Dean&Francis

ISSN 2959-409X

MS003542

A Study of Bioactive Antimicrobial Glass-Ceramics' Composition, Synthesis, Mechanisms, and Biomedical Applications

Shuhan Yao

Dalian No.8 High School,Dalian 116021,China

Abstract:

Bioactive and antimicrobial glass-ceramics have garnered significant interest due to their distinctive attributes, high bioactivity, supreme mechanical strength, and effective antibacterial characteristics. These materials provide extensive application potential in orthopedics and dentistry, mainly where infection control and tissue integration are paramount. The bioactivity of glass ceramics facilitates their integration with human tissues and concurrently suppresses microbial proliferation via processes including ion release, diminishing the likelihood of implant-associated infections. This study seeks to elucidate the creation and implementation of bioactive antimicrobial glass ceramics, emphasizing design concepts, synthesis techniques, antibacterial mechanisms, and biological features of these materials. Specifically, how enhancements in the manufacturing process influence the physical and chemical characteristics of the materials, consequently augmenting their antibacterial efficacy and biocompatibility. Furthermore, the prospective uses of these materials in the biomedical domain, such as their use in bone regeneration, dental implants, and healing wound dressings, will be examined, along with anticipated future development trajectories. As this research continues, bioactive antimicrobial glass-ceramics are anticipated to provide innovative choices for improving the medical safety and biological efficacy of medical implants, therefore improving biomaterial technology.

Keywords: Bioactive glass-ceramics; antibacterial properties; ion release control

1. Introduction

The appearance of antibiotic-resistant bacteria poses a substantial challenge to universal healthcare, necessitating prompt advancement of novel strategies for the prevention and cure of infection.[1-3] The accelerating necessity for bio-materials that improve bone regeneration has facilitated advancement in biological and multi-functional composites science. [4, 5] Owing to extensive utilization and potential promise in implanting areas, antibacterial and bioactive glass-ceramics have attracted significant interest in recent years. [6] These prevailing materials provide a representative amalgamation of diverse beneficial effects, including bone-bonding ability and antibacterial characteristics, rendering them especially appropriate for biomedical implants,[7] bone repair,[8] and surgical instruments' coatings [9].

Distinguished by the establishment of a robust link with bone tissue via bioactivity, Bioactive glass-ceramics functioned by the creation of hydroxyapatite (one typical mineral existing inside real bone with superficial exposure to physiological fluids.[10] This representative property facilitates implants' incorporation into the host bone, which is necessary for successful orthopedic and dental applications with long-serving times. [11] Compared to ordinary materials, bioactive glass-ceramics served not only as structural scaffolds but also actively engaged in the healing process by enhancing osteogenesis and providing a favorable surrounding for bone cell proliferation.[12] These features enable them to serve as ideal candidates for enhancing patient recovery after bone damage and degeneration. Besides their bone-regenerative features, several glass ceramics may be designed to exhibit inherent antibacterial characteristics, hence mitigating the risk of post-surgical infections. Antibacterial methodologies of bioceramic-based glass-ceramics are shown in Figure 1. This figure illustrates the antibacterial mechanism of bioceramic-based scaffolds, including drug-induced method, ion-mediated strategy, and physical stimulation strategy, as well as their combination. The drug-induced methodology consisted of the introduction of antibiotics within the scaffold structures, enabling a well-regulated and long-term sustained release to generate effective antibacterial effects. The ion-mediated methodology utilizes the release of antibacterial ions, such as Zn^{2+}, Cu^{2+}, and Ag^{+}, to suppress bacterial growth and DNA replication by breaking cell walls and inhibiting their metabolic activities. [13] Physical stimulus methods functioned by electrical charges under applied pressure, therefore inhibiting bacterial physiological functions.

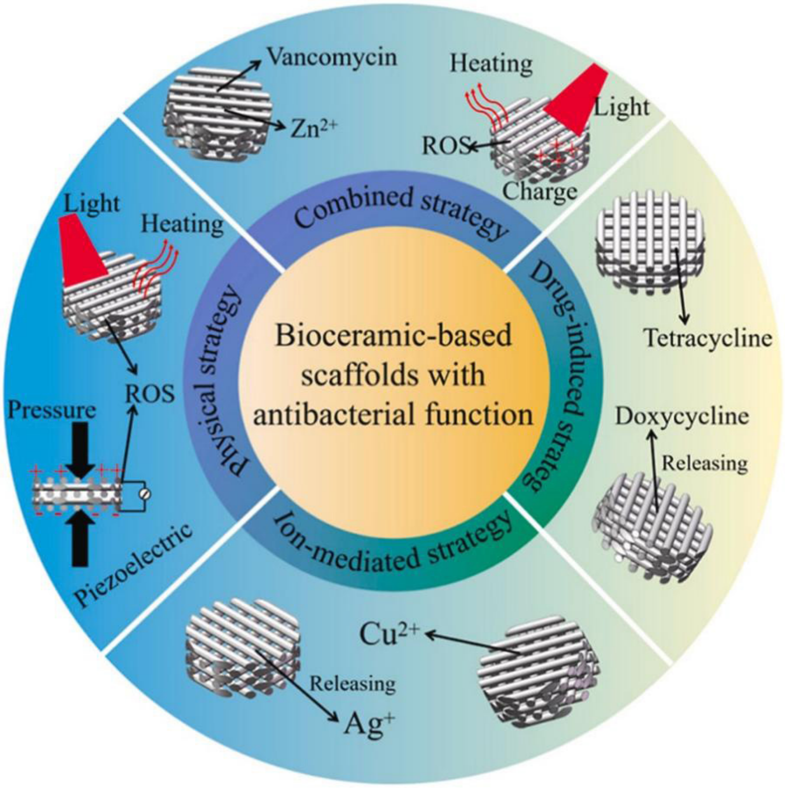

Fig. 1. Antibacterial methodologies of bioceramic-based scaffolds based on various antibacterial mechanisms.

There is great expectation that bioactive antibacterial glass ceramics could significantly enhance the quantities of successful dental and orthopedic implant placements. In light of the alarming rise of multidrug-resistant bacteria caused by the inappropriate and even excessive utilization of antibiotics, their capability of infection reduction is becoming

ISSN 2959-409X

increasingly more important than ever.[14] y providing the desired antimicrobial function surrounding the implanting site, these materials could reduce the necessity for systemic antibiotics and, perhaps, slow the advancement of antibiotic resistance. Preventing early-stage infections and biofilm growth on implants is significant, and bioactive glass ceramics could be tailored to expose therapeutic ions at controlled rates, offering lasting antibacterial effects.[15] Even with the considerable advancements in bioactive antimicrobial glass ceramics production, notable deficiencies in the existing study require more investigation. Most current research primarily concentrates on these materials' bioactivity or antibacterial characteristics alone, frequently neglecting the complex interplay between synthesis methods and their cumulative impact on bioactivity and antibacterial effectiveness.[16] Moreover, the impact of diverse design factors on these glass ceramics' mechanical durability and sustained biocompatibility has yet to be a thorough performance outcome, especially in intricate in vivo contexts.[17] This study aims to solve these deficiencies by comprehensively analyzing the composition and structure design, conventional synthesis, and multi-functioning bioactive antimicrobial glass ceramics, emphasizing the importance of a holistic approach to improving their daily performance and broadening their medicinal applications.[18]

