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# Review of bredigite-based 3D-printed bone scaffolds in biomedical application

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## ABSTRACT

The use of three-dimensional (3D) bio-scaffolds for bone regeneration has gained significant attention due to the increasing demand for effective bone graft substitutes. Among various bioceramics, bredigite ($Ca_7MgSi_4O_{16}$) has emerged as a promising candidate due to its excellent bioactivity, suitable mechanical properties, and controlled biodegradability. Recent advancements in 3D printing technologies have enabled the fabrication of porous bredigite-based scaffolds with tunable structural and biological characteristics, facilitating improved cell adhesion, proliferation, and osteogenic differentiation. This review provides a comprehensive analysis of the latest developments in bredigite-based 3D-printed scaffolds, focusing on their fabrication techniques, mechanical behavior, and potential biomedical applications. Additionally, the key future directions for optimizing these scaffolds are discussed.



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## 1. Introduction

In recent years, bone disorders have become increasingly common due to the aging population, and synthetic biomaterials are increasingly being used to replace bone grafts [1-3]. When bone grafts were first developed to restore damaged bone, they were based on biomechanical properties, but advances in bone tissue engineering have enabled more sophisticated approaches, including scaffolds incorporating drugs, gene delivery systems, and growth factors [4, 5]. The most common bone scaffolds are made from porous, degradable materials that provide mechanical support and allow bone healing and regeneration to occur [6, 7]. Biocompatibility is one of the key requirements for bone scaffolds, which entails support of cellular activity while not causing tissue toxicity [8, 9]. Furthermore, bone scaffolds should closely match the mechanical characteristics of the host bone, taking into account differences between cancellous and cortical bone [10].Scaffolds must also be bioresorbable, allowing bone tissue to form while degrading at a controlled rate. Bone tissue engineering continues to face the challenge of designing scaffolds that have the ideal balance of mechanical properties, bioresorbability, and biocompatibility [11]. As a technology used for preparing bone tissue engineering scaffolds, 3D printing has quickly become widespread. In order to prepare a bone scaffold, CT scans or magnetic resonance imaging are used to obtain images of the repair site in three dimensions, which are then "sliced" by CAD software into layers and imported into a 3D printer. The device stacks the supplies in layers in accordance with the layered data for the bone scaffold [12].It has been shown in prior research certain glasses and ceramics containing Mg, Ca, and Si can be used as biomedical materials due to their high bioactivity [13].

A magnesium-based silicate bioceramic, based on magnesium, has gained attention as a potential bone regeneration material because of its bioactive properties. Among them is Bredigite (BRT, $Ca_7MgSi_4O_{16}$), which is rich in calcium, magnesium, and silicon, essential bioactive elements. Several studies have shown that BRT bioceramics are bio comparable, promote apatite formation, and have good mechanical properties. Additionally, BRT bioceramics have the ability to influence stem cell behavior by releasing a range of ions [14-16]. Three-dimensional (3D) printing can also be used to fabricate personalized BRT scaffolds. A unique advantage of 3D printing in regenerative medicine is its ability to fabricate rapidly, precisely, and controllably[17]. Bioceramic materials and 3D printing technology may offer a promising alternative to onlay grafts, thus facilitating the use of bioceramic materials. A biomaterial's ability to modulate bone regeneration has been identified as osteoimmunomodulation, based on the convergence of osteoimmunology and immunomodulation [18]. A porous scaffold prepared using 3D printing technology with an appropriate biodegradability and biocompatibility is typically used as a matrix material to support cells adhering and growing in bone defect areas, as well as regenerating tissues and restoring organ function by stimulating tissue regeneration [19-21].

In this review, we aim to investigate the current advancements in bredigite-based 3D-printed bone scaffolds, focusing on their design, fabrication methods, and potential applications in biomedical fields. Our innovation lies in synthesizing recent research findings to provide a holistic understanding of how bredigite scaffolds can enhance bone regeneration processes. We will also highlight the unique properties of bredigite that distinguish it from other materials, such as its superior bioactivity and mechanical performance, and discuss the implications of these characteristics for future applications.

## 2. Properties of bredigite

### *2.1. Chemical composition*

A calcium-magnesium orthosilicate ($Ca_7MgSi_4O_{16}$) is formed when calcium-rich continental and magnesium-rich mantle material interact under certain pressure-temperature conditions. Identified at Scawt Hill, Northern Ireland, its composition, phase stability, and structure have been studied extensively. There are minor Ca-Mg substitutions in Bredigite, but no significant Ba. As a result of limitations in single-crystal X-ray diffraction data, its structure remains unresolved up to 1372°C. Ba's larger ionic radius hindered the study of Ba-bearing syntheses, leading to different proposed structures for phases with Ba [22].

Bredigite contains essential elements for bone regeneration, such as calcium (Ca), magnesium (Mg), and silicon (Si). This chemical composition makes bredigite a valuable bioactive ceramic [14, 19]. The superior biocompatibility, bioactivity, and mechanical properties of magnesium-containing silicate ceramics make them ideal for bone tissue engineering (BTE). In addition to promoting bone regeneration, these ceramics release specific ions like magnesium and silicon. Among this group of bioactive ceramics, $Ca_7MgSi_4O_{16}$ exhibits these properties, making it an excellent candidate for BTE applications.

