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BIOGLASS AND HERBAL THERAPEUTICS: A REVOLUTIONARY APPROACH TO ENHANCING ORAL HEALTH MANAGEMENT

Riya Dsilva¹, Arti Gachake² and Vaibhav Shinde^{*1}

Department of Pharmacognosy¹, Poona College of Pharmacy, Erandwane, Pune - 411038, Maharashtra, India.

Department of Prosthodontics and Crown and Bridge Bharati Vidyapeeth (Deemed to be) University Dental College and Hospital², Pune - 411043, Maharashtra, India.

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Correspondence to Author: Dr. Vaibhav Shinde

Assistant Professor & HOD
Department of Pharmacognosy,
Poona College of Pharmacy,
Erandwane, Pune - 411038,
Maharashtra, India.

E-mail: vaibhavshinde847@gmail.com

ABSTRACT: In recent decades, oral health management has witnessed a paradigm shift by integrating bioactive materials into dental therapeutics. Among these, bioactive glasses (BGs) that were originally developed by Larry Hench in 1969 have garnered significant attention because of their distinctive capacity to bond with bones and soft tissues of the body, while stimulating biological responses that promote healing and regeneration. Bioglass was the first synthetic material that formed a chemical bond with bone. The principal mechanism underlying the bioactivity of BGs lies in their surface reactions in aqueous environments, where they release therapeutic ions like Ca^{2+} , Na^+ , PO_4^{3-} , and Si^{4+} , that lead to the formation of a hydroxycarbonate apatite (HCA) layer that mimics natural bone mineral. Furthermore, functionalization of bioactive glasses (BGs) with therapeutic metal ions like Ag^+ , Zn^{2+} , Cu^{2+} , Sr^{2+} and herbal bioactives has emerged as a promising strategy to enhance their antimicrobial, osteogenic, angiogenic, and anti-inflammatory properties, thereby broadening their applications in dental and ocular implantology, orthopedics, and wound healing. Despite the widespread recognition of its benefits, the translation of BGs into mainstream clinical practice has been limited by challenges related to mechanical strength, processing focused on the development of mesoporous Bioglasses, nanostructured BGs, and BG-polymer composites, aiming to optimize their handling characteristics, bioactivity, and controlled drug delivery capabilities. This review intends to highlight the in-depth analysis of Bioglass in the management of oral health, covering its mechanisms of action, therapeutic potential, clinical outcomes, and emerging innovations.

INTRODUCTION: Oral health is a fundamental component of overall well-being, encompassing the health of teeth, gums, and the entire oral-facial system that enables essential functions such as speaking, smiling, chewing, and expressing emotions¹.

According to the World Health Organization (WHO), oral diseases affect approximately 3.5 billion people worldwide, with untreated dental caries (tooth decay) in permanent teeth being the most common issue.

Recognising the significant burden possessed by oral diseases, the WHO has developed a Global Oral Health Action Plan for 2023–2030. This plan outlines strategic objectives and actions aimed at improving oral health on a global scale. It emphasizes integrating oral health into universal health coverage, promoting preventive care, and

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addressing common risk factors such as tobacco use, unhealthy diets, and harmful alcohol consumption². Maintaining optimal oral health is challenging due to various factors. Primarily, the socioeconomic disparities limit their approach to dental care, which disproportionately affect marginalised and low-income groups who are more likely to suffer from periodontal diseases and dental caries³. Poor oral hygiene, infrequent dental visits, and high sugar intake also contribute to declining oral health. Systemic conditions like diabetes and cardiovascular diseases can worsen oral issues, highlighting the link between oral and general health⁴. Mental health disorders like depression, negatively impact personal care and oral hygiene habits⁵. Moreover, oral health is impacted not only by systemic health conditions and disorders but also by hormonal fluctuations during pregnancy, which can lead to a deterioration of oral health, including an increased risk of gingivitis and periodontitis⁶. To address these issues, a variety of oral care formulations are available to maintain oral hygiene and prevent dental diseases that include toothpastes, mouthwashes, gels, and chewing gums containing active agents such as fluoride, triclosan, cetylpyridinium chloride, and essential oils⁷. However, the modern dental science is moving beyond the use of traditional, inert materials towards a new generation of innovative biomaterials. One such bioactive material that has significantly contributed in healing bone defects and restorative oral surgeries is Bioglass⁸. It has a unique and potent property of bioactivity that helps to form a rapid and robust bond with bone and soft tissues⁹. Bioglass is a pioneering bioactive material that has transformed the landscape of oral health care by offering unique regenerative and antimicrobial properties¹⁰. Originally developed for bone repair, Bioglass has found extensive

applications in dentistry because of its capacity to adhere to both soft and hard tissues, promote mineralisation in dental implants, alleviate dentin hypersensitivity, and promote tissue and craniofacial regeneration¹¹⁻¹³. This is very crucial in treating a wide variety of oral and dental issues, unlike the other oral treatment alternatives like fluoride, triclosan, chlorhexidine, etc that usually have adverse effects associated with their therapeutic use.

