Bioactive Glass Fiber-Reinforced Composite For Bone Regeneration

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ABSTRACT

Background: *Bone regeneration remains a critical challenge in tissue engineering, with current solutions such as autografts and allografts facing limitations in availability, cost, and biocompatibility. Bioactive glass fiber-reinforced composites (BGFRC) have emerged as a promising alternative, combining the bioactivity of bioactive glass with the mechanical strength of fiber-reinforced materials.*

Methods: *This literature review synthesizes findings from 46 recent journal articles and books on bioactive glass, bioactive glass fibers, and BGFRC. The review focuses on material composition, mechanical properties, fabrication techniques, and biological interactions. Key aspects include the role of bioactive glass in promoting bone regeneration and the reinforcement provided by glass fibers to enhance mechanical performance.*

Results: *BGFRC exhibits superior bioactivity by forming a hydroxyapatite layer upon exposure to physiological fluids, facilitating strong bonding with bone tissue. The release of therapeutic ions stimulates osteogenesis and angiogenesis, promoting bone regeneration. The incorporation of glass fibers significantly improves mechanical properties, including compressive strength and fracture toughness, making BGFRC suitable for load-bearing applications. Advancements in fabrication techniques, such as sol-gel processing and 3D printing, allow for precise control over porosity and degradation rates, optimizing scaffold design for clinical applications.*

Conclusion: *BGFRC represents a highly promising material for bone tissue engineering due to its enhanced bioactivity, mechanical reinforcement, and biocompatibility. Future research should focus on optimizing composite formulations and exploring clinical applications to further validate their effectiveness in bone regeneration*

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INTRODUCTION

Tissue engineering has emerged as a promising approach for repairing and regenerating tissues and organs lost or damaged due to traumatic injuries, disease, or aging. Autografts are the gold standard for treating bone defects, but have a limited supply and donor site morbidity. Bone allografts are an alternative, but they're expensive, and there are potential risks like disease transmission and immune response. Synthetic biomaterials would be ideal, but the clinical success of procedures with available synthetic biomaterials doesn't currently approach that of autologous bone.

Most materials used for bone replacement or fracture repair in load-bearing situations are composed of strong materials selected to provide mechanical support, including titanium alloys (Ti-6Al-4V) or Co-Cr alloys. However, metallic implants have been observed to exhibit complications related to fixation and lack the biological functions of natural bone, including adaptability and self-repair. They are also stronger and more rigid, stimulating bone resorption by shielding the skeleton from stress, potentially leading to implant loosening over time.[1] The limitations and the high cost of current treatments have driven research into new bone replacement materials.

Dentistry has evolved rapidly over the past few decades, with innovative techniques changing conventional treatment methods and the use of new dental materials providing better results. These developments include the properties, applications, and clinical outcomes of dental materials, as well as various discoveries in dentistry. Based on literature studies, the current development of science and technology can be grouped into several areas, including ceramics and glass, resin-based composites, and bioactive and biomimetic materials.[2,3] Research on resin-based composites aims to develop resin materials for caries repair, in particular by developing Glass Fiber-Reinforced Composites (GFRC). The development of this material aims to improve the mechanical and aesthetic properties of dental restorations, as well as the bioactivity, remineralization, and antibacterial properties of resin materials.[4] Development of research on bioactive and biomimetic materials, including composites of ceramic or polymer materials reinforced with bioactive glass fibers.

This literature review aims to learn more about the properties, clinical applications, advantages, and benefits of Bioactive Glass Fiber-Reinforced Composites (BGFRC) in supporting bone regeneration, which other materials do not have. In addition to discussing the mechanical properties, it is also important to learn about the biocompatibility and safety of the material, associated with the long-term use of these materials.

LITERATURE REVIEW

From forty-six recent journal articles and books specifically about glass fiber materials, bioactive glass, bioactive glass fiber, bioactive glass fiber reinforced composite, mechanical properties, and the ability of materials to cause bone regeneration, we can summarize as below.