2. Materials Design and Synthesis of Bioactive Glass-Ceramics

Careful consideration of bioactivity, biocompatibility, and antibacterial efficacy is necessitated when fabricating bioactive antibacterial glass ceramics. [19] A popular foundation material is a glass system, which usually includes silicate, phosphate, or borate [20], with the incorporation of elements such as Zn^{2+}, Cu^{2+}, and $Ag^{+}$to impart antibacterial qualities.[21] The combination of these substances not only makes the material more effective in promoting bone regeneration and creating an ideal environment for tissue formation and entitles it to antimicrobial qualities while implanting operations. A crucial aspect in the design and optimization of bioactive glass ceramics has already achieved dynamic equilibrium between antibacterial characteristics and bioactivity. The glass ceramic must possess the capacity to interact with adjacent bone tissue while simultaneously inhibiting bacterial colonization. [22] This dual function requires accurate manipulation of the glass composition, enabling the release of therapeutic ions that promote bone healing and prevent infection. The utilization of various glass systems and dopants allows researchers to tailor the material's properties to satisfy specific clinical requirements, making bioactive antibacterial glass ceramics increasingly versatile for several biomedical applications.[23]optical, and radiation shielding properties of potassium borate glass doped with samarium ions</title><secondary-title>Optik</secondary-title></titles><periodical><full-title>Optik</full-title></periodical><pages>170738</pages><volume>278</volume><dates><year>2023</year></dates><isbn>0030-4026</isbn><urls></urls></record></Cite></EndNote>

2.1 Selection of Glass Systems

Silicate-based glass ceramics are common due to their enhanced bioactivity, customizable degradation rates, and mechanical stability. Silicate glasses demonstrate significant bioactivity by readily generating hydroxyapatite layers in physiological settings, promoting strong adherence to bone tissue. Hoppe et al. [24] found that silicate-based glasses stimulate bone formation through their ionic dissolution products, which enhance osteogenesis. Since proper integration with host bone is of the utmost importance in orthopedic and dental applications, their bioactivity makes them an ideal choice. Islam et al. [25] found that the release of bioactive ions that improve bone regeneration can be regulated by adjusting the composition of silicate glasses, thereby tailoring their decomposition rate. One advantage of phosphate-based glasses is their increased solubility, which might be helpful in situations where rapid disintegration is required. These glasses are particularly advantageous in situations necessitating rapid resorption, such as temporary implants or scaffolds that must be replaced by native bone tissue within a short period. Bretcanu et al.[26] demonstrated that phosphate glass scaffolds exhibit rapid hydroxyapatite formation and significant mass loss, making them highly suitable for bone repair applications. Compared to silicate glasses, those based on borate provide a better option because of their increased bioactivity and faster conversion to hydroxyapatite. There are several biological applications for borate glasses due to their great flexibility and the fact that they may be altered to attain different degradation rates. Ensoylu et al.[27] found that borate-based glass scaffolds exhibit rapid apatite formation and offer excellent drug delivery capabilities for bone tissue engineering. Since quick bioactivity and ion release are crucial for encouraging tissue repair, borate-based solutions are particularly useful for bone regeneration and wound healing. Table 1 enumerates the standard constituents (in wt%) of prevalent bioactive antibacterial glass ceramics, encompassing traditional formulations such as 45S5, 13-93, and S53P4. Comparing the amounts of SiO_2, CaO, P_2O_5, Na_2O, B_2O_3, K_2O, MgO, and other constituents in different glass types offers researchers a fundamental reference for choosing and constructing material compositions that fulfill certain bioactivity and antibacterial performance criteria.

Table 1 Typical composition of bioactive antimicrobial glass-ceramics.

Glass Type	Typical composition/(wt%)
45S5	45SiO2-24.5Na2O-24.5CaO-6P2O5
13-93	53SiO2-6Na2O-12K2O-5MgO-20CaO-4P2Os
13-93B3	53B2O3-6Na2O-12K2O-5MgO-20CaO-4P2Os
S53P4	53SiO2-20CaO-23Na2O-4P2Os
70S30C	70SiO2-30CaO
58S	58SiO2-33CaO-9P2O5
1-98	52.7SiO2-1B2O3-6Na2O-11K2O-5MgO-22CaO-2P2Os
P50C35N15	71P2O5-19.7CaO-9.3Na2O

2.2 Incorporation of Antibacterial Agents

Antimicrobial characteristics are commonly imparted to the glass matrix by incorporating valuable metal ions, including Zn^{2+}, Cu^{2+}, and Ag^{+}. Because these metal ions usually kill Gram-positive and Gram-negative bacteria equally well, it is the antibiotic choice to avoid infections related to medical implants. Various scientific research has confirmed that Ag^{+} could kill bacteria by destroying their cell walls, blocking enzymes, and preventing DNA replication. Kim et al.[28] shown that silver ions undermine bacterial viability by causing structural damage to the cell membrane and disrupting essential cellular functions. Moreover, studies on silver-infused glass materials indicate that the incorporation of silver enhances antibacterial effectiveness without significantly diminishing the material's mechanical strength, making it suitable for medical applications. [29] However, the quantity of silver must be meticulously regulated, as elevated concentrations can harm human cells. Zhao et al. [30] emphasized the significance of regulated silver release, demonstrating that excessive concentration might induce cytotoxicity while preserving antibacterial effectiveness against a wide range of pathogens. Figure 2 illustrates the various modes of antibacterial action of AgNPs. First, AgNPs bind to the cell membrane of bacteria, which alters its shape and permeability, leading to leakage of cellular contents and ATP and loss of transport function. Second, AgNPs penetrate cells and nuclei. These are responsible for the production of reactive oxygen species. Conclusively, AgNPs affect cellular signaling by changing phosphotyrosine levels, impairing some critical cellular activities that attain antibacterial effectiveness. Zinc and copper are often utilized as dopants because they promote osteogenesis and confer antibacterial characteristics. Bone mineralization and growth depend on zinc, a trace metal. Not only does it have antibacterial qualities, but it also increases osteoblast activity. Fig.2 depicts the attachment of silver nanoparticles (AgNPs) to bacterial cell membranes, their subsequent penetration into cells and nuclei, and the initiation of various processes, including alterations in membrane permeability, damage to proteins and DNA, generation of reactive oxygen species (ROS), and disruptions in cell signaling pathways. The synergistic effects allow AgNPs to suppress bacterial proliferation efficiently, illustrating silver ions' primary mechanism of action in antibacterial glass ceramics.