### *2.2. Mechanical properties*

Bone scaffolds should mimic the mechanical properties of host bone in order to ensure effective load transfer and support. A cortical bone's Young's modulus is 15–20 GPa, while a cancellous bone's modulus is 0.1–2 GPa. It is challenging to design an ideal scaffold because the compressive strength ranges between 100–200 MPa for cortical bone and 2–20 MPa for cancellous bone [6].

Recent research shows that magnesium-containing silicate ceramics such as bredigite have superior bioactivity, biocompatibility, and mechanical properties compared to hydroxyapatite (HA). As a result of a polymer sponge approach, bredigite scaffolds demonstrate a 90% porosity, large pore sizes, good degradation rates, and satisfactory mechanical properties. Apatite-mineralization ability and mechanical properties of bredigite bioceramics contribute to their success in bone regeneration applications [14, 19].

### *2.3. Biocompatibility*

According to literature reports, $CaO\text{-}SiO_2$ containing glasses and glass-ceramics have excellent bioactivity and bond well with living bones and soft tissues. The calcium and silicate ions influence apatite nucleation and bone-like HA production as well as osteoblast cell metabolism and bone bonding. In addition to magnesium, magnesium has been suggested as a growth factor for osteoblasts. With an effect comparable to insulin (a known growth

factor for osteoblasts), it stimulates osteoblast proliferation directly [23]. Bredigite a ceramic belonging to the ternary system $CaO$-$SiO_2$-$MgO$, has been regarded as a potential biomaterial for artificial bone. Wu et al. [24] demonstrated that bredigite has improved mechanical strength as compared to HA and wollastonite ceramics based on studies examining degradation, bioactivity, and cytocompatibility. Moreover, bredigite forms apatite when dissolving in simulated body fluid (SBF), and its ions stimulate osteoblast proliferation, which makes it an ideal candidate for bone regeneration [23]. It is crucial for bone scaffolds to be biocompatible to ensure that they will support cellular processes, such as adhesion, proliferation, and extracellular matrix formation without causing toxicity to the host [6].

Bredigite is one of the most highly biocompatible silicate ceramics with demonstrated osteoconductive properties, and it contains magnesium. Furthermore, bredigite bioceramics are well known for their ability to stimulate bone formation through biomolecular signaling and recruiting progenitor cells, which makes them ideal for BTE applications [6, 19].

### *2.4. Bioactivity*

A key characteristic of bredigite is that it releases bioactive ions, such as magnesium and silicon, which stimulate bone regeneration and regulate stem cell behavior. Furthermore, Bredigite scaffolds exhibit controlled biodegradability, which allows them to gradually resorb in vivo while creating space for new bone [14].

Bredigite's bioactive properties allow it to influence the immune response and encourage osteogenesis by interacting with host cells like macrophages, which are essential in the regeneration process. These characteristics render bredigite an exceptionally effective solution for tackling clinical issues associated with critical-sized bone defects [25].

## 3. 3D Printing techniques for bone scaffolds

### *3.1. Overview of 3D printing technologies*

An emerging digital manufacturing technique called 3D printing can quickly prepare and precisely manipulate structural and morphological characteristics to target regenerative applications. A porous scaffold produced by 3D printing with controlled biodegradability and good biocompatibility is usually used as a matrix material for supporting the attachment and growth of critical cells in the area of bone defects, as well as regeneration of target tissues [19].

Among the essential forms of bioprinting, 3D bioprinting is a method of assembling biomaterials by layer-by-layer deposition with computer assistance. It is widely used in tissue engineering, regenerative medicine, pharmacokinetics, and other biological studies to construct living tissues and organs. Biomedical scaffolds can be shaped, sized, and porosity adjusted to adjust the interactions between cells and materials [26].

Researchers have found that cell-material interaction plays a major role in tissue engineering, allowing cells to migrate, proliferate, and differentiate. Manufacturing scaffolds should take into consideration the size, design, and interconnectivity of its pores. A scaffold's architecture can be more controlled with 3D printing, since the printed object corresponds to the model developed. Moreover, the model and printing processes are very easy, so researchers can run many experiments quickly. By making scaffolds with a variety of designs and pore sizes, we can study how geometry and architecture affect cellular response and mechanical behavior [27].

Ceramic powders, metal powders, and other powders are used to shape in 3DP technology. Printing a part's cross-section using an adhesive, such as silicone, instead of sintering it together. Adhesive-bonded parts are, however, weak and require post-processing [28]. Nevertheless, adhesive-bonded parts have limited strength, which requires post-processing. It involves bonding the uppermost layer, descending the forming cylinder (corresponding to layer thickness 0.013–0.1 mm), rising the powder supplying cylinder, pushing out powder, and spreading the powder with the spreading roller. Powders are pressed and packed. According to the forming data in the section below, the computer can control the spray head to spray the adhesive construction layer selectively. By doing so, the powder is finally bonded three-dimensionally. There are a number of advantages to using 3DP technology, including the ability to use a wide variety of raw materials, the smooth scaffold surface, and the ability to use cells directly on the scaffold. Cells, growth factors, and proteins can be printed directly [12].

### *3.2. Comparison of techniques of 3D printing*

A variety of additive manufacturing methods have revolutionized the production of bone scaffolds for tissue engineering. Among them are stereolithography (SLA), selective laser sintering (SLS), fused deposition modelling (FDM), and electron beam melting (EBM) [29, 30].