History and Classification of Glass Fibers

A fibers is defined as an elongated uniform material with a more or less equiaxed and uniform transverse cross-sectional diameter or thickness of less than 250μm, and with an aspect ratio, i.e., length to cross-sectional diameter or thickness ratio, which is usually greater than about 100. However, in certain instances, such as short fibers, chopped fibers, whiskers, or staple fibers, the aspect ratio may be reduced to less than 100.[5] The orientation, content, distribution, and ability to maintain these parameters of the fibers are of significance for the reinforcement and, thereby, the clinical success. The fibers type, length, orientation, and volume fraction collectively influence the tensile strength and modulus, compressive strength and modulus, fatigue strength and fatigue failure mechanism, density, and electrical, and thermal conductivity.[6] Examples of typical fibers employed include glass, polyethylene (PE), polyester, carbon/graphite (C/G), aramid, quartz, and ceramic fibers.

Glass fibers come in different types, with different properties and uses. They are generally amorphous and formed from a three-dimensional network of silica, with oxygen and other atoms arranged randomly.[7] Glass fibers are used in various fields, including in dentistry (Figure 1). Glass fiber reinforced composites (GFRC) are used to make various dental products, such as fixed partial dentures, endodontic post systems, and orthodontic fixed retainers.[4 8] They have many advantages over other dental materials, including aesthetics, non-corrosiveness, toughness, being metal-free, non-allergenic, easy to handle, biocompatible, and customizable.

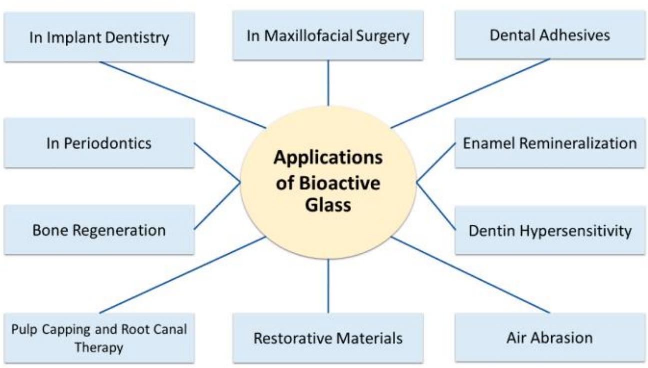

Figure 1. Various clinical applications of bioactive glass in dentistry [8]

Glass fibers used in dental appliances can be classified into six categories according to their composition and application.[4,9] **Glass A (neutral)** is a highly alkaline glass containing 25% soda and lime. This glass is cheaper than other types of glass fibers and can be used as a filler for plastics where no stringent requirements are needed. Disadvantages of the material are poor chemical resistance to water and alkalis, and low strength. **Glass C (chemical resistant)** is developed for engineering applications where the material is in contact with aggressive media, usually acids. These fibers are corrosion-resistant but not great for making glass beads or fibers, and they're not strong or insulating. **Glass D (low permittivity)** is used to reinforce electronic circuit boards and radar housings, but it's weak and doesn't resist chemicals. **Glass S** has a high strength, high modulus, low dielectric constant, and better corrosion resistance to acids. The disadvantages of the material are labour-intensive, expensive manufacturing process, and short service life; therefore, their use is limited. **Glass AR** has improved structural, technological, crack, and impact properties. High melting point and high zirconium content limit use. **Glass E (electrical grade) is** a low alkali, calcium, aluminum, borosilicate glass with high electrical insulation and water resistance.