ISSN 2959-409X

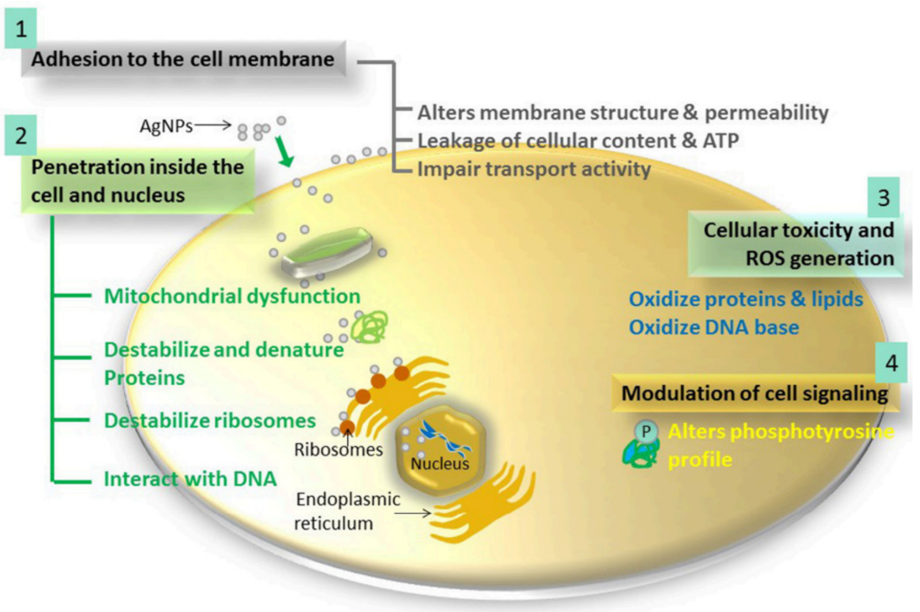

Fig.2 The four principal mechanisms of antibacterial activity of AgNPs.[31]

2.3 Synthesis Methodologies

It is possible to produce bioactive antibacterial glass-ceramics by the sol-gel process, melt-quenching, and controlled crystallization. The low-temperature method and exact control over the composition of the sol-gel technique enable the incorporation of heat-sensitive dopants and nanostructured materials fabrication. Bellantone et al. [32] found that sol-gel-derived bioactive glasses incorporating Ag^{+} ions demonstrate significant antibacterial properties without promoting bacterial resistance, which aligns to enhance ion release and bioactivity. Making glass ceramics using this technique makes it easier to increase their surface area, improving their bioactivity. When the microstructure and porosity of the material need to be precisely controlled, glasses made using sol-gel techniques are the way to go. One standard glass-making method is the "melt-quenching" process, which comprises rapidly cooling heated raw materials. Figure X shows a schematic of the glass-ceramic production process that includes melt-quenching. Vuong et al. [33] demonstrated that bioactive glasses synthesized by melt-quenching exhibit enhanced homogeneity, which ensures consistent performance in clinical settings and aligns well with their application in load-bearing environments like screws and bone plates. One important step in making bioactive glass ceramics is controlled crystallization. Crystalline phases can form inside a glass matrix if the glass's heat treatment is carefully controlled. Nawaz et al.[34] revealed that specific thermal treatment conditions can promote the formation of crystalline phases like combeite, enhancing mechanical strength without compromising bioactivity. Optimal bioactivity, mechanical characteristics, and degradation rates can be achieved by combining amorphous and crystalline phases, making controlled crystallization a key technique for advanced biomaterial development. Figure 3 clearly shows two classic preparation routes: (a) the traditional melt-quench process obtains glass or glass-ceramic products through high-temperature melting, quenching and subsequent heat treatment; (b) the sol-gel method hydrolyses and condenses the precursor solution, and then dries and sinters to achieve bioactive glass with controllable nanostructure and porosity. This schematic diagram helps readers understand the manufacturing processes and key steps from raw materials to the final bioactive glass-ceramic materials.

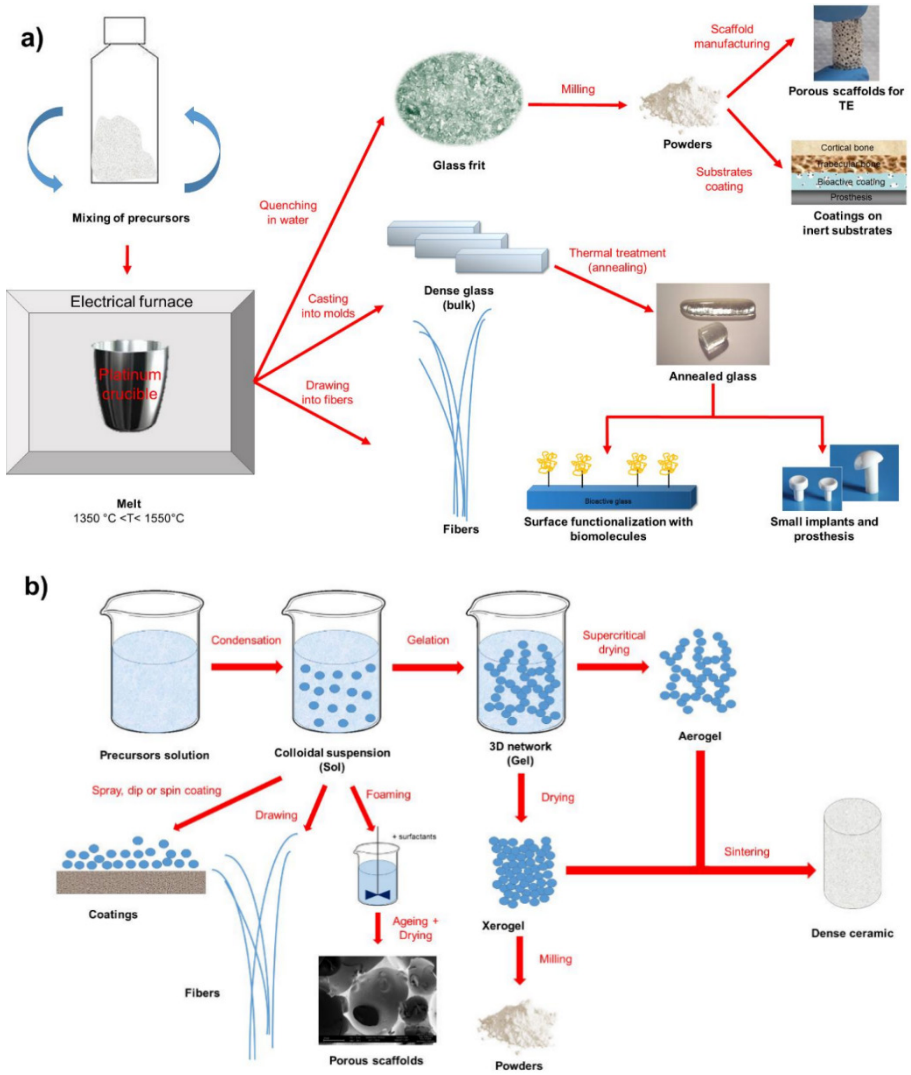

Fig.3 Schematic illustration of (a) melt-quenching method and (b) sol-gel process for bioactive glass synthesis.

3. Antibacterial Mechanisms

Metal ion release is the primary mechanism by which glass-ceramics antibacterial properties manifest. Verné et al.[36] found that silver ions released from bioactive glass-ceramics can disrupt bacterial membranes and inhibit enzymatic activity. Similarly, Palza et al. [37] demonstrated that releasing biocide metal ions from sol-gel-derived glass-ceramics leads to ROS generation. These findings collectively underscore the role of metal ion release in mediating antibacterial activity, making such glass ceramics effective tools for biomedical applications. Figure 4 depicts the multi-target assault of metal ions (e.g., Ag^{+}, Cu^{2+}, Zn^{2+}) and free radicals (R*) on bacterial cells, encompassing the suppression of cell wall production, disruption of protein synthesis and metabolic pathways, as well as damage to DNA/RNA. The synergistic processes elucidate the practical and wide-ranging antibacterial activity induced by metal ion doping in bioactive glass ceramics.