Brief History and the Bioglass Revolution: The history of Bioglass dates back to the 1960s with the ground breaking work of Professor Larry Hench, who sought to develop a material that could form a living bond with bone¹⁴. At that time, metals were commonly used as implants in orthopaedic surgeries. However, over time, these metals would corrode inside the body, posing health risks and potentially causing toxicity¹⁵. This led to the development of the first-generation Bioglass, known as 45S5, which demonstrated a remarkable ability to stimulate bone growth, representing a major shift from the inert materials previously used. This silica-based material bonds directly to bone and stimulates gene activation for osteogenesis within 48 hours of implantation, promoting rapid bone regeneration. This unique bioactivity redefined implant material goals, emphasizing natural healing processes, making Bioglass a cornerstone in biomaterials science and the field of bioactive ceramics¹⁶. Subsequent advancements over the following decades focused on tailoring Bioglass compositions to control their degradation rates and improve their mechanical properties for specific applications like wound healing, tissue engineering and the multifaceted world of oral health¹⁷. **Table 1.** Represents the evolution of Bioglass over decades and its significant characteristics.

TABLE 1: EVOLUTION OF BIOGLASS

Year	Significance	Details
1969	Discovery of Bioglass	Development of 45S5 Bioglass by Sir Larry Hench that bonded with bone tissue ¹⁸
1970-1980	Conduction of Clinical trials	Clinical trial study proved success of Bioglass in orthopedic and dental implants also avoids immune rejection ¹⁹ .
1990s	Commercialization of Bioglass	Products like Perioglass and NovaBone enter the market for use in bone grafts and periodontal repair ²⁰
2000s	Development of Bioglass ceramics	Bioglass with advanced structural features for load-bearing applications ²¹
2010	Advanced applications	Integration with polymers, 3D printing and use in cancer therapy and tissue engineering ²²

The Fundamental Mechanism of Bioglass Bioactivity: Bioglass is primarily a family of bioactive glasses composed of silicon dioxide, sodium oxide, calcium oxide, and phosphorous pentoxide. These materials exhibit both bioactivity and biodegradability, enabling the controlled release of therapeutic ions that modulate cellular responses. Owing to these properties, they are well-suited for diverse biomedical applications, including bone substitution and replacement, as well as the regeneration of both soft and hard tissues²³. Bioglass can be classified into three primary classes: silicate, borate, and phosphate Bioglass, based on the type of network-forming

oxides. They can be synthesized using either the melt quenching method or the sol-gel method²⁴. Bioglass is typically composed of calcium sodium phosphosilicate, has revolutionized oral care by offering a unique mechanism as described in **Fig. 1**, that promotes healing and remineralisation of dental tissues. Its bioactivity stems from its ability to interact with bodily fluid like saliva which initiates a cascade of chemical reactions that result in the formation of a mineral layer similar to natural tooth enamel. When Bioglass is introduced into the oral environment, such as through toothpaste or dental treatments, it begins a multi-phase process as represented in **Fig. 1**.

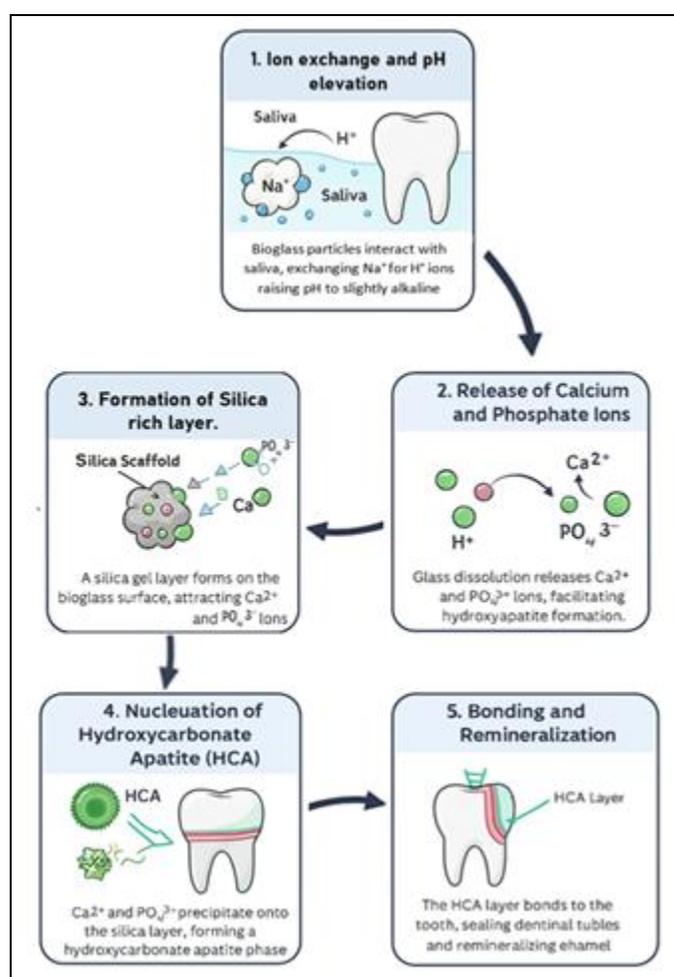


FIG. 1: MECHANISM OF ACTION OF BIOGLASS ON TOOTH SURFACE

Bioglass and other biomaterials have played a significant role in bone repair for more than 30 years. Their effectiveness is largely attributed to their versatile properties, which can be tailored to enhance specific biological responses in both orthopedic and dental fields. For instance, Bioglass can promote the formation of new bone tissue, facilitate the healing process, and even provide

antibacterial effects²⁵. The formation of Hydroxycarbonate apatite layer (HCA) releases ions like Ca^{2+} , Si^{4+} , Na^+ , PO_4^{3-} which directly influence cellular signalling and promote bone regeneration²⁶.