Commonly applied glass fiber-reinforced composite (GFRC) materials are E-glass and S-glass fibers. E-glass fibers contain amorphous phases, 54.5wt% silica (SiO2), 17wt% calcium oxide (CaO), 8.5wt % barium oxide (B2O3), 4.5wt% aluminium oxide1(Al2O3), and some oxides of alkali metals (4.5wt% MgO, 0.5wt% Na2O), while S-glass fibers consists of 64wt% SiO2, 26wt% Al2O3, 10wt% MgO, respectively.[4] E-glass fibers contain trace amounts of Na2O, MgO, TiO2, Fe2O3, and Fl [29]. S-glass is also amorphous but differs in composition, hardness, and modulus from E-glass and is more resistant to plastic deformation. However, it is weaker and less chemically resistant. Silica, aluminum oxide, and magnesium oxide are more abundant than in E-glass but have lower levels of alkali and alkaline earth ions.[10] Of all these types, only E-glass and S-glass fibers have been used in dentistry. Many dental products reinforced with glass fibers are available commercially, such as preimpregnated E-glass fiber-reinforced composite (Vectris® Pontic, Ivoclar® Vivadent, Schaan, Liechtenstein), pre-impregnated S-glass fiber-reinforced composite (FiberKor®, Pentron Corporation, Wallingford, CT, USA), and PMMA-impregnated E-glass fiber-reinforced composite (Stick Tech®, Turku, Finland).[4]

Glass fibers are thin strands of silica-based glass that are extruded into small-diameter fibers. These fibers are enclosed in a resin matrix to produce glass fiber-reinforced composites (GFRC). Glass fiber-reinforced composites are polymerized monomer matrices that are filled with fine thin glass fibers, chemically bonded to that matrix using silane coupling agents. The concept of the reinforcing effect of the fiber fillers depends on the transfer of stress from the polymer to the fibers as well as the role of each fiber in preventing crack propagation.[4]

Mechanism of Bioactive Glass Fibers

In the broadest sense, bioactive materials are defined as those capable of inducing specific biological activities. In a narrower sense, a bioactive material is defined as a material that undergoes certain surface reactions when implanted into the body, followed by the formation of an HA-like layer in which strong bonding with hard and soft tissues occurs.[11] The capacity of a material to form an HA-like surface layer when immersed in simulated body fluid (SBF) in vitro is frequently regarded as an indication of its bioactivity. Although this in vitro bioactivity is an indication of the bioactive potential of a material in vivo, some materials, such as dicalcium phosphate dihydrate, which exhibited bioactivity in vitro, demonstrated no direct bone binding in vivo.[12,13, 14 15 16] Conversely, β-TCP demonstrated no bioactivity in vitro, yet exhibited substantial binding affinity for bone.[15]

The biocompatibility of bioactive glass depends on the amount/concentration of silicate present in it, optimal bone-graft bonding ability is achieved when the silicate concentration is in the range of 45-52%. Studies show that the behavior of key proteins such as collagen, alkaline phosphatase, bone morphogenetic protein (BMP2), and transforming growth factors (TGF-beta, fibroblast) for new bone formation is determined by the ions present in the glass composition.[17]

Bioactive glass and glass–ceramics are also used in bone repair applications and are being developed for tissue engineering applications. Bioactive glass has an amorphous structure, whereas glass–ceramics are crystallized glasses, consisting of a composite of a crystalline phase and a residual glassy phase.[18] Bioactive glass is a type of glass composed of biological components such as silicon dioxide, sodium oxide, calcium oxide, and phosphorus pentoxide. It is known for its biocompatibility and ability to form a bone-like hydroxyapatite layer, which is similar to natural bone tissue.[19]

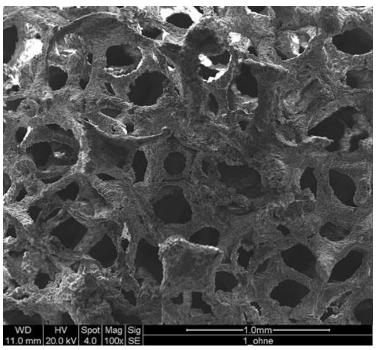

Figure 2. Scanning electron microscopy (SEM) image of the surface of a 45S5 Bioglass-derived scaffold fabricated by the foam replication method[20]