ISSN 2959-409X

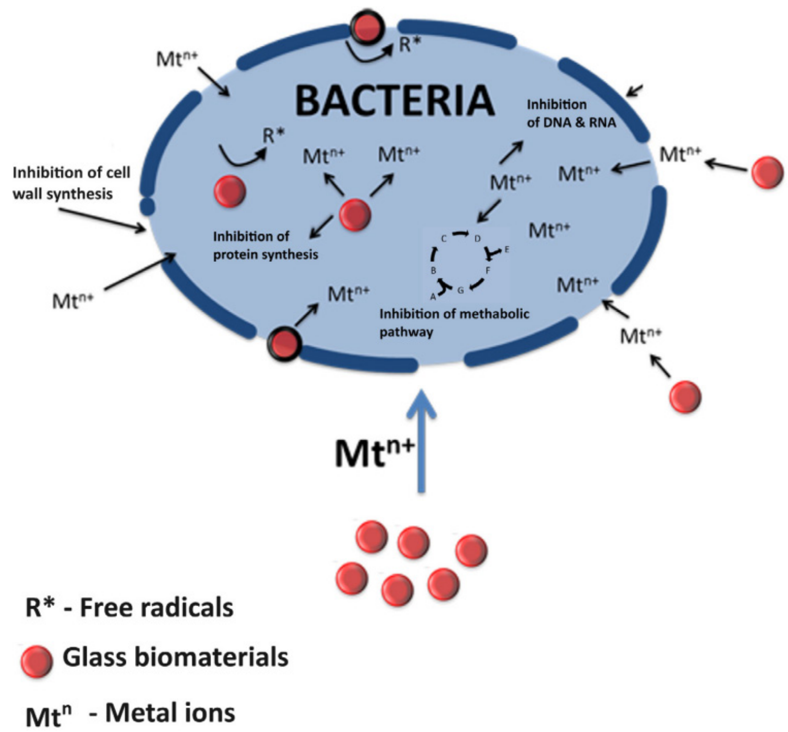

Fig. 4 Summary of the proposed pathways linked to the antibacterial properties of metal ions.

3.1 Ion Liberation and Cell Wall Compromise

Bacterial cell membranes are usually exposed to various antibacterial metal ions discharged from the glass matrix, including Ag^+ and Cu^{2+}. Ishida et al.[38] Ag^+ and Cu^{2+} ions disrupt bacterial cell walls by inducing ROS generation and inhibiting cell wall synthesis, resulting in membrane and structural damage, ultimately causing bacterial lysis. Bacterial cell walls are structurally deteriorated and become increasingly permeable when positively charged metal ions get in touch with negatively charged components of bacterial membranes. Zhang et al.[39] demonstrated that Ag^+ ions steadily released from silver-doped membranes irreversibly damage bacterial membranes, leading to significant antibacterial activity (2, Zhang et al., 2022). Owing to this deteriorating phenomenon, the bacterial cell membrane gradually becomes less stable, eventually leading to continuous lysis and death of diverse bacteria. The beneficial effects of copper ions on bacterial cell walls are strong. Raja et al.[40] highlighted that copper ions embedded in phosphate glass act synergistically to enhance antibacterial effects. Copper ions can displace essential cations while directly interacting with membrane components. This displacement progressively undermines the bacterial membrane, increasing its susceptibility to external stress and ultimately leading to cell death. The ability of these metal ions to target vital cellular structures makes them highly effective in preventing bacterial colonization and biofilm formation on medical equipment.

3.2 Generation of Reactive Oxygen Species

Reactive oxygen species (ROS) are highly reactive molecules that facilitate the inactivation of germs. As a representative type of transition metal ions, the cycling back and forth between the Cu+ and Cu2+ states enables copper ions to promote the generation of reactive oxygen species through Fenton-like processes. ROS are continuously produced and make surviving conditions unsuitable for normal bacteria, eventually resulting in their death. Limiting limitation to the implantation site, the antiba makes the antibacterial effect protect neighboring healthy tissue from potential damage. Chen et al. [41] found that copper ions, specifically from CuO, activate molecular oxygen, generating reactive oxidants, including high-valent copper species (≡Cu(III)), which play a key role in organic compound oxidation and may enhance antibacterial effects. Miller et al. [42] also demonstrated that copper ions influence metal-binding compounds, which enhance ROS production and, subsequently, the antibacterial potential.

3.3 Enzyme Inhibition

Zinc ions can inhibit metalloproteinases; they are involved in bacterial biofilm development and maintenance. Zinc inhibits these enzymes by limiting biofilm growth on implant surfaces, which is necessary to mitigate persistent infection hazards. Once established, biofilms are infamously challenging to eradicate because they provide bacteria with a safe sanctuary where they may resist treatments and the host's defenses. Cuajungco et al. [43] found that zinc's inhibitory effects on metalloproteinases limit biofilm growth by disrupting bacterial enzyme activities, thereby preventing biofilm formation on medical devices. Because they prevent the early formation of biofilms, zinc-doped bioactive glass ceramics significantly improve the long-term performance of medical implants. Thompson [44] highlighted that metal carrier proteins play a significant role in zinc's ability to influence enzymatic reactions, which can be essential in managing bacterial growth on implant surfaces. By manipulating the composition and ion release profile, researchers may enhance the antibacterial capabilities of glass ceramics. Weiss et al.[45] demonstrated that the regulation of zinc-dependent enzymes is crucial for controlling biofilm formation and bacterial persistence, underscoring zinc's importance in ensuring the longevity of medical implants. This opens up new possibilities for safer and more effective solutions for patients who need bone replacement or implanted devices and specific therapeutic needs.

4. Biological Performance and Biocompatibility

The biocompatibility of bioactive antibacterial glass ceramics is essential for their efficacy in medicinal applications. These materials are designed to ensure compatibility with biological tissues, minimizing the likelihood of undesirable immunological reactions. They facilitate natural healing processes in the body by promoting cell proliferation and tissue integration. Sánchez-Salcedo et al.[46] Incorporating silver nanoparticles into mesoporous bioactive glasses significantly enhances their antibacterial activity, providing a promising approach for bone tissue engineering. Moreover, their antimicrobial characteristics inhibit bacterial colonization, therefore reducing the incidence of infections following implantation. This dual capability shows sophisticated design efforts integrating biological compatibility with antibacterial efficacy. Ebrahimi et al.[47] demonstrated that doping bioactive glasses with Ag2O and MgO significantly improved their biocompatibility and antibacterial properties, making them suitable for clinical applications. Moreover, the structural integrity of these glass ceramics guarantees long-term stability in medical settings, rendering them appropriate for diverse applications like bone transplants and dental implants. Zhou et al. [17] further confirmed that bioactive glass compounds, such as S53P4 and 45S5, show robust antibacterial properties, particularly against biofilms, crucial for reducing post-implantation infections. The meticulous regulation of their composition and microstructure allows customized features that fulfill particular medical needs, exemplifying the advancements in material science designed to enhance patient outcomes.