Moreover, Bioglass can have antimicrobial effects by raising pH and directly inhibiting the

progression of caries causing and periodontopathogenic like *Streptococcus mutans* and *Porphyromonas gingivalis*^{27, 28}. Incorporating ions such as lithium, strontium, magnesium, or cerium can further enhance antibacterial and remineralizing properties²⁹.

Current Treatments for Oral Care: The most commonly used agent in various oral care formulations is Fluoride, which is widely known for its ability to strengthen tooth enamel and prevent dental caries. When used in recommended doses, fluoride is generally considered safe. However, excessive exposure can lead to dental fluorosis, oral irritation, and, in rare cases, systemic toxicity^{30, 31}.

Another important active ingredient is Triclosan, an antibacterial agent that has shown to improve gingival health and reduce plaque formation when used in dentifrices. However, clinical studies have reported that triclosan-containing oral products can lead to oral mucosal irritation and taste disturbances. Moreover, it is also considered the most common endocrine disruptor³².

A systematic review highlighted that users of triclosan mouthrinses frequently experienced taste alterations and mucosal irritations, leading to its removal from use in the European Union and the United States³³.

Cetylpyridinium chloride, a quaternary ammonium compound, exhibits antimicrobial properties effective against plaque and gingivitis. While being effective in reducing dental plaque and gingivitis, its prolonged use is associated with several side effects, like tooth and tongue staining and temporary loss or alteration of taste in a few cases³⁴.

Also, oral burning, taste alterations, ulcers and stomatitis were also reported in some cases³⁵. Among mouthwashes, chlorhexidine gluconate is considered the gold standard for its broad-spectrum antimicrobial activity and substantivity, making it effective in managing gingivitis and periodontitis. However, its long-term use is associated with side effects such as tooth staining, altered taste sensation, increased calculus formation, and, in rare cases, mucosal irritation³⁶.

Bioglass is such a bioactive material that significantly surpasses current conventional oral treatment options by actively engaging with biological tissues. It has a distinct ability to release ions like Ca^{2+} , Si^{4+} , and PO_4^{3-} that directly stimulate cellular regeneration, offer inherent antimicrobial properties by increasing local pH, and can serve as a smart delivery system for therapeutic agents.

This versatile material facilitates true tissue restoration and enhances the stability of dental repairs for a prolonged period of time. It adopts a proactive approach to disease prevention, surpassing the limitations of conventional materials that provide only structural support or temporary relief.

Bioglass in Oral Health: Applications and Latest Advancements: In dentistry, Bioglass has been explored across multiple disciplines including periodontics, restorative dentistry, endodontics, and implantology³⁷. Bioactive glasses are beneficial in toothpaste formulation due to their ability to release antibacterial agents, promote remineralization, and reduce hypersensitivity. One such bioactive glass is NovaMin, which serves as an active ingredient in toothpaste to enhance remineralisation and alleviate tooth sensitivity. NovaMin, which is composed of calcium-sodium-phosphate silicate, releases calcium and phosphate ions.

These ions help raise the pH level, facilitating the deposition of calcium phosphate, and its conversion to hydroxyapatite³⁸. In a study of toothpaste containing fluoride and Bioglass, it was reported that bioactive glass has the potential to prevent mineral loss on bleached enamel³⁹. In periodontology, BG particles have been successfully used for the regeneration of periodontal tissues, showing comparable or superior results to traditional graft material⁴⁰.

In implant dentistry, BG coatings on titanium surfaces promote osseointegration and may prevent peri-implant diseases by modifying the peri-implant microbiome⁴¹. Moreover, its incorporation into dental adhesives and restorative materials offers the potential for enhanced remineralization and antibacterial properties, especially beneficial in managing caries-prone patients⁴².

