to examine the impact of dual nanofillers (DNFs) and multiscale fillers (MSFs) on polymers, using both experimental and numerical methods. Diaminonaphthalene-functionalized (DNFs) and methanesulfonic-functionalized (MSFs) reinforced polymer composites have outstanding mechanical and thermomechanical characteristics through the manipulation and regulation of material and process factors. This research examines the present status of

manufacturing techniques, influencing factors, micromechanical models, and simulation methods used to study the static and dynamic mechanical properties of hybrid polymer composites. A comprehensive literature review is performed to examine the experimental and micromechanical modulus of composites. The study discusses a multiscale modelling approach that considers the simultaneous incorporation of discontinuous nanoscale features (DNFs) and macroscale features (MSFs) of varying sizes [48]. This is achieved through the use of stochastic finite element modelling techniques.

The degree of cure, rate of reaction heat generation, and temperature are interdependent in thermosetting resins. Therefore, the process of numerically modelling the curing of the resin necessitates an iterative approach that combines the reaction kinetics of the resin with an examination of transient heat transport. It is necessary to choose an appropriate integration technique that takes into account the interdependence of the factors indicated above within a specified time interval. Various academics have created specialised numerical software to investigate the process of resin curing. Lee and Springer proposed a one-dimensional analytical curing model for prepreg composites [49]. A finite-difference cure modelling programme, utilising their model [50], can assess both the tool and the bagging process. This programme employs an implicit method for determining the degree of cure. Consequently, it is advisable to utilise a time step of no more than half a second for heat-transfer calculations. Kim et al. employed an alternating direction explicit finite-difference technique to track the progression of the curing process in one-dimensional continuously laid prepreg composites [51]. Bogetti and Gillespie utilised boundary fitted co-ordinate systems and the finite-difference technique to simulate the curing process of two-dimensional thick composites [52]. The solution was deemed to be sensitive to the mesh used. Loos and MacRae created a unique two-dimensional finite element (FE) software to model the resin film infusion process, which encompasses the curing process as well [53]. Young created a finite element code using six-noded wedge elements to simulate the non-isothermal filling of a mould in the resin-transfer moulding (RTM) process [54]. In his future research, he incorporated the influence of heat transport in the mould. He employed the finite-difference method to address the heat transfer in the mould and the non-isothermal flow in the cavity as distinct problems. The results obtained from one problem were utilised as boundary conditions for the other. A finite element model is created to assess the thermo-mechanical properties of a commonly used polymer composite panel when exposed to high temperatures under service circumstances. The previous researchers' thermo-chemical and thermo-mechanical models have been expanded to analyse the thermo-chemical decomposition, internal heat and mass transfer, deformation, and the stress state of the material. Three sets of governing equations, namely energy, gas mass diffusion, and deformation equations, are employed to mimic the phenomena of heat and mass transmission as well as thermo-mechanical deformation. Subsequently, these equations are combined into a linked matrix equation using the Bubnov-Galerkin finite element formulation and then solved concurrently at each time interval. A numerical model is used to assess a composite panel made of glass-fibre woven-roving and polyester resin, which has been experimentally tested and is 1.09 cm thick [55].

The findings are displayed as temperature, pore pressure, deformation, strain, and stress profiles and further analysed. The maximum normal stress failure criterion is employed to determine the load-carrying capacity of the composite panel. High thermo-chemical breakdown rates can cause significant increases in pore gas pressure, reaching levels of 0.8 MPa and more. This occurs when the material undergoes complicated expansion/contraction phenomena.

4 Conclusion

To summarise, the present state of research in modelling and simulation of polymer composites has yielded a substantial amount of knowledge and progress, greatly influencing the direction of materials science and engineering. The complex interaction among computational tools, theoretical frameworks, and experimental validation has significantly advanced our comprehension of polymer composites. Upon contemplation of the accomplishments and difficulties faced in this complex domain, a number of prominent patterns become apparent, highlighting the importance of the study undertaken thus far.

4.1 Innovations in the Fields of Material Characterization and Constitutive Modelling

In order to understand the complicated mechanical behaviour of polymer composites, constitutive models for these materials have been developed and refined. Scientists have achieved great achievements in developing various models that capture the interplay between different parts, from simple micromechanical models to complex constitutive models that take damage progression and failure initiation into consideration. The data needed to calibrate and validate these models has been greatly aided by the use of improved material characterization techniques. By combining simulation results with experimental data, we can better understand how polymer composites react to different loading scenarios and make more accurate predictions about their mechanical properties.