4.1 In Vitro Investigations

In addition to aiding osteoblast growth and other cell types in mammals, bioactive glass ceramics have been shown in vitro to effectively suppress common infections, including Staphylococcus aureus and Escherichia coli. This study frequently mixes bacterial strain cultures with mammalian cells to determine if glass-ceramic samples are cytocompatible and effective against germs. The results demonstrate that the discharge of metal ions from a glass matrix significantly reduces bacterial viability while leaving surrounding human cells unharmed. F. Kurtuldu et al. [48] found that bioactive glass nanoparticles doped with cerium and gallium exhibit antibacterial activity against S. aureus and E. coli without causing cytotoxicity towards osteoblast-like cells. More crucially for bone formation, bioactive glass-ceramic surfaces can improve osteoblast adhesion and proliferation. Jos Crush et al.[49] showed that the composition of bioactive glasses can be manipulated to maximize osteogenesis and angiogenesis, promoting bone and blood vessel growth. This dual role prevents infections and promotes bone repair and integration. This process is necessary for bones to heal. The glass-ceramic's excellent biocompatibility and possible uses in regenerative medicine are shown by its ability to create an environment suitable for cell attachment, growth, and differentiation. According to Shicheng Huo et al.[50], some glass-ceramic materials with controlled porosity also help tissue renewal by facilitating cell entry and nutrient distribution. Figure 5 illustrates the many uses of three-dimensional miniature bone models, such as micro scaffolds, microgels, cell pellets, and organoids, in disease research, pharmacological testing, regenerative medicine, and physiological simulation. These new models offer researchers a testing platform that more accurately simulates the actual physiological environment, hence facilitating the optimization of bioactive glass-ceramics application strategies in bone repair and regeneration.

ISSN 2959-409X

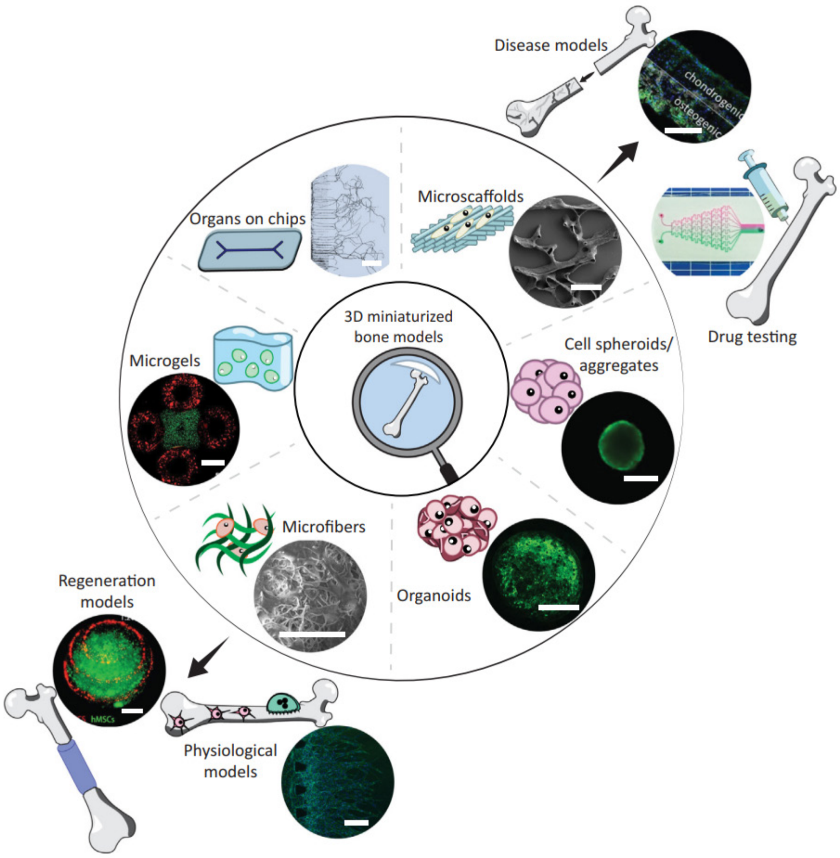

Figure 5. Cutting-edge miniature in vitro bone models.

4.2 In Vivo Investigations

some glass-ceramic materials with controlled porosity also help tissue renewal by facilitating cell entry and nutrient distribution. Figure 5 illustrates the many uses of three-dimensional miniature bone models, such as micro scaffolds, microgels, cell pellets, and organoids, in disease research, pharmacological testing, regenerative medicine, and physiological simulation. These new models offer researchers a testing platform that more accurately simulates the actual physiological environment, hence facilitating the optimization of bioactive glass-ceramics application strategies in bone repair and regeneration. [51] found that surface modifications, including nanoscale modifications of implants, can further enhance bone regeneration and integration by improving osseointegration and reducing infection risks. Traditional bioactive glass ceramics mixed with antimicrobials like silver or copper significantly improve bone formation and inhibit bacterial growth, suggesting that implant-related diseases may become less common. Francesca et al. [52] observed that surface coatings, including bioactive glass, play a vital role in enhancing osseointegration while reducing bacterial-related infections and minimizing the chances of peri-implantitis. These materials have unique antibacterial qualities, which reduce the need for systemic antibiotics. This lowers the risk of side effects and stops the development of drug resistance. R. Eftekhar et al. [53] further demonstrated that using businglass-based materials in dental implants promotes bonbone growth and has antibacterial properties, minimizing chronic inflammation and improving tissue healing. Studies conducted on live organisms have shown that bioactive glass ceramics do not elicit negative immunological responses such as persistent inflammation or sensitivities to foreign bodies. This provides important evidence that these materials have a good chance of lasting as implanted ones. Because of how naturally occurring these materials are, they improve mechanical stability and stimulate the body's healing processes by blending in with surrounding tissues. Bioactive antibacterial glass ceramics have several potential medical applications, including dental implants, spinal fusion, and fracture healing.

5. Applications in Biomedical Engineering

Antibacterial bioactive glass-ceramic for orthopedic and dental purposes mostly has applications in bone graft substitutes, coating of implants, and scaffolds for the tissue engineering of bones; these biomaterials want to promote bone growth while bringing along antibacterial action. Zhao et al. [54] discussed various dental bone grafts and substitute materials that promote bone regeneration and their efficiency in dental implant success. Due to this fact, antimicrobial infection with medical implantation cannot be ruled out besides going further to ensure good integration between biological systems and tissues. Chen et al.[55] found that the lack of effective antibacterial properties in many biomaterials limits their application, and they emphasize the importance of incorporating antibacterial properties in materials to prevent infection in bone defect treatments. Due to these reasons, bioactive antibacterial glass-ceramics have diversified versatility, making them tailor-made for specific therapeutic needs; hence, their efficiency in many medical and dental applications. Ramburrun et al.[56] reviewed the development of antimicrobial materials for dental applications, highlighting the potential of such materials to reduce infections and improve the longevity of implants and prosthetics. Figure 6 clearly illustrates the kinetics of ion release from the bioactive glass surface and its various biological effects on osteogenesis (enhancing osteoblast proliferation and differentiation), angiogenesis (promoting endothelial cell proliferation and neovascularization), and antibacterial activity (by disrupting bacterial membranes and elevating pH). The picture highlights the synergistic influences of material microstructure, chemical composition, and surface characteristics on ion release and ultimate biological qualities, serving as a crucial reference for designing multifunctional, bio-responsive glass-ceramic materials.