#### *3.2.1. Fused deposition modeling (FDM)*

A Fusion Deposition Model, also called a Fused Lamination Model, involves the melting of filamentous hot-melt materials [31]. A three-dimensional nozzle selectively covers the workbench material based on its cross-sectional structure. After rapidly cooling, a cross-sectional layer forms. Once one layer has been formed, the machine table descends (that is, the layer thickness) and forms the next layer. Heat-shrinkable polymers are usually used in fusion lamination, such as ABS, polyamides, polyester, polycarbonate, polyethylene, and polypropylene [32]. There are many advantages of FDM in scaffold fabrication, including low energy consumption, durability, low temperature, good accuracy, low cost, safe and efficient operating technique, and the ability to make thermoplastic items with complex geometries [33].

#### *3.2.2. Selective laser sintering (SLS)*

The 3D microstructure of bone scaffolds was important for reproduction and cell adhesion. As a result of the introduction of 3D measurement techniques in bone research, it became possible to capture the real architecture of bone scaffolds without assumptions about their type [34]. A femur specimen from a canine was reconstructed and analyzed, and indices of 3D structure were compared. Direct 3D analysis revealed significant differences between two scaffolds in structural characteristics. Scaffolds prepared by FDM showed a denser and plate structure, lower porosity, thinner trabecular bone than scaffolds prepared by SLS. As opposed to the rod-shaped scaffolds prepared by SLS, which resembled real canine femur specimens and had a higher interconnectivity, scaffolds prepared by SLS had a stronger interconnection [35].

Scaffolds are created by sequentially fusing regions of powder bed, layer by layer, via a computer-controlled scanning laser beam. There are many benefits to using SLS to fabricate tissue engineering scaffolds that other SFF methods may lack. The process of layer-by-layer additive fabrication in SLS allows

scaffolds to have complex internal and external geometry. The second advantage of using powdered biomaterials to fabricate scaffolds is that virtually any powdered biomaterial that does not decompose under a laser beam can be used. Furthermore, SLS can be used to create intricate biphasic scaffold geometries without the use of organic solvents, and filaments aren't required (like in FDM). Multiple materials can be incorporated, and it is fast and cost-effective, making it a good technology for tissue engineering scaffolds [36].

A study investigated the use of SLS to manufacture porous scaffolds for applications in bone tissue engineering. This technique, like most SFF techniques, uses additive fabrication to produce models and prototype parts quickly based on 3D CAD models, 3D digitizing data from the system, computed tomography, and magnetic resonance imaging. In this technique, layers of the physical object are manufactured one on top of another, transforming the 3D problem into a bi-dimensional one. A layer-by-layer construction of objects is based on CAD information exported in the industry-standard triangulation language (STL) [37].

The majority of biocompatible polymers comply with SLS manufacturing techniques. Bioceramics and biopolymers, such as poly(e-caprolactone), were successfully combined in SLS to fabricate complex scaffolds for bone tissue engineering [36].

Furthermore, SLS-fabricated scaffolds can be modified to incorporate growth factors like vascular endothelial growth factor (VEGF), enhancing blood vessel formation and bone regeneration in animal models. These advancements in SLS technology offer a versatile approach to creating biomimetic scaffolds with tailored properties for bone tissue engineering applications.

### *3.2.3. Stereolithography (SLA)*

Photosensitive resin is a crucial raw material used in the process of stereolithography, an advanced 3D printing technique. In this process, a high-precision laser is meticulously controlled by a computer system [38]. The computer scans each individual layered section of the object being fabricated, moving point by point to precisely expose the liquid photosensitive resin. In order to create a thin layer of the amount, a thin resin layer is scanned and cured by photopolymerization. After the first layer has been cured, the worktable moves down one layer. The previously cured resin is then reapplied with a new layer of liquid resin until a solid model is obtained in three dimensions. A stereolithography printer can print high-resolution objects with complex structures in a short timeframe and with a varied range of products, as well as high-resolution items at a variety of sizes. Nevertheless, it has drawbacks, including limited printable materials, which can be toxic, and the need to clean impurities after printing [39].

It is difficult to find biocompatible resins that have good processing properties for SLA. Additional challenges include photoinitiators and radicals, as well as entrapment of unreacted monomers and residuals. These impurities may impair bone regeneration in vivo and induce cytotoxicity by altering bone matrix synthesis. Nevertheless, it has been demonstrated both in vitro and in vivo that adding HA to resin produces scaffolds better suited for bone regeneration due to increased osteoblast attachment [40].

### *3.2.4. Electron beam melting (EBM)*

Metal powder or plastic bondable materials are used in 3D printing to construct objects layer by layer. An important aspect of 3D printing technology is electron beam melting (EBMT), which enables the creation of an interface necessary for bone growth support [41]. A study by Zhang et al. [42] describes the application of EBM in the preparation of a titanium trabecular bone reconstruction system that was applied for the treatment of early femoral head necrosis. Long-term follow-up results indicated that patients' hip joints functioned well after surgery.

Since EBM is reproducible, it is an excellent method for preparing porous materials. In a study by Palmquist et al, [43] porous implants were prepared with electron beam melting and implanted in sheep's bilateral femurs and backs. Upon removal of the implants after 26 weeks, it was demonstrated to have outstanding long-term soft tissue biocompatibility and extreme bone integration.