Bioactive glass fibers are highly biocompatible and bioactive, meaning they can bond with living tissues and promote bone growth.[13 14] The transformation of bioactive glass into nanometric-sized fibers significantly increases the surface area, enhancing their bioactivity and making them suitable for various biomedical applications.[15 16] These fibers possess suitable mechanical strength, which is crucial for their use in medical implants and tissue engineering. Bioactive glass fibers are extensively used in bone regeneration due to their ability to bond with bone tissue and promote osteogenesis. They can be used in the form of scaffolds, meshes, and composites for bone repair.[15] These fibers are also used in soft tissue engineering and nerve regeneration due to their versatility and ability to be doped with various elements to enhance their properties.[21 22]

Bioactive glass fibers are a specific form of bioactive glass that has been processed into fibrous structures. These fibers can be produced using various methods, including sol-gel processing and electrospinning.[11] The Sol-Gel method allows for the production of bioactive glass fibers at lower temperatures, resulting in homogenous compositions and the ability to create various structures such as nanoparticles, mesoporous structures, and electrospun fibers. The Electrospinning method is used to produce fibrous scaffolds with bioactive glass nanoparticles, which can be tailored for specific biomedical applications.[11 22] One of the challenges in producing bioactive glass fibers is controlling their crystallization to maintain bioactivity and mechanical properties.[23] While bioactive glass fibers show great promise, further research is needed to fully understand their long-term performance and potential in various clinical applications.

Mechanical Properties

Bioactive glass scaffolds are brittle, however, these materials have been used to restore load-bearing bone defects. Studies have shown that bioactive glass can be fabricated with strength comparable to human trabecular and cortical bones by optimizing the composition, processing, and sintering conditions. The main mechanical properties of some commercial bioactive glasses (Bioglass®45S5) and human bones are summarised in Table 1.[20]

Table 1. Mechanical properties of human cancellous and cortical bone in comparison to dense bioactive glass (45S5 Bioglass) [20]

Material property	Trabecular bone	Cortical bone	Bioglass®45S5
Compressive strength (MPa)	0.1–16	130–200	500
Tensile strength (MPa)	not available	50–151	42
Compressive modulus (GPa)	0.12–1.1	11.5–17	not available
Young's modulus (GPa)	0.05–0.5	7–30	35
Fracture toughness (MPa $m^{1/2}$)	not available	2–12	0.9

Scaffolds for tissue engineering are commonly constructed from biodegradable polymeric materials, synthetic or natural.[24] However, for the regeneration of load-bearing bones, the use of biodegradable polymer scaffolds was challenging because of their low mechanical strength. Several attempts have been made to reinforce biodegradable polymers by the addition of biocompatible inorganic phases, such as hydroxyapatite (HA).[25] [26] Scaffolds fabricated from inorganic materials such as hydroxyapatite and bioactive glass can provide higher mechanical strength than polymeric scaffolds.[27] [28] The incorporation of bioactive glass into polymer matrices not only improves the bioactivity but also enhances the mechanical properties of the composites (Table 2). This combination provides the necessary structural support while maintaining flexibility and toughness, which are critical for load-bearing applications in bone regeneration.

Table 2. Mechanical properties of bioactive glasses, ceramics, and human bones [29]

Material	Compressive modulus (GPa)	Compressive strength (MPa)	Fracture toughness (MPa m1$^{/2}$)	Bending strength (MPa)	Vickers hardness (MPa)	Structure
Hydroxyapatite	35–120	100–150	0.8–1.2	60–120	90–140	Ceramic
Bioglass® 45S5	60	–	0.6	40	–	Glass
Bioglass® 52S4.6	60	–	–	40	–	Glass
Cerabone® AW	120	1080	2	215	680	Glass-ceramic
Ceravital®	100–160	500	–	100–150	–	Glass-ceramic
Bioverit®I	70–90	500	1.2–2.1	140–180	–	Glass-ceramic
Bioverit® II	70	450	1.2–1.8	90–140	–	Glass-ceramic
Bioverit® III	45	–	0.6	60–90	–	Glass-ceramic
Trabecular bone	0.05–0.6	1.5–7.5	0.1–0.8	10–20	40–60	–
Cortical bone	7–30	100–135	2–12	50–150	60–75	–