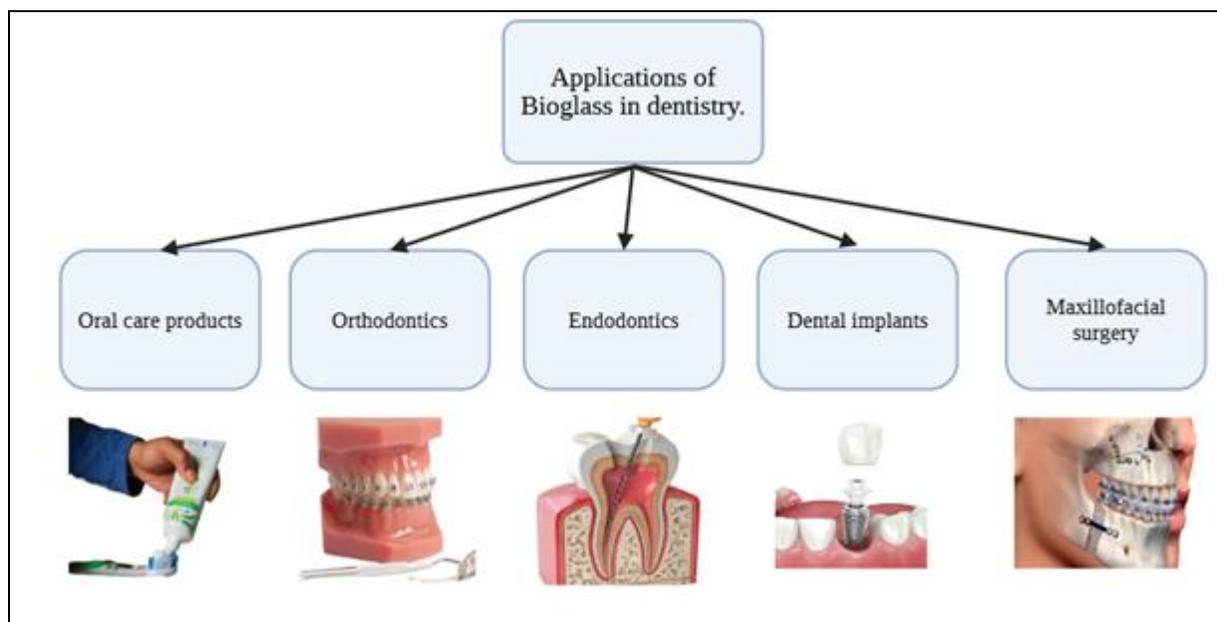


FIG. 2: APPLICATIONS OF BIOGLASS IN DENTISTRY

Dentin Hypersensitivity (DH): Bioglass plays an important role in managing dental hypersensitivity, which is a clinical condition characterised by sharp stabbing pain due to exposed dentin tubules in response to thermal or chemical stimuli⁴³. There is a perception of pain arising from the stimulation of mechanoreceptors in the dental pulp due to fluid movement within exposed dentinal tubules. Managing DH would require occluding the exposed tubules or modulating the nerve responses⁴⁴. The mechanism by which Bioglass alleviates pain associated with dentin hypersensitivity (DH) involves covering exposed dentin tubules. Bioglass has the unique ability to form a hydroxycarbonate apatite (HCA) layer that blocks external stimuli, reducing sensitivity and relieving pain. This biomimetic mineralisation also occludes the tubules and integrates with the natural tooth structure, providing durable relief. Fluoride-containing Bioglass formulations further enhance this effect by forming a fluorapatite layer, which is more resistant to acid attack and offers longer-lasting protection⁴⁵.

Systemic reviews and in-vitro studies report that when desensitizers like fluoride or gelatin modifications are added to the composition of Bioglass, there is significant reduction in long-term and short-term symptoms of DH⁴⁶. The clinical applications of Bioglass in treating dentin hypersensitivity (DH) include its use in toothpastes, desensitizing treatments, and restorative materials.

One well-known formulation of Bioglass is NovaMin, which is widely used in dentistry. Studies have shown that NovaMin-containing toothpastes can significantly reduce sensitivity within a few weeks of use, often outperforming traditional agents like potassium nitrate⁴⁷. Moreover, Bioglass has shown antimicrobial properties, contributing to improved gingival health and reduced plaque accumulation, which indirectly benefits DH management⁴⁸. The **Fig. 3**, shows the antibacterial effect of Bioglass on remineralisation and treating hypersensitivity⁴⁹.

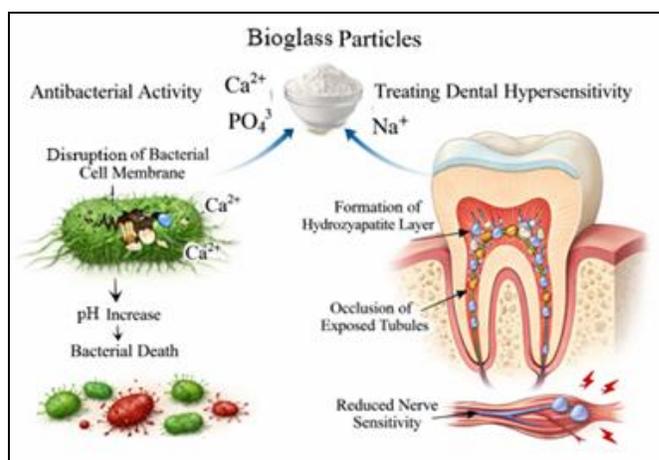


FIG. 3: BIOGLASS IN TREATING DENTIN HYPERSENSITIVITY

In Maxillofacial Surgery and Restorative Dentistry: In the field of maxillofacial surgery, bioactive glass serves as a commonly used bone graft alternative for the restoration of craniofacial

defects and the repair of orbital floor injuries⁵⁰. Once implanted, it initiates a cascade of surface-level reactions, beginning with the exchange of sodium (Na⁺) and calcium (Ca²⁺) ions from the glass with hydrogen ions (H⁺) present in bodily fluids. This ionic interchange promotes the development of silanol (Si-OH) groups on the material's surface⁵¹.