## 4. Design considerations for bredigite scaffolds

### *4.1. Synthesis of bredigite*

### *4.1.1. Sol-gel*

The sol-gel method can be used to manufacture Bredigite powders by combining TEOS, magnesium nitrate hexahydrate, and calcium nitrate tetrahydrate in a specific ratio. The process involves hydrolysis, reaction, drying, and calcination steps. The resulting powders should be dispersed in a PVA solution to form a slurry, which is used to coat a polyurethane foam template [44].

Pure $Ca_7MgSi_4O_{16}$ powders are produced using the sol-gel technique. These bredigite powders consist of polycrystalline particles ranging from 1 to 10 μm in size. The in vitro bioactivity of the bredigite powders is assessed by examining their ability to form HAp in SBF and analyzing how the ionic products from bredigite dissolution affect osteoblast proliferation. The findings revealed that bredigite promotes the formation of nanocrystalline HAp after being immersed in SBF for 10 days. Additionally, the Ca, Si, and Mg ions released from bredigite dissolution at specific concentration levels enhance osteoblast proliferation. Our research suggests that bredigite is bioactive and could be utilized in the development of new biomaterials [13]. Maryam Rahmati et al. [45] studied the synthesis of single-phase bredigite nanopowder using a modified sol–gel method, resulting in particle sizes of 38–48 nm. There in vitro bioactivity tests showed that this nanopowder developed a bone-like apatite layer faster than micro-sized bredigite. After 3 days of soaking, they observed numerous uniform worm-like apatite crystallites smaller than 100 nm on the surface, with additional tiny apatite sediments forming after 28 days. The researchers suggested that apatite formation in SBF occurs through the dissolution of Ca (II) ions from bioceramics, followed by H+ ion exchange, which leads to silanol (Si-OH-) formation and the attraction of calcium ions to negative phosphate ions in the fluid.

Similarly, Wu et al. [15] prepared a new $Ca_7MgSi_4O_{16}$ by sintering sol–gel-derived bredigite powder compacts for 8 hours at 1350 °C. A certain concentration range of bredigite dissolution products significantly increased cell growth. Furthermore, osteoblasts adhered well to bredigite ceramics and proliferated well.

### *4.1.2. The space holder technique*

There have been several reports on the use of volatile or solute materials as space holders, such as carbamide, starch, ammonium bicarbonate, or sodium chloride [46].

A nanostructured bredigite scaffold was fabricated using a space holder technique for bone repair and restoration by Ghomi et al. [47] This study showed that a highly interconnected porous scaffold with approximately 86% total porosity, pores ranging

from 400 to 600 μm, and a compressive strength of 1.1 MPa was successfully fabricated. As a result of its nanosize and porosity, the scaffold provides a large specific surface area, making it a good candidate for bone regeneration during tissue engineering.

### *4.1.3. Electrospinning technique*

Nanofibrous scaffolds are fabricated using different techniques, but electrospinning is the most widely used because of its ease of use and relatively low cost [48].

The use of electrospinning techniques to produce bredigite nanoparticles was described by Kouhi et al. [48] A pre-treatment of bredigite was found to improve nanoparticle dispersion. By incorporating T-BR nanoparticles, the PHBV nanofibrous scaffolds demonstrated remarkable improvements in mechanical properties. The results also demonstrated that adding BR or T-BR nanoparticles significantly altered the bioactivity and biodegradability of the scaffolds. The researchers showed that T-BR nanoparticles could improve the mechanical performance and bioactivity of PHBV nanofibers when incorporated into them.

## *4.2. Bredigite-based 3D-printed bone scaffolds*

For fabricating bone tissue-engineered scaffolds, 3D printing is a fast prototyping method that can be used [49]. A triply periodic surface model construction (TPMS) was used to investigate the mechanical, degradation, and biologic properties of bredigite, as shown in Fig. 1. With the same porosity, TPMS scaffolds performed significantly better than open-rod scaffolds. TPMS scaffolds have better protein adsorption abilities than open-rod scaffolds, cells adsorb more readily on their surfaces, and the proliferation rate is higher in the TPMS model than the open-ended rod model based on biological properties [50].

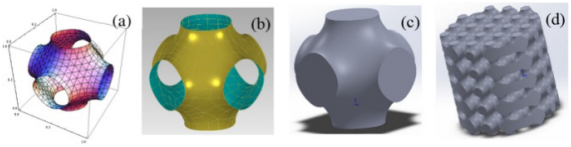


**Fig. 1.** Scaffold model design process. Models of (a) single-cell curved surfaces, (b) single-cell solid surfaces, and (c) single-cell TPMS bone surfaces [51].

In the study, Xuan et al. [25] developed and investigated bredigite (BRT) bioceramic scaffolds with two different structures: The first one (BRT-O) has an ordered arrangement and the second one (BRT-R) has a random morphology. BRT bioceramic powder containing Si, Mg, and Ca, $Ca_7MgSi_4O_{16}$ was produced using the sol-gel method process (Fig. 2). Based on the results, the BRT-O scaffolds enhanced osteogenic differentiation and migration of bone marrow-derived mesenchymal stem cells (BMSCs) in vitro by polarizing macrophages towards the pro-regenerative M2 phenotype. The BRT-O scaffolds promoted bone regeneration in rabbits and increased CD68+CD206+ macrophage polarization in vivo. Furthermore, BRT-O scaffolds promoted osteogenic difference of bone core mesenchymal stem cells (BMSC) in a rat model, correlating with increased macrophage infiltration and osteogenesis-related marker expression.