This finding confirms that glass composition and sintering parameters also affect the mechanical properties of glass-ceramic scaffolds. Upon immersion in SBF, Fu et al.[1] observed a nanostructured HA layer formed on the surface of the porous scaffolds within seven days, indicating the in vitro bioactivity of the scaffolds. Such HA nanocrystals are found in human bone and are believed to be beneficial for increased cell adhesion, proliferation, and greater tissue growth into the scaffold. In a recent study, Fu et al.[20] fabricated bioactive glass scaffolds with oriented (i.e., columnar and lamellar) microstructures and found that at an equivalent porosity of 55–60%, the columnar scaffolds had a compressive strength of 25 ± 3 MPa, compressive modulus of 1.2 GPa, and pore width of 90–110 lm, compared to values of 10 ± 2 MPa, 0.4 GPa, and 20–30 lm, respectively, for the lamellar scaffolds. The compressive strength of these columnar bioactive glass scaffolds is 1.5 times higher than the highest strength reported for trabecular bone (0.1–16 MPa).

Multi-directional, anisotropic mechanical properties of scaffolds have also been reported by Baino et al.[20] They prepared glass-ceramic fluoro-apatite scaffolds and investigated their mechanical, structural, and bioactive properties upon soaking in simulated body fluid (SBF). The scaffolds had interconnected macropores (23.5–50% porosity) and orthotropic mechanical properties, with compressive strength values in the range of 20–150 MPa. Thick hydroxyapatite layers were formed on the surface of the scaffolds after seven days of immersion in SBF, demonstrating the scaffold's excellent bioactivity. Compressive strength values reported are considerably higher than those found for bioactive glass-ceramic scaffolds with similar porosities (porosity = 54–73%) prepared by the foam replication technique. The latter scaffolds formed from SiO2–P2O5–CaO–MgO–Na2O–K2O bioactive glass had a compressive strength of 1.3–5.4 MPa.

Bioactive Glass Fiber Reinforced Composites (BGFRC)

Calcium phosphate-based bioceramics, such as HA, Ca10(PO4)6-(OH)2, β-tricalcium phosphate (β-TCP), Ca3(PO4)2, and biphasic calcium phosphate (BCP), a mixture of HA and β-TCP composed of the same ions as bone, are the inorganic materials that have received the most attention for bone repair applications. HA resorbs slowly and undergoes little conversion to a bone-like material after implantation. However, β-TCP scaffolds often have lower strength than HA scaffolds, making them challenging to use in the repair of load-bearing bone. BCP with different HA to β-TCP ratios can be used to manipulate the degradation rate and other properties.[18]

Glass fiber reinforced composites (GFRC) have gained significant attention in dentistry due to their favorable mechanical properties and aesthetic benefits. The materials are amorphous, homogeneous, and structurally a three-dimensional network of silica, oxygen, and other randomly arranged atoms. GFRC is known for its superior biomechanical performance, particularly in tension and flexure, which makes it suitable for various dental applications.[30 31] The fibers provide strength and stiffness, while the matrix polymer binds the fibers together, forming a continuous phase around the reinforcement.[32]

GFRC combines the bioactivity of glass or Bioactive Glass Fiber Reinforced Composites (BGFRC) with the mechanical strength of fibers, addressing the brittleness of pure bioactive glass. This makes them suitable for structural bone repair, especially in load-bearing sites.[33] Advances in the mechanical properties of BGFRC, such as enhanced compressive strength and toughness, make them suitable for load-bearing bone repair. For instance, the inclusion of nanofibers in bioactive glass matrices has shown a 94% enhancement in compressive strength.[34]