Bioglass serves as a highly effective bone graft substitute in maxillofacial surgery due to its osteoconductive and osteostimulatory properties⁵². After a tooth is extracted, the alveolar bone naturally resorbs, leading to a loss of bone volume. This can complicate or even prevent the placement of dental implants. Bioglass, often used in particulate form, is placed into the extraction socket to preserve the alveolar ridge. The bioactive properties of the glass promote the formation of new bone, maintaining the ridge's height and width for future prosthetic rehabilitation⁵³.

In restorative dentistry, bioactive glass is incorporated into various materials such as composites, liners, and adhesives to improve both functional and therapeutic properties. Its ability to release calcium and phosphate ions supports the remineralization of demineralized enamel and dentin, helping restore the mineral content of teeth. Additionally, the ion release raises local pH, creating an environment that inhibits the growth of cariogenic bacteria, thereby providing an antimicrobial effect. In cases of dentin hypersensitivity, bioactive glass helps by occluding exposed dentinal tubules, significantly reducing sensitivity and discomfort⁵⁴. Furthermore, when used in restorative materials, it can improve their mechanical integrity while offering long-term therapeutic advantages⁵⁵.

Periodontal Regeneration: Periodontics is a dental specialty dedicated to the prevention, diagnosis, and management of conditions affecting the tooth-supporting structures, collectively referred to as the periodontium⁵⁶. These include the gingiva (gums), alveolar bone, cementum, and periodontal ligament. Periodontists primarily address gingivitis which is a reversible gum inflammation and periodontitis, a chronic condition that can lead to permanent damage such as bone deterioration and tooth loss if not properly treated.

Effective periodontic care is vital for preserving oral health and avoiding severe complications⁵⁷. In this domain, Bioglass is employed to repair periodontal defects by stimulating bone regeneration. When introduced to periodontal lesions, Bioglass particles react with bodily fluids, releasing sodium, calcium, and phosphate ions⁵⁸. This ionic exchange initiates the formation of a silica gel layer on the particle surface, which is subsequently overlaid by a calcium-phosphate-rich phase. This layer crystallises into hydroxycarbonate apatite (HCA), a compound structurally similar to natural bone mineral. The HCA coating supports osteoblast attachment and proliferation, thereby enhancing bone growth and facilitating periodontal tissue regeneration⁵⁹.

Dental implantology is a specialized field focused on the surgical placement, restoration, and long-term maintenance of dental implants. A dental implant is a biocompatible medical device that is surgically positioned in the jawbone to replace a natural tooth root. This implant provides a stable foundation for prosthetic teeth, such as crowns, bridges, or dentures, effectively restoring both function and aesthetics for patients with missing teeth⁶⁰.

The bioactive surface of Bioglass-coated implants encourages the formation of a strong bond between the implant and the surrounding bone tissue. Additionally, the antimicrobial properties of Bioglass help in minimizing the risk of peri-implant infections, contributing to the long-term success of dental implants. It also serves as a coating material to enhance osseointegration. The osteostimulative effect of Bioglass, characterized by its ability to stimulate osteoblast activity and bone matrix formation, further underscores its utility in implant dentistry⁶¹.

The rising demand for robust implants, driven largely by an aging population and a surge in trauma cases, presents significant challenge and to overcome this the Bioglass has been doped with various elements like the zirconium dioxide (ZrO₂) and magnetite. Studies indicate that doping of 45S5 Bioglass with Zirconium dioxide improves the activity and results in more durable and biocompatible implants⁶².

Dental and Orthodontic Adhesives: In orthodontics, Bioglass is incorporated into adhesives and sealants to mitigate enamel demineralization, a common issue during fixed appliance therapy. The mechanism involves the release of calcium and phosphate ions as mentioned in the above mechanism that leads to the formation of aHCA layer on the enamel surface. This layer remineralizes early carious lesions and serves as a barrier against acid attacks. Studies have demonstrated that orthodontic adhesives enhanced with Bioglass nanoparticles exhibit superior remineralizing effects and antibacterial properties, especially when doped with strontium ions, which further promote apatite formation and inhibit bacterial growth⁶³.

Endodontic therapy, Bioglass is utilized in root canal sealers and fillers to improve sealing ability and promote periapical healing⁶⁴. It also exhibits antibacterial properties by elevating the local pH and releasing ions that disrupt bacterial cell walls, thereby reducing the risk of reinfection. The bioactive layer upon contact with body fluid is rich in silica that facilitates the adhesion and proliferation of osteoblasts, promoting bone regeneration and sealing of the root canal system⁶⁵.