## *4.3. Integration of bioactive components*

The integration of bioactive components with bredigite has been a focus of recent research in regenerative medicine, particularly for orthopedic and dental applications [52]. Several approaches have been developed to enhance the functional properties of bredigite-based materials. Khandan et al. [53] conducted a study to investigate the mechanical and biological properties of bredigite-magnetite ($Ca_7MgSi_4O_{16}$-$Fe_3O_4$) nanocomposites, adjusting the magnetite content to 0, 10, 20, and 30 wt%.

The researchers fabricated cylindrical scaffolds using a 3D printer. The results demonstrated that the characteristics of the scaffolds were highly dependent on the concentration of magnetite. The sample with 30 wt% magnetite showed the best performance, with a fracture toughness of 2.69 MPa·$m^{1/2}$ and a Young's modulus of 29 GPa. Additionally, an increase in bredigite content resulted in a rise in pH levels in simulated body fluid (SBF), due to the interaction of $Ca^{2+}$ ions present on the scaffold's surface. The sample with 10 wt% magnetite exhibited a rough, irregular texture, while the one containing 30 wt% magnetite had a smooth, flat surface interspersed with coarse projections. In terms of biodegradation, it was found that pure bredigite degraded more quickly than the 20 wt% magnetite sample, a difference attributed to the dissolution of Si ions in the absence of magnetite.

In Fe-Pd alloys, metal matrix composites (MMCs) with bioceramics where the ceramic phase composition and distribution can be controlled could improve both biocompatibility and bioactivity [54, 55]. A combination of these discoveries has led to the development of Fe-Pd-bredigite biocomposites with superior bioactivity, excellent biodegradation, and favorable biocompatibility. A study examines the degradation of Fe-Pd-bredigite biocomposites in SBF, illustrated by corrosion in Fig. 3. Corrosion starts at the Fe matrix near Pd-rich intermetallic particles (IMPs) at grain boundaries, forming micro-galvanic cells due to Pd's high corrosion potential.

This oxidizes the Fe matrix to ferrous ions, while electrons reduce oxygen at Pd-rich IMPs, leading to local alkalization and forming ferrous and ferric hydroxides. Bredigite, a biodegradable ceramic, creates added corrosion sites, speeding up degradation compared to bioceramics like hydroxyapatite and diopside. It is faster degradation forms corrosion pits, exposing more Fe matrix and enhancing corrosion. Interfacial defects between bredigite and the Fe matrix allow corrosion medium invasion, increasing the overall rate. The findings emphasize bredigite's crucial role in boosting the corrosion behavior of metallic matrices in biocomposites [56].

Bredigite, when combined with other materials, such as β-tricalcium phosphate and ciprofloxacin, forms effective composite scaffolds for bone treatment applications. These composites leverage the unique properties of bredigite to enhance overall performance in biomedical applications [57].

A research by Rezaei Shahraki et al. [58] examined the creation of gelatin/polylactic acid/bredigite composite scaffolds for bone tissue regeneration via freeze-drying. The addition of 5 wt% bredigite raised the compressive strength of the 1Gel3PLA scaffold to over 0.57 MPa. While reducing the Gel:PLA ratio from 1:3 to 1:2 increased porosity to 71.4%, the addition of bredigite generally decreased porosity. In vitro tests in simulated body fluid (SBF) demonstrated apatite layer formation, and MTT assays showed that 5 wt% bredigite boosted cell viability to over 90%. Human osteoblastic (MG-63) cells on these scaffolds exhibited enhanced cell proliferation and mineral deposition. The findings suggest that Gel-PLA scaffolds with 5 wt% bredigite hold promise as materials for bone tissue regeneration.

Bredigite/titanium dioxide composite scaffolds were developed using the gelcasting method with chitosan (Ch) coatings to enhance properties. Adding titanium dioxide increased compressive strength (0.299 to 0.687 MPa) and reduced porosity.

Chitosan coating further improved compressive strength (0.585 to 2.339 MPa) and decreased porosity (83% to 63%). Antibacterial tests showed inhibition zones of 22 mm against Escherichia coli and 29 mm against Staphylococcus aureus.

MG63 cell tests confirmed no toxicity and supported cell growth, proliferation, and adhesion. These results indicate the scaffold's strong potential for bone tissue engineering [59]. In another study compared 3D-printed bredigite (Bre) scaffolds with PDA and PDA-fullerol modifications (Bre@PDA and Bre@PDA-Ful). In Fig. 4 SEM, the analysis showed that all scaffolds had a uniform pore structure, with no significant morphological differences due to the nanoscale coatings. XPS confirmed successful surface modification, with the Bre@PDA group showing a higher (N1s) peak due to amine and amide bonds, while fullerol slightly reduced this peak in the Bre@PDA-Ful group. Mechanical testing showed no significant difference in compressive strength among the groups. However, the modified scaffolds (Bre@PDA and Bre@PDA-Ful) had improved hydrophilicity, as indicated by lower water contact angles. All scaffolds showed similar degradation rates (~30%) over five weeks, with a gradual pH increase that benefits cell proliferation and differentiation. Overall, the PDA and PDA-fullerol modifications enhanced surface properties without compromising mechanical strength, making the composite scaffolds more suitable for bone tissue engineering than pure bredigite scaffolds [60].