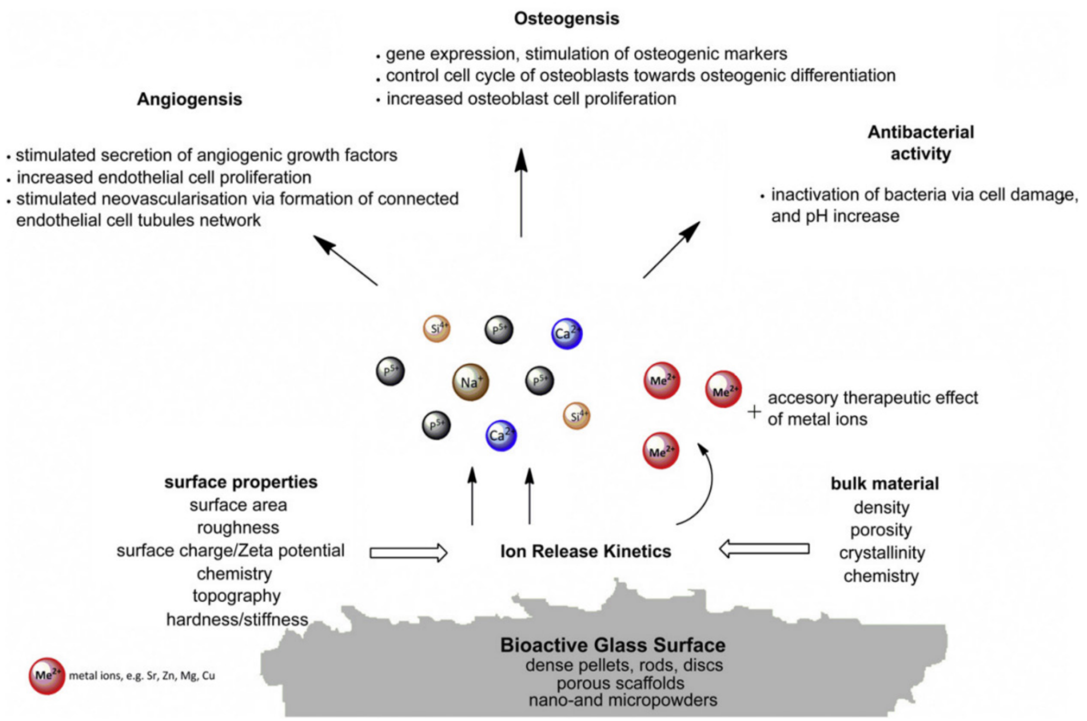

Fig. 6 Overview of biological responses to ionic dissolution products of bioactive glasses.

5.1 Orthopedic Prosthetics

Glass-ceramic coating of metallic implants has been universally employed in orthopedic surgery, which could improve osseointegration and reduce postoperative infection risks. Owing to their optimum mechanical strength, certain metals are commonly utilized in diverse processing steps and application circumstances, including joint replacement and fracture fixation. The problem with these implants is ensuring strong integration with the host bone and avoiding bacterial colonization that may lead to implant failure. Thus, to overcome such difficulties, various procedures increase the hydroxyapatite on implant surfaces for good contact at the interface between the tissue bone and implant. Lu et al. [57] found that multifunctional coatings, such as bioactive surfaces on titanium implants, are essential to enhance both osseointegration and antibacterial properties, providing insight into recent surface modification strategies. Glass-ceramic coatings not only enhance the osseous, but this increased osseointegration also favors the long-time stabilizing of the implant against

ISSN 2959-409X

mechanical stresses. Besides having good biological properties, further advantages are that glass-ceramics contain many groups that could act as antibiotics al and reduce the formation of infection, one generally diffused complication after ortho surgery. Shaaban et al. [58] demonstrated that bioactive glasses possess optical and radiation characteristics, which could be integrated into coatings to enhance infection resistance and improve bone bonding. The same implies serious complications, including both removing the implant and a prolonged antibiotic course that may cause several side reactions without any specific treatment. The antibacterial ion-releasing bioactive glass-ceramic coatings may provide a more effective local defense against bacterial colonization and, thus, reduce systemic drugs and minimize the development of antibiotic resistance. Melo Esteves et al.[59] highlighted that antimicrobial and antibiofilm coatings on implants are critical for preventing bacterial infections and improving the success rate of titanium dental implants. Such a coating can act in a two-way manner, enhancing osseointegration and preventing infection, significantly improving orthopedic implant success rates.

5.2 Dental Applications

Specific applications in dentistry include root canal fillers, dental implant coatings, and bone graft substitutes. Considering these bioactive glass ceramic-based root canal fillers, mechanical reinforcement and antibacterial resistance are cardinal factors for successful endodontic treatment. H. Simila et al. [60] found that bioactive glass containing sol-gel materials enhances the mechanical properties of restorative materials, which also plays a key role in the durability and performance of dental implants and root canal fillers. Its antibacterial action will kill the remaining bacteria within the root canal itself, thereby minimizing the chances of the recurrence of infection and prolonging the efficacy of the treatment provided. Gang et al.[61] developed a novel bioactive glass-based root canal sealer that improves sealing ability and biocompatibility, showing promise in preventing reinfection during endodontic treatments. These coatings favored hydroxyapatite synthesis, thus affecting implant integration with the surrounding bone and holding its longevity. J. Makanjuola et al. [62] reviewed the improvements in glass-ionomer cement, showing how bioactive glass can improve remineralization and antibacterial properties, which are critical for dental materials' performance. Releasing antibacterial ions can prevent bacterial colonization on the implant surface, thus reducing the chance of peri-implantitis and enhancing the overall dental implant outcome. Bioactive glass-ceramic applications have increased the mechanical stability of implants in dentistry by promoting good oral health and decreasing infection rates.

5.3 Tissue Engineering

Utilizing bioactive antibacterial glass ceramics as tissue scaffolds represents a fresh frontier in biomaterials investigation. Bioactive glass-ceramic scaffolds could provide representative frameworks that could temporarily enhance mutual attachment, cell proliferation, and differentiation related to cell regeneration. These distinctive bioactive glass-ceramic scaffolds elicit a biological response of healing through the ions release, enhancing osteogenesis and angiogenesis. Kurtuldu et al. [48] found that cerium and gallium-doped mesoporous bioactive glass nanoparticles (MBGNPs) exhibited significant antibacterial activity and in vitro bioactivity, making them candidates for bone tissue engineering. Besides promoting tissue healing, the antibacterial properties of scaffolds could also prevent infection through all the healing stages. Chen et al. [55] demonstrated that various antibacterial biomaterials, including bioactive glass scaffolds, effectively combat bone infections by inhibiting bacterial growth. Incorporating antibacterial agents into the glass-ceramic matrix entitles these scaffolds to local antibacterial action, reducing the possibility of infection without systemic medication. Bioactive antibacterial glass-ceramic scaffolds have dual functionality: they provide structural support and prevent infections, making them highly serviceable for bone tissue regeneration and other regenerative applications.