Combining BGFRC with biodegradable polymers improves the mechanical properties of the composite, making it more suitable for bone applications.[29] For instance, the tensile strength of BG-SiC fiber composites significantly increases with the addition of SiC fibers.[35] Reinforcing polymers with BG fibers significantly improves the initial mechanical properties of the composites, making them more suitable for load-bearing applications. Early clinical trials with fiber-reinforced composite implants in pediatric skull bone reconstruction have shown promising results, with good functional and cosmetic outcomes. Despite improvements, the mechanical properties of some BG composites still need enhancement for more demanding bone applications.[36] In conclusion, bioactive glass fiber-reinforced composite provides structural reinforcement and toughness, which are essential for load-bearing applications. The mechanical properties of BGFRCs can be tailored by adjusting the composition and processing methods, allowing for the creation of materials with specific strengths and degradation rates.[29]

Bioactive Glass Fiber Reinforced Composite for Bone Regeneration

Since the discovery of 45S5 bioactive glasses (Bioglass® 45S5) by Larry L. Hench, who intended to develop a graft material compatible with the human body, when he knew about the host rejection of inert metal and plastic materials used mainly for amputation cases. Bioactive glasses can bond with bone tissue and promote osteointegration by forming a calcium phosphate layer when exposed to physiological fluids.[37] After implantation, bioactive glasses form an amorphous calcium phosphate (ACP) or crystalline hydroxyapatite (HA) phase on their surface, bonding strongly with the surrounding tissue (Figure 3).[8] The material also stimulates gene expression, enhancing osteoinduction,[37] exhibit excellent biocompatibility and controlled degradation rates, which are crucial for bone regeneration.[36] [38]

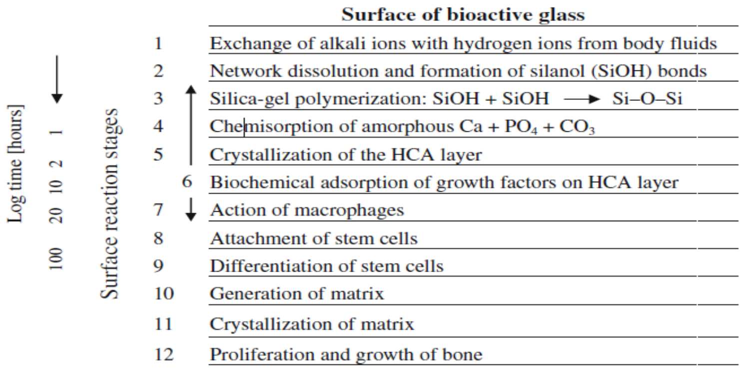

Figure 3. The sequence of interfacial reactions involved in forming a bond between bone and a bioactive glass [20]

Bioactive glass fiber reinforced composites (BGFRC) are increasingly being explored for their potential in bone regeneration due to their unique properties that facilitate interaction with biological tissues. A calcium phosphate layer enhances osteointegration, which is crucial for the stability and functionality of the implant. Bioactive glasses also release ions that activate osteogenic genes and stimulate angiogenesis (formation of new blood vessels), which is crucial for effective bone healing. The ionic release including elements like calcium, phosphate, strontium, and copper, stimulates gene expression and promotes osteoinduction, leading to the differentiation of osteoblasts and the suppression of osteoclast activity.[6 39] This is achieved through the release of therapeutic ions like zinc, which enhance vascularization and bone regeneration.[40 41] The ability to fabricate thin margins (0.8 mm) for implants allows for minimally invasive surgical procedures, reducing patient recovery time and improving outcomes. [42] BGFRC has been successfully used in reconstructing large skull bone defects in pediatric patients, showing good functional and cosmetic outcomes with minimal complications.[42]

Studies have shown that BGFRC supports the adhesion, proliferation, and differentiation of various cell types, including dental pulp stem cells and bone marrow mesenchymal stem cells. These cells adhere to the composite fibers, proliferate, and produce a mineralized matrix, which is essential for bone regeneration.[2,3] In vitro studies demonstrate that BGFRC can form hydroxyapatite on their surfaces when immersed in simulated body fluid (SBF), indicating their bioactivity and potential to support bone tissue formation.[2] The design of BGFRC, including controlled porosity and fiber alignment, plays a significant role in facilitating cell alignment and proliferation, which are essential for restoring both the quality and quantity of bone tissue.