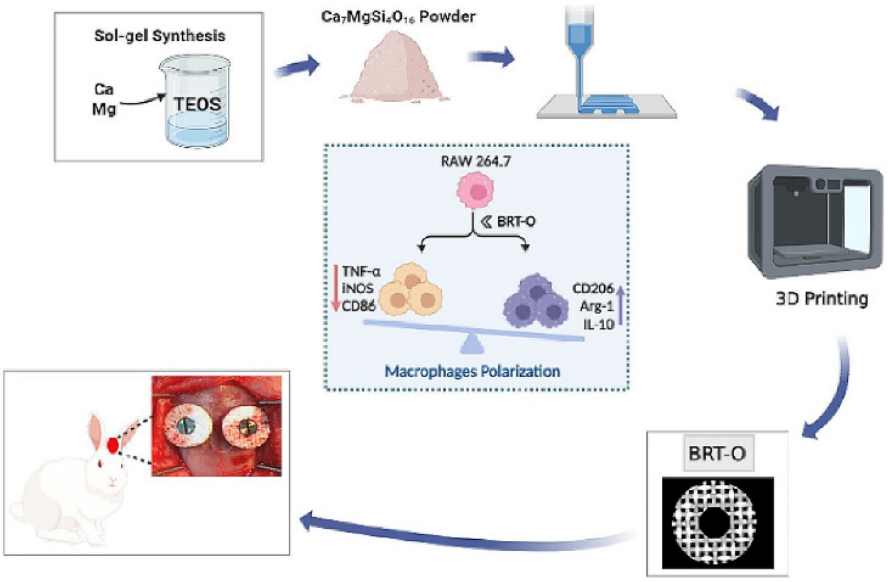


**Fig. 2.** Perpetration of BRT bioceramic [25].

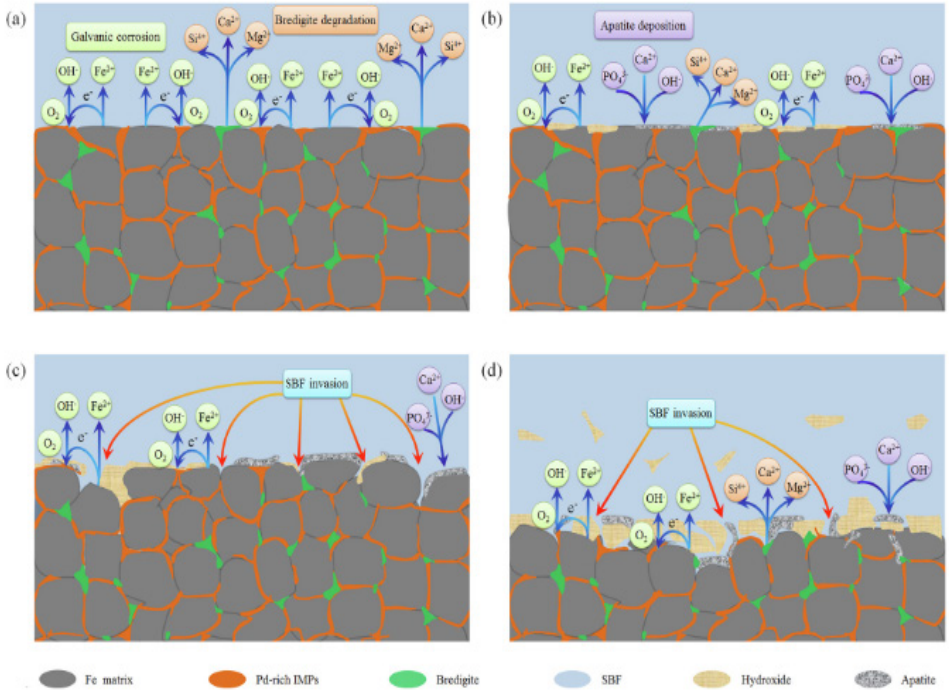


**Fig. 3.** An illustration of how Fe-Pd-bredigite biocomposites degrade: (a) galvanic corrosion occurs between Pd-rich IMPs and the Fe matrix, followed by degradation of bredigite; (b) hydroxides and apatite deposition; (c) SBF infiltration through corrosion pits caused by bredigite degradation; (d) exposing new Fe matrix to SBF, resulting in ongoing degradation [56].