6. Challenges and Future Directions

There are promising solutions ensured by bioactive antibacterial glass-ceramics for some medical treatments; the materials have some challenges, which must be overcome to ensure long-term success and safety. Among several principal challenges is providing long-term stability of implant materials in the body, maintaining their structure over extended duration, especially under load-bearing, and preventing failure of implants, as well as various complications. Other challenges concern the precise control of the ion release rate. The therapeutic ions released from the glass-ceramic matrix are essential for antibacterial action and tissue regeneration; uncontrolled or fast release can cause cytotoxicity or diminished efficiency. Hence, it is prettysignificant to fine-tun both composition and degradation rate to achieve a sustained release of bioactive ions in a balanced manner. Taye et al.[63] found that metallic ion-doped bioactive glasses, notably those incorporating silver, copper, and zinc, exhibit enhanced antibacterial properties and high bioactivity due to their tuneable ion release mechanisms. Besides that, apprehension exists about the bacterial resistance that might develop against metal ions, especially in case elements like silver or copper are used. Though the mode of antibacterial action for these metal ions differs from those of conventional antibiotics, continuous contact with a sub-lethal concentration in the long term may well result in adapting the bacterial population to it, reducing the material's effectiveness. This challenge requires a much more detailed investigation into optimizing ion concentrations, or the combination of various antibacterial agents, to minimize the prospect of resistance. Future investigation probably will lie in the optimization of the bioactive glass-ceramic composition for conditions required in specific applications: assuring proper material properties for particular clinical needs, either by modifying the relative proportions of specific components or with the addition of new dopants towards the achievement of enhanced bioactivity, antibacterial properties, and mechanical strength. Materials' clinical safety and efficacy depend on long-term biological interactions such as immune response and ion release over a long period. The development of added therapeutic functionalities to multifunctional composites is also being researched, such as anti-inflammatory or angiogenic properties that would further enhance the healing process and patient outcomes. Overcoming these challenges could facilitate the advancement of reliable and effective bioactive antibacterial glass ceramics.

7. Conclusion

Bioactive antibacterial glass ceramics serve as desirable biomedical materials in the fight against implant-related infections and the promotion of tissue regeneration. Advances in antibacterial materials would facilitate the further development of increasingly effective and versatile glass ceramics.

References

1. Mills, J.P. and D. Marchaim, *Multidrug-resistant gram-negative bacteria: infection prevention and control update.* Infectious Disease Clinics, 2021. 35(4): p. 969-994.

2. Avershina, E., V. Shapovalova, and G. Shipulin, *Fighting antibiotic resistance in hospital-acquired infections: current state and emerging technologies in disease prevention, diagnostics and therapy.* Frontiers in microbiology, 2021. 12: p. 707330.

3. Mielke, M., *Prevention and control of nosocomial infections and resistance to antibiotics in Europe–Primum non-nocere: elements of successful prevention and control of healthcare-associated infections.* International Journal of Medical Microbiology, 2010. 300(6): p. 346-350.

4. Zhang, Y., et al., *In situ bone regeneration enabled by a biodegradable hybrid double-network hydrogel.* Biomaterials science, 2019. 7(8): p. 3266-3276.

5. Cheng, W., et al., *Injectable hydrogel systems with multiple biophysical and biochemical cues for bone regeneration.* Biomaterials science, 2020. 8(9): p. 2537-2548.

6. Fernandes, J.S., et al., *Multifunctional bioactive glass and glass-ceramic biomaterials with antibacterial properties for repair and regeneration of bone tissue.* Acta biomaterialia, 2017. 59: p. 2-11.

7. Zhang, E., et al., *Antibacterial metals and alloys for potential biomedical implants.* Bioactive materials, 2021. 6(8): p. 2569-2612.

8. Zamborsky, R., et al., *Infection in bone allograft transplants.* Exp Clin Transplant, 2016. 14(5): p. 484-490.

9. Binyamin, G., B.M. Shafi, and C.M. Mery. *Biomaterials: a primer for surgeons*. in *Seminars in pediatric surgery*. 2006. Elsevier.

10. Ohtsuki, C., M. Kamitakahara, and T. Miyazaki, *Bioactive ceramic-based materials with designed reactivity for bone tissue regeneration.* Journal of the Royal Society Interface, 2009. 6(suppl_3): p. S349-S360.

11. Ur Rehman, M.A., et al., *Electrophoretic deposition of PEEK/bioactive glass composite coatings on stainless steel for orthopedic applications: an optimization for in vitro bioactivity and adhesion strength.* The International Journal of Advanced Manufacturing Technology, 2020. 108: p. 1849-1862.

12. Zhai, W., et al., *Stimulatory effects of the ionic products from Ca–Mg–Si bioceramics on both osteogenesis and angiogenesis in vitro.* Acta biomaterialia, 2013. 9(8): p. 8004-8014.

13. Godoy-Gallardo, M., et al., *Antibacterial approaches in tissue engineering using metal ions and nanoparticles: From mechanisms to applications.* Bioactive Materials, 2021. 6(12): p. 4470-4490.

14. Pajares-Chamorro, N., et al., *Resurrection of antibiotics that methicillin-resistant Staphylococcus aureus resists by silver-doped bioactive glass-ceramic microparticles.* Acta Biomaterialia, 2019. 96: p. 537-546.

15. Fuchs, M., et al., *Therapeutic ion-releasing bioactive glass ionomer cements with improved mechanical strength and radiopacity.* Frontiers in Materials, 2015. 2: p. 162876.

16. Savvova, O., et al., *Development of Antibacterial Glazing for Ceramic Tiles.* Voprosy khimii i khimicheskoi tekhnologii, 2022. 3: p. 60-66.

17. Zhou, P., B.L. Garcia, and G.A. Kotsakis, *Comparison of antibacterial and antibiofilm activity of bioactive glass compounds S53P4 and 45S5.* BMC microbiology, 2022. 22(1): p. 212.

18. Ratha, I., et al., *In vitro bioactivity and antibacterial properties of bismuth oxide modified bioactive glasses.* Journal of Materials Research, 2018. 33(2): p. 178-190.

19. Li, M., et al., *Light-transmitting lithium aluminosilicate*

ISSN 2959-409X

glass-ceramics with excellent mechanical properties based on cluster model design. Nanomaterials, 2023. 13(3): p. 530.

20. Yang, X., et al., *Incorporation of B2O3 in CaO-SiO2-P2O5 bioactive glass system for improving strength of low-temperature co-fired porous glass ceramics.* Journal of non-crystalline solids, 2012. 358(9): p. 1171-1179.

21. Bhojwani, P., et al., *Recent advances in antimicrobial and biosynthesis properties of bioglass and nanoparticles: A narrative review.* Multidisciplinary Reviews, 2024. 7(12): p. 2024286-2024286.

22. Gristina, A., *Biomaterial-centered infection.* Clinical orthopaedics and related research, 2004. 427: p. 4-12.

23. Sayyed, M., et al., *Impact of lead oxide on the structure, optical, and radiation shielding properties of potassium borate glass doped with samarium ions.* Optik, 2023. 278: p. 170738.

24. Hoppe, A. and A.R. Boccaccini, *Bioactive glasses as carriers of therapeutic ions and the biological implications.* 2016.

25. Islam, M.T., et al., *Bioactive calcium phosphate–based glasses and ceramics and their biomedical applications: A review.* Journal of tissue engineering, 2017. 8: p. 2041731417719170.

26. Bretcanu, O., et al., *Novel resorbable glass-ceramic scaffolds for hard tissue engineering: from the parent phosphate glass to its bone-like macroporous derivatives.* Journal of biomaterials applications, 2014. 28(9): p. 1287-1303.