Caries Prevention and Remineralisation:

Bioglass possesses exceptional antimicrobial properties that are valuable in biomedical applications. Its action is mainly due to the release of ions like Na^+ , Ca^{2+} , and PO_4^{3-} in physiological fluids, raising local pH and creating an alkaline environment that inhibits bacterial growth. This ionic release also alters osmotic pressure around microbial cells, causing dehydration and cell lysis⁶⁶. Furthermore, Bioglass can physically damage bacterial membranes, leading to cell death. Therefore, its activity is enhanced by doping with antimicrobial metal oxides such as zinc, cobalt, and copper, with combinations resulting in synergistic effects that can be up to 100 times more effective. Silver-doped Bioglass exhibited both bacteriostatic and rapid bactericidal activities. Furthermore, the porous structure of this biomaterial facilitates the controlled release of metal ions, allowing for a sustained delivery of the antibacterial agent to dental materials⁶⁷. Prevalence of various *Enterococcus species* have been reported in the oral cavity⁶⁸.

The antimicrobial activity of Bioglass reduces bacterial colonization, prevents infections, and promotes tissue healing thereby benefiting dentistry, orthopedics and wound care⁶⁹. A study reported that Bioglass 45S5 exhibited antimicrobial effects against *E. faecalis* using direct exposure test (DET) was used to evaluate the antimicrobial effect⁷⁰. The given **Fig. 4**, represents the antibacterial action of Bioglass in treating Dental caries⁷¹.

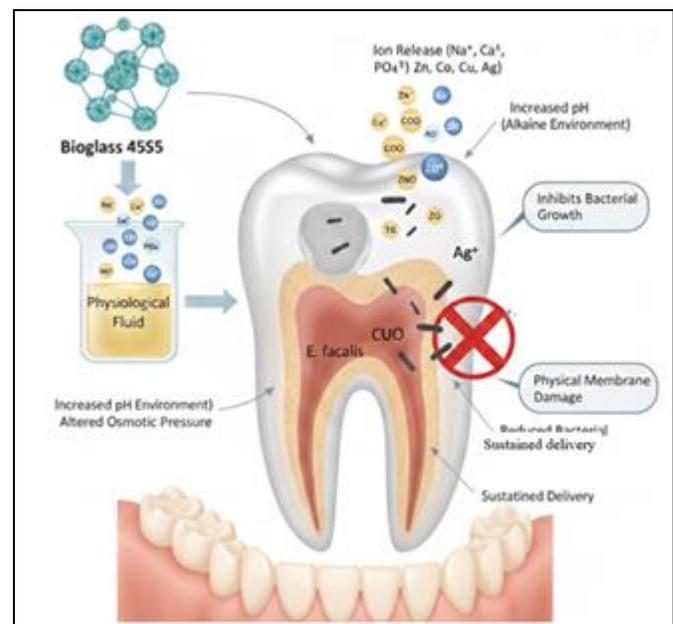


FIG. 4: ANTI-BACTERIAL ACTION OF BIOGLASS IN TREATING DENTAL CARIES

Other Emerging Oral Health Applications:

In orthodontics, Bioglass is incorporated into adhesives, sealants orthodontic brackets to mitigate enamel demineralization, a common issue during fixed appliance therapy⁷². The mechanism involves the formation of HCA layer on the enamel surface. This layer remineralises early carious lesions and serves as a barrier against acid attacks. Studies have demonstrated that orthodontic adhesives enhanced with Bioglass nanoparticles exhibit superior remineralizing effects and antibacterial properties, especially when doped with strontium ions, which further promote apatite formation and inhibit bacterial growth⁷³.

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The bioactive layer upon contact with body fluid is rich in silica that facilitates the adhesion and proliferation of osteoblasts, promoting bone regeneration and sealing of the root canal system^{74,75,76}.

The given **table 2** represents commercially available products of Bioglass.

TABLE 2: MARKETED PRODUCTS CONTAINING BIOGLASS

Material	Composition and structure
PerioGlas®	Contains calcium, sodium, phosphate and silica; it is a granulated form of 45S5 Bioglass®. Particle size: 90–710 µm
Biogran®	Same composition as 45S5 Bioglass® (calcium, sodium, phosphate, and silica); particles of narrow size range. Particle size: 300–360 µm
BonAlive®	Special Bioglass (S53P4) consists of 53% SiO ₂ , 23% Na ₂ O, 20% CaO, and 4% P ₂ O ₅ as weight percent. Particle size: 500–800 µm
NovaMin®	Identical with 45S5 Bioglass®, contains only calcium, sodium, phosphate, and silica in an amorphous matrix. Particle size: 18 µm

Doping of Bioglass with Other Chemicals/Herbs: Bioglass is often enhanced with herbal extracts to improve its properties for medical applications. This doping increases antimicrobial activity, aiding in infection prevention during bone and dental repairs. The natural compounds in herbs promote healing and tissue regeneration, creating a synergistic effect that boosts the performance of Bioglass. This combination offers a holistic approach that utilises both Bioglass and the benefits of medicinal plants. Bioglass has been infused with various metals such as cobalt, zinc, and silver, which provides advantageous properties of these metal ions in addition to the benefits offered by the Bioglass itself⁷⁷.