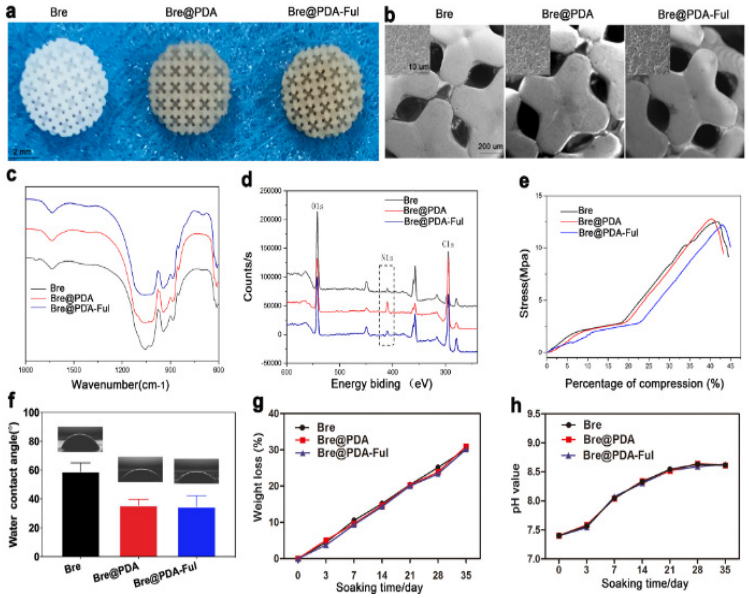


**Fig. 4.** Characterization a) Digital images showcasing the bredigite (Bre) scaffold, the PDA-modified bredigite (Bre@PDA) scaffold, and the fullerol/PDA modified bredigite (Bre@PDA-Ful) scaffold. b) SEM representations of the scaffolds. c) FTIR spectra corresponding to the scaffolds. d) XPS spectra of the scaffolds. e) Stress-compression curves recorded for the scaffolds. f) Water contact angle measurements for the scaffolds. g) Degradation curves of the scaffolds. h) pH levels of the medium after degradation [60].

## 5. Biomedical applications of bredigite-based scaffolds

Bredigite-based scaffolds are emerging as a versatile and innovative solution in the field of biomedical engineering, particularly in areas such as bone tissue engineering, dental applications, bone regeneration, and regenerative medicine. Their unique properties make them suitable for various applications designed to enhance healing and regeneration processes in the body, as shown in Fig. 5.

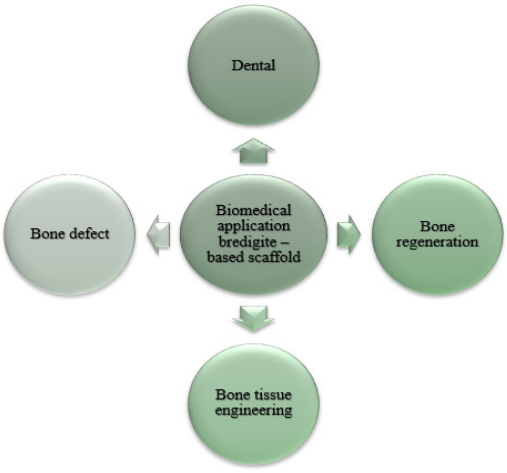


**Fig. 5.** Biomedical applications of bredigite-based scaffolds.

### 5.1. Bone tissue engineering

Biological ceramics have a wide range of applications in the biomedical field. This medical substance is biocompatible and does not form adjacent fibrous tissue, allowing it to be utilized safely within the body [61]. The mechanical properties and bioactivity of silicate bioceramics (e.g., calcium-magnesium-silicon) make them more desirable than phosphate bioceramics (e.g., calcium phosphates) in TE applications. It has been shown that Ca-Mg-Si ceramics enhance bioactivity, biocompatibility, mechanical properties, and crystallinity in bone TE scaffolds. Bredigite has some suitable mechanical properties as well as biocompatibility and osteogenic characteristics, there are still definite aspects in which further enhancement can be made to these bioceramics [22]. In a study by Dongxue Liu et al. [62] bone tissue engineering scaffolds have been increasingly utilized to repair bone defects. The scaffold was fabricated using a Sol-gel method combined with 3D printing, as illustrated in Fig. 6. A TPMS model structure was used to investigate the mechanical, degradation, and biological stuffs of bredigite. A pressure test showed that TPMS scaffolds performed expressively better than open-rod scaffolds with the same porosity. Furthermore, the TPMS model exhibited better protein adsorption ability and cell adhesion, with higher cell proliferation numbers and rates compared to the open-ended rod model.

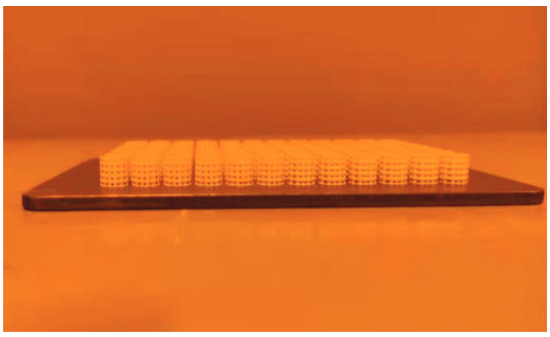

**Fig. 6.** Bredigite-based scaffold for bone tissue engineering [62].

### 5.2. Bone regeneration

Bone tissue engineering has introduced various biomaterials with key properties like biocompatibility, osteogenesis, osteoconduction, and osteoinduction [63]. These scaffolds offer a potential alternative to onlay bone grafts, although most research focuses on bone defect models rather than onlay grafts. Bioceramic scaffolds with hierarchical designs can replicate natural bone

structures and are gaining attention. Bredigite (BRT, $Ca_7MgSi_4O_{16}$), a ceramic biomaterial containing calcium, silicon, and magnesium oxides, has shown strong potential for promoting bone growth and blood vessel formation [64]. Furthermore, 3D printing allows the creation of customized BRT scaffolds for advanced bone tissue engineering [18]. Flexible polymeric sponges provide a novel template for highly porous hydroxyapatite scaffolds [65].