27. Ensoylu, M., A.M. Deliormanlı, and H. Atmaca, *Preparation, characterization, and drug delivery of hexagonal boron nitride-borate bioactive glass biomimetic scaffolds for bone tissue engineering.* Biomimetics, 2022. 8(1): p. 10.

28. Kim, J.S., et al., *Antimicrobial effects of silver nanoparticles.* Nanomedicine: Nanotechnology, biology and medicine, 2007. 3(1): p. 95-101.

29. Gargiulo, N., et al., *Silver-containing mesoporous bioactive glass with improved antibacterial properties.* Journal of Materials Science: Materials in Medicine, 2013. 24: p. 2129-2135.

30. Zhao, L., et al., *Antibacterial nano-structured titania coating incorporated with silver nanoparticles.* Biomaterials, 2011. 32(24): p. 5706-5716.

31. Dakal, T.C., et al., *Mechanistic basis of antimicrobial actions of silver nanoparticles.* Frontiers in microbiology, 2016. 7: p. 1831.

32. Bellantone, M. and L.L. Hench, *Bioactive behaviour of sol-gel derived antibacterial bioactive glass.* Key Engineering Materials, 2001. 192.

33. Vuong, B.X., *Evaluation of bioactive glass synthesized by alkali-mediated sol-gel process.* Vietnam Journal of Chemistry, 2019. 57(1): p. 80-84.

34. Nawaz, Q., et al., *New insights into the crystallization process of sol-gel–derived 45S5 bioactive glass.* Journal of the American Ceramic Society, 2020. 103(8): p. 4234-4247.

35. Gautam, C. and A. Madheshiya, *Fabrication methods of lead titanate glass ceramics and dielectric characteristics: a review.* Journal of Materials Science: Materials in Electronics, 2020. 31(15): p. 12004-12025.

36. Verné, E., et al., *Synthesis and characterisation of bioactive and antibacterial glass–ceramic Part 1–Microstructure, properties and biological behaviour.* Advances in applied ceramics, 2008. 107(5): p. 234-244.

37. Palza, H., et al., *Designing antimicrobial bioactive glass materials with embedded metal ions synthesized by the sol–gel method.* Materials Science and Engineering: C, 2013. 33(7): p. 3795-3801.

38. Ishida, T., *Insights into Metallic Ag+, Cu2+, Zn2+ Ions-Induced Bacteriolytic Mechanism against S. Aureus and E. Coli.* Catalysis Research, 2023. 3(1): p. 1-12.

39. Zhang, S., et al., *Silver (i) metal–organic framework-embedded polylactic acid electrospun fibrous membranes for efficient inhibition of bacteria.* Dalton Transactions, 2022. 51(17): p. 6673-6681.

40. Raja, F.N., et al., *Synergistic antimicrobial metal oxide-doped phosphate glasses; a potential strategy to reduce antimicrobial resistance and host cell toxicity.* ACS Biomaterials Science & Engineering, 2022. 8(3): p. 1193-1199.

41. Chen, N., et al., *Activation of molecular oxygen by tenorite and ascorbic acid: Generation of high-valent copper species for organic compound oxidation.* Journal of Hazardous Materials, 2022. 440: p. 129839.

42. Miller, B.W., et al., *Halogenated metal-binding compounds from shipworm symbionts.* Journal of Natural Products, 2022. 85(3): p. 479-484.

43. Cuajungco, M.P., M.S. Ramirez, and M.E. Tolmasky, *Zinc: Multidimensional effects on living organisms.* Biomedicines, 2021. 9(2): p. 208.

44. Thompson, M.W., *Regulation of zinc-dependent enzymes by metal carrier proteins.* Biometals, 2022. 35(2): p. 187-213.

45. Weiss, A., et al., *Zn-regulated GTPase metalloprotein activator 1 modulates vertebrate zinc homeostasis.* Cell, 2022. 185(12): p. 2148-2163. e27.

46. Sánchez-Salcedo, S., et al., *Antibacterial effect of 3D printed mesoporous bioactive glass scaffolds doped with metallic silver nanoparticles.* Acta Biomaterialia, 2023. 155: p. 654-666.

47. Ebrahimi, M., S. Manafi, and F. Sharifianjazi, *The effect of Ag2O and MgO dopants on the bioactivity, biocompatibility, and antibacterial properties of 58S bioactive glass synthesized by the sol-gel method.* Journal of Non-Crystalline Solids, 2023. 606: p. 122189.

48. Kurtuldu, F., et al., *Cerium and gallium containing mesoporous bioactive glass nanoparticles for bone regeneration: Bioactivity, biocompatibility and antibacterial activity.* Materials Science and Engineering: C, 2021. 124: p. 112050.

49. Crush, J., et al., *Bioactive glass: methods for assessing angiogenesis and osteogenesis.* Frontiers in Cell and Developmental Biology, 2021. 9: p. 643781.

50. Huo, S., et al., *Formation of a novel Cu-containing bioactive glass nano-topography coating with strong bactericidal capability and bone regeneration*. Composites Part B: Engineering, 2023. 253: p. 110521.
51. Silva, R.C., et al., *Titanium dental implants: an overview of applied nanobiotechnology to improve biocompatibility and prevent infections.* Materials, 2022. 15(9): p. 3150.
52. Accioni, F., et al., *Latest trends in surface modification for dental implantology: Innovative developments and analytical applications.* Pharmaceutics, 2022. 14(2): p. 455.
53. Eftekhar Ashtiani, R., et al., *The Role of Biomaterials and Biocompatible Materials in Implant-Supported Dental Prosthesis*. Evidence-Based Complementary and Alternative Medicine, 2021. 2021(1): p. 3349433.
54. Zhao, R., et al., *Bone grafts and substitutes in dentistry: A review of current trends and developments*. Molecules, 2021. 26(10): p. 3007.
55. Chen, Z.-Y., et al., *Antibacterial biomaterials in bone tissue engineering.* Journal of Materials Chemistry B, 2021. 9(11): p. 2594-2612.
56. Ramburrun, P., et al., *Recent advances in the development of antimicrobial and antifouling biocompatible materials for dental applications.* Materials, 2021. 14(12): p. 3167.
57. Lu, X., et al., *Multifunctional coatings of titanium implants toward promoting osseointegration and preventing infection: recent developments*. Frontiers in Bioengineering and Biotechnology, 2021. 9: p. 783816.
58. Shaaban, K.S., et al., *Physical, optical, and radiation characteristics of bioactive glasses for dental prosthetics and orthopaedic implants applications*. Radiation Physics and Chemistry, 2022. 193: p. 109995.
59. Esteves, G.M., et al., *Antimicrobial and antibiofilm coating of dental implants—past and new perspectives*. Antibiotics, 2022. 11(2): p. 235.
60. Simila, H.O. and A.R. Boccaccini, *Sol-gel bioactive glass containing biomaterials for restorative dentistry: A review.* Dental Materials, 2022. 38(5): p. 725-747.
61. Huang, G., et al., *A novel bioactive glass-based root canal sealer in endodontics.* Journal of dental sciences, 2022. 17(1): p. 217-224.
62. Makanjuola, J. and S. Deb, *Chemically activated glass-ionomer cements as bioactive materials in dentistry: a review. Prosthesis. 2023; 5: 327–345*.
63. Taye, M.B., *Biomedical applications of ion-doped bioactive glass: A review.* Applied Nanoscience, 2022. 12(12): p. 3797-3812.