Herbs can be integrated into Bioglass to have combined benefits of the Bioglass and phytoconstituents present in the herbs⁷⁸. Bioglass can be doped with various potent herb extracts to have synergistic action, multi-functionality, controlled release and improved biocompatibility and therefore increasing their effectiveness in treating dental conditions and effective against *Streptococcus mutans* strains⁷⁹. The process of incorporating herbs into Bioglass majorly depends on the nature of the herb-extract, crude powder, purified compound etc. Various methods employed for the same are loading into porous Bioglass, surface coating, and direct incorporation during synthesis, etc. Herbs that have well documented oral benefits and that can be potentially combined with Bioglass include- Green tea, Red Clover, Turmeric, Neem, Liquorice, Chamomile, Aloe vera, Miswak, etc⁸⁰. Studies have reported that Bioglass doped with curcumin showed promising

wound healing activity. Curcumin enhances the anti-inflammatory and antimicrobial effects, making this combination a promising option for improving tissue regeneration and reducing infection risks in wound care⁸¹. Research has shown that Bioglass infused with *Boswellia sacra* extract exhibits antibacterial properties and promotes tissue healing and regeneration⁸².

The future of Bioglass infused with herbs for oral health can offer innovative possibilities for treatment. One significant advancement is the creation of customized therapies, such as 3D-printed Bioglass-herb composite scaffolds that can be tailored to the unique anatomy of individual patients and their specific disease conditions⁸³. Additionally, targeted drug delivery systems could be developed, allowing these Bioglass-herb combinations to release therapeutic compounds in response to specific triggers, such as pH changes in inflamed tissues or during the production of acid by bacteria. Another potential application is in the prevention of peri-implantitis, which is a significant cause of dental implant failure⁸⁴. Herb-doped Bioglass coatings on dental implants could be designed to create surfaces that actively prevent the formation of biofilms and reduce inflammation around the implants. Furthermore, these Bioglass-herb composites might be utilized in regenerative endodontics to help rejuvenate damaged pulp tissue and encourage the regeneration of dentin. Recent advancements in the use of Bioglass include the addition of quercetin, which helps reduce oxidative stress and consequently diminish periodontal bone defects through various molecular mechanisms⁸⁵.

Bioglass in Other Fields: In Orthopedics, Bioglass and other biomaterials have played a significant role in bone repair for more than 30 years. Their effectiveness is largely attributed to their versatile properties, which can be modified to enhance biological responses⁸⁶. For instance, Bioglass can facilitate new bone tissue, enhancing the healing process, and even provide antibacterial effects²⁵. When the Bioglass comes in contact with physiological fluid, it forms a HCA layer it releases ions like Ca^{2+} , Si^{4+} , Na^+ , PO_4^{3-} which directly influence cellular signalling and promote bone regeneration²⁶. Bioglass enhances proliferation of osteoprogenitor cells, regulates gene expression and promotes angiogenesis which is critical for delivering nutrients and oxygen essential for bone healing⁸⁷.

The therapeutic effectiveness of Bioglass in Wound Healing is initiated by its dissolution in physiological fluids, which releases a variety of beneficial ions like calcium (Ca^{2+}), silicon (Si^{4+}), and phosphorus (P_2O_5). This ion exchange mechanism leads to a local increase in pH, creating an alkaline microenvironment that is detrimental to bacterial proliferation, thereby offering an inherent antibacterial effect⁸⁸. The released ions also modulate cellular behavior, promoting the migration and proliferation of key cells such as fibroblasts and keratinocytes that are vital for tissue regeneration. Furthermore, Bioglass has been shown to induce angiogenesis, the formation of new blood vessels, which is critical for supplying the wound with essential nutrients and oxygen⁸⁹. By regulating the inflammatory phase and promoting the proliferative and remodeling phases, Bioglass facilitates the deposition of new collagen and the formation of organized tissue, ultimately leading to accelerated wound closure with reduced scarring, making it a powerful tool for managing both acute and chronic wounds⁹⁰.

Bioglass also plays a significant role in the management of chronic and diabetic ulcers by enhancing wound healing and improving the quality of regenerated tissue⁹¹. Its therapeutic effect is driven by the release of bioactive ions, which stimulate angiogenesis that is the process of development of new blood vessels and this helps to regulate the inflammatory response by encouraging the activity of anti-inflammatory macrophages^{92,93}.

Emerging application of Bioglass, includes its application in cosmetic and cosmeceutical fields. The patent underscores the incorporation of Bioglass into topical formulations that aim at enhancing skin appearance, particularly in reducing fine lines and improving texture. When applied topically, Bioglass particles interact with moisture on the skin, initiating an ion exchange that leads to the formation of a hydroxycarbonate apatite-like layer. This biomimetic process not only supports skin regeneration but also contributes to a smoother, more hydrated surface.