A study designed three-dimensional HA-$Ca_7MgSi_4O_{16}$ composite scaffolds with varying amounts of bredigite (0, 5, 10, and 15 wt%) using the space holder approach to enhance the mechanical weakness of pure HA scaffolds. These scaffolds featured pore sizes ranging from 220 to 310 μm, porosity between 63.1% and 75.9%, and a density of 1.1 ± 0.04 g/cm³. As the bredigite content increased, micropore size decreased, sintering improved, and mechanical properties, such as compressive strength and modulus, significantly increased, especially at 15 wt%. The HA-15 wt% bredigite scaffold demonstrated superior bioactivity, biodegradability, and cell growth compared to pure HA in MTT assays, highlighting its potential for bone regeneration applications [14].

### *5.3. Bone defect*

An important aspect of clinical practice is repairing bone defects that are of critical size as a result of trauma or tumors; artificial scaffolds appeared to offer better outcomes in this particular case [66]. In addition to being a promising candidate for bone tissue engineering, $Ca_7MgSi_4O_{16}$) bioceramic exhibits excellent physicochemical properties as well as biological activity [19].

As a treatment for bone infections, a study developed nanostructured bredigite (Bre) –amoxicillin (AMX) scaffolds using space holders. In addition to high porosity (80–82%), the scaffolds demonstrated controlled antibiotic release and high compressive strength. Using Bre– (3-10%) AMX scaffolds, Staphylococcus aureus and Escherichia coli bacteria were effectively killed with increased antibacterial activity. Using the scaffolds, 20% of the drug was released over 8 hours, followed by sustained drug release, making them ideal for preventing infection. Bre–(3–5%)AMX scaffolds showed tremendous mechanical properties, sterile activity, and no cytotoxicity, making them a promising alternative for bone infection treatment [67].

### *5.4. Dental applications*

The application of bredigite-based 3D-printed bone scaffolds in dental procedures presents a promising avenue for advancing restorative treatments, particularly in bone tissue engineering [68]. Bredigite, a calcium-magnesium silicate, has demonstrated biocompatibility and bioactive properties beneficial for bone regeneration.

The porous structure of 3D-printed bredigite scaffolds allows for improved nutrient diffusion, cell infiltration, and vascularization, which are crucial for the successful integration and functionality of dental implants and other reconstructive procedures [69].

A study developed bredigite scaffolds using coprecipitation and polymeric foam methods, followed by fluoride doping and PLGA coating. These treatments improved pore structure, enhanced apatite formation, increased compressive strength, and boosted cell viability, with the combined approach showing the greatest effect [70]. Another research examined the effects of bredigite and β-TCP extracts on human dental pulp cells (hDPCs). Bredigite extracts increased cell growth, proliferation, and expression of pluripotency-related genes (Stro1, Oct4, Sox2), while also enhancing multilineage differentiation, unlike β-TCP [71].

## 6. Conclusion

The review of bredigite-based 3D-printed bone scaffolds highlights the significant potential of bredigite as a biocompatible and bioactive material in the field of biomedical applications. Bredigite possesses unique properties, such as its ability to support cell proliferation, promote osteoconductivity, and facilitate the gradual release of bioactive ions, make it an excellent candidate for creating scaffolds that mimic the natural bone environment. The advancements in 3D printing technology further enhance the customization and precision of scaffold design, allowing for tailored solutions that address specific clinical needs. Moreover, the integration of bredigite with other materials and the exploration of various printing techniques have shown promising results in improving the mechanical properties and biological performance of scaffolds.

Looking ahead, several key areas warrant further investigation. Continued research into the chemical and physical modification of bredigite to enhance its mechanical properties and degradation rates will be crucial. Exploring composite materials that combine bredigite with polymers or other bioactive ceramics could lead to improved scaffold performance. While in vitro studies have demonstrated the potential of bredigite-based scaffolds, comprehensive in vivo studies are necessary to evaluate their long-term biocompatibility, integration with host tissues, and functional outcomes in real biological environments.

The development of patient-specific scaffolds using advanced 3D printing techniques could revolutionize bone repair strategies. Research should focus on integrating patient-specific data, such as imaging and biomechanical properties, to create customized scaffolds. Enhancing the vascularization of 3D-printed scaffolds is essential for successful bone regeneration. Future studies should explore the incorporation of growth factors, stem cells, or bioactive molecules that promote angiogenesis within bredigite scaffolds.

## Author contributions

**Fatemeh Sharif Jafari:** Conceptualization, Manuscript drafting, writing—review and editing. **Aramis Moradi:** Manuscript drafting, writing—review and editing. **Reyhaneh Nasr Azadani:** Literature search, data collection, and writing—original draft preparation. **Sana Radmehr:** Manuscript drafting and writing—review and editing. **Saeid Gholizadeh:** Manuscript revision and writing—review and editing. **Aida Mahdian:** Manuscript editing, reference management, and writing—review and editing.

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The authors declare no conflict of interest.

## Data availability

No data is available.

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