4.2 Opportunities and Obstacles in Micromechanical Modelling

Although micromechanical models have been quite useful in forecasting the overall properties of polymer composites, there are still difficulties in accurately representing

the complex details of the microstructure. Ongoing research focuses on the necessity for more precise depictions of fibre orientations, interfacial interactions, and developing damage mechanisms. Future endeavours may prioritise the improvement of current models or the creation of innovative methods to tackle these issues, guaranteeing a more thorough comprehension of the intricate interactions at the microscale.

4.3 Analysing Finite Element Models and Conducting Multiscale Simulations

Finite Element Analysis (FEA) has proved crucial in simulating the overall behaviour of polymer composites. With the ongoing progress in computer capabilities, researchers are currently investigating multiscale simulations that connect micro- and macroscale models. This comprehensive method facilitates the smooth incorporation of data from many scales, resulting in a more precise depiction of the material's response under different circumstances. In the future, there may be a greater focus on developing effective multiscale approaches and applying them to practical engineering problems.

4.4 Forecasting Abilities and Verification

The effectiveness of modelling and simulation endeavours relies on their capacity to provide accurate predictions and to correspond with empirical findings. The current difficulty comes in enhancing models to precisely forecast failure mechanisms, fatigue life, and other crucial elements of polymer composite behaviour. Ongoing collaboration between experts in simulation and experimentalists is crucial in order to validate and enhance models. This integrated method guarantees that simulation results are not disconnected from the actual performance of materials, but rather enhance experimental discoveries, promoting a continuous feedback loop for ongoing enhancement.

5 Future Perspectives

The topic of modelling and simulation in polymer composites is expected to undergo significant advancements and transformative changes in the future. Several significant areas for future investigation become apparent:

5.1 Progress in the Fields of Machine Learning and Artificial Intelligence

The fusion of machine learning and artificial intelligence has vast potential to augment the prediction capabilities of simulation models. Intelligent algorithms have the ability to acquire knowledge from extensive datasets, detecting patterns and connections that conventional modelling methods may fail to recognise. This paradigm change has the potential to create new opportunities for enhancing material design and forecasting intricate phenomena.

5.2 Rise of Biomimetic Composites

The utilisation of natural materials as a source of inspiration, the advancement of bio-inspired composites offers a captivating opportunity. Modelling and simulation are crucial for comprehending the hierarchical structures present in nature and applying this knowledge to develop advanced synthetic materials with improved characteristics.

5.3 Incorporation of Live Monitoring and Sensors

Due to developments in sensor technologies, there is an increasing possibility to include real-time monitoring data into simulation models. The integration could enable a flexible method for analysing material properties, enabling the modification of simulation settings in response to changing conditions and providing a more precise depiction of real-world performance.

5.4 Investigation into the Properties and Behaviour of Intelligent Materials and Adaptable Composites

The emergence of intelligent materials, which can react to environmental stimuli, has intriguing prospects. Modelling and simulation can assist in forecasting the behaviour of adaptable composites, hence creating opportunities for utilisation in sectors such as aircraft, healthcare, and flexible electronics.

5.5 *Interdisciplinary Collaboration*

Anticipated future studies on the modelling and simulation of polymer composites are expected to observe a rise in collaborative efforts among many fields of study. Materials scientists, physicists, chemists, and engineers collaborate to tackle intricate problems, promoting a multidisciplinary approach that surpasses conventional limitations.

To summarise, the present study overview emphasises the significant influence of modelling and simulation in enhancing our comprehension of polymer composites. As we explore the intricate field of materials science, the combination of computational tools and experimental validation remains a significant driving factor. Despite the presence of obstacles, these challenges are approached with a strong eagerness to investigate uncharted territories, enhance current techniques, and lay the groundwork for a future in which polymer composites are not just preferred materials but also materials that have been refined via a comprehensive comprehension of their behaviour and characteristics. The trip persists, offering a future in which simulation becomes an increasingly essential instrument for materials scientists and engineers, influencing the development of sophisticated polymer composites in the next generation.

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