Challenges and Future Perspectives: Despite the significant bioactivity and compatibility of Bioglass, it faces several challenges that limit its widespread clinical and industrial application. One of the major challenges faced is its mechanical fragility. Traditional Bioglass compositions, such as 45S5, exhibit poor tensile strength and brittleness, making them unsuitable for load-bearing applications like orthopedic implants⁹⁴. Researchers have attempted to overcome this by developing composites or incorporating reinforcing agents, but achieving a balance between bioactivity and mechanical integrity remains complex. Another significant challenge lies in the processing and fabrication of Bioglass-based materials. The high melting temperatures and sensitivity to crystallization during sintering complicate the manufacturing of porous scaffolds and injectable formulations. Also, Rapid dissolution can lead to local pH changes and cytotoxicity, while slow degradation may hinder integration with host tissue⁹⁵.

From a clinical perspective, regulatory approval and translational hurdles also pose barriers. The variability in composition, particle size, and delivery methods across different formulations makes standardization difficult. Additionally, long-term *in-vivo* data on Bioglass performance, especially in soft tissue applications, is still limited. This affects clinician confidence and slows down broader adoption beyond dental and bone repair contexts⁹⁶.

Future perspectives: Bioglass is advancing rapidly with promising innovations. Nanocomposites combining Bioglass with polymers are improving strength and promoting remineralisation, with

emerging self-healing variants that could extend restoration life. 3D and 4D printing technologies enable custom scaffolds for tissue regeneration, tailored to patient-specific defects. Bioglass-based bioinks in 3D bioprinting offer precise reconstruction of oral tissues with excellent biocompatibility⁹⁷. Additionally, Bioglass is being explored as a smart drug delivery system for antibiotics and growth factors, enhancing targeted therapy for dental conditions like peri-implantitis and periodontal regeneration⁹⁸. Injectable Bioglass is gaining momentum as a versatile material for

regenerative therapies, offering minimally invasive solutions tailored to complex tissue defects. Future developments focus on enhancing its mechanical and biological performance through multifunctional composites, while also enabling controlled delivery of drugs and growth factors. Innovations like responsive formulations and stem cell integration aim to create dynamic, personalized treatments. With progress in customization and scalable production, injectable Bioglass is set to play a key role in dentistry, orthopedics, and soft tissue repair⁹⁹.

Clinical Trial Studies of Bioglass:

TABLE 3: CLINICAL TRIALS OF BIOGLASS

NCT Number	Conditions	Study Status	Sex	Phases	Locations
NCT03786302	Pulpotomy	Terminated	All	Phase2	Faculty of Dentistry, 21512, Egypt
NCT04767243	Chronic Periodontitis Bone Loss Intrabony Periodontal Defect	Completed	All	Phase4	Department of Periodontology, 133207, India
NCT05049915	Pseudoarthrosis of Bone	Unknown	All	Na	University Hospital Heidelberg, 69118, Germany
NCT05260853	Invasive Ventilation Weaning	Unknown	All	Na	Thoraxklinik Heidelberg, 69120, Germany
NCT05974228	Chronic Wound	Unknown	All	Na	NA
NCT03798184	Self-etch Selective-etch Bioactive Glass Direct Resin Composite	Unknown	All	Na	University of Valencia, Spain
NCT05484492	Alveolar Bone Resorption	Recruiting	All	Phase4	University of Louisville, 40202, United States
NCT02982681	Periodontal Diseases Bone Resorption	Completed	All	Phase3	NA
NCT01878084	Bone Loss Vertical Alveolar Bone Loss Horizontal Alveolar Bone Loss	Completed	All	Na	Tissue Engineering Laboratories, Egypt
NCT02316080	Dentin Hypersensitivity	Completed	All	Phase4	University of Sao Paulo, 14040904, Brazil

Patents Related to Bioglass:

TABLE 4: DIFFERENT PATENT RELATED TO BIOGLASS

Title	Link
Bioglass fermentation cylinder	https://patents.google.com/patent/CN222119207U/en
A surface-modified bioactive glass tooth desensitizer and its preparation method and application	https://patents.google.com/patent/CN119385842A/en
A plant-based bioactive glass and its application in oral care products	https://patents.google.com/patent/CN119302878A/en
Sponge comprising a recombinant collagen-like peptide (clp) and bioactive glass	https://patents.google.com/patent/WO2025016819A1/en
Stable bioactive glass formulations	https://patents.google.com/patent/US20240366482A1/en
Bletilla polysaccharide-mesoporous bioactive glass-gelatin hydrogel and application thereof	https://patents.google.com/patent/CN117771428A/en
A bioactive glass composite hydrogel scaffold material and its preparation method and application	https://patents.google.com/patent/CN116099041B/en
Storage device for Bioglass toothpaste	https://patents.google.com/patent/CN218594919U/en
Bioactive borated glass with addition of phosphorus pentoxide	https://patents.google.com/patent/BR102022019645A2/en

Micro-nano Bioglass restoration toothpaste and preparation process thereof	https://patents.google.com/patent/CN114557895A/en
Method for preparing Bioglass powder with different particle sizes in batch	https://patents.google.com/patent/CN110818270A/en
The preparation method of porous Bioglass dressing	https://patents.google.com/patent/CN106474535A/en
Mesoporous silica-loaded Bioglass composite material	https://patents.google.com/patent/CN106038333B/en
Bioglassfiber