BGFRC can be used to create scaffolds that deliver drugs in a controlled manner, enhancing the healing process and preventing infections.[43] Combining bioactive glass with polymers like chitosan or alginate enhances the mechanical properties and bioactivity of the scaffolds, making them more effective for bone tissue engineering.[44] Bioactive glass is also often combined with polymers like polycaprolactone (PCL), starch-poly-ε-caprolactone (SPCL), and chitosan to form composites that mimic the structure of natural bone.[38] These combinations enhance the flexibility and processability of the composites while maintaining their bioactive properties.

DISCUSSION

Bioactive glass fiber reinforced composites (BGFRC) are emerging as promising materials for bone regeneration due to their unique combination of bioactivity, mechanical strength, and osteoconductive properties. Bioactive glasses can bond with bone tissue and promote osteointegration by forming a calcium phosphate layer when exposed to physiological fluids.[37] The material also stimulates gene expression, enhancing osteoinduction,[37] exhibit excellent biocompatibility and controlled degradation rates, which are crucial for bone regeneration.[36 38]

A key part of bone tissue engineering is the scaffold, a porous structure that, under the right conditions, helps new tissue form by providing a matrix with interconnected porosity and surface chemistry that encourages cell growth, proliferation, and nutrient and metabolic waste transport.[45] Glasses are appealing as scaffold materials because they can be easily altered to change their chemical composition and degradation rate. The ideal scaffold design must balance tissue ingrowth, nutrient transport, and angiogenesis with resorption regulation. The properties of glasses can be tailored by changing their composition or thermal or environmental processing history.[45] This allows for designing glass scaffolds with different degradation rates, which can align with bone growth and remodelling.

The ideal scaffold Also should be biocompatible (not toxic) and should promote cell adhesion and proliferation, exhibit mechanical properties that are comparable to those of the tissue to be replaced after in vitro tissue culture, have a porous three-dimensional (3-D) architecture to allow cell proliferation, vascularization and diffusion of nutrients between the cells seeded within the matrix and the surroundings, degrade at a rate that matches the production of new tissue, into nontoxic products that can be easily resorbed or excreted by the body, be capable of being processed economically into anatomically relevant shapes and dimensions, and be sterilized for clinical use.[45]

Bioactive glass fiber reinforced composites (BGFRC) have shown significant promise in bone tissue engineering because they can be used to create porous scaffolds that support bone regeneration. These scaffolds are designed to be osteoconductive and osteoinductive, promoting new bone formation and vascularization.[36 46] It has been shown to support cell attachment, proliferation, and differentiation, which are crucial for effective bone tissue engineering. It also stimulates osteogenesis and angiogenesis, enhancing the healing process. [36 44] The degradation rate of BGFRC can be modulated to match the rate of new bone formation, ensuring that the scaffold supports the tissue until it is no longer needed. Techniques such as 3D printing and freeze-drying allow for the precise fabrication of BGFRC scaffolds with complex geometries and controlled porosity, which are essential for mimicking the natural bone structure. [34 46]

BGFRC represents a highly promising material for bone tissue engineering due to its enhanced bioactivity, mechanical reinforcement, and biocompatibility. Future research should focus on optimizing composite formulations and exploring clinical applications to further validate their effectiveness in bone regeneration.

CONCLUSION

In conclusion, bioactive glass fiber-reinforced composites interact with biological tissues through chemical bonding, ion release, and structural support, making them highly effective for bone regeneration applications. Their ability to promote osteointegration, support cell proliferation, and enhance mechanical properties positions them as promising materials in the field of bone tissue engineering. Bioactive glass fiber-reinforced composites offer a versatile and effective solution for bone tissue engineering, with applications ranging from scaffolds for bone regeneration to load-bearing implants and drug delivery systems. Their ability to combine bioactivity with enhanced mechanical properties makes them a promising material for future clinical applications. Ongoing research and development are focused on optimizing these materials to overcome current limitations and expand their clinical applications.

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CONFLICT OF INTEREST

All authors declared no conflict of interest in drafting and publishing this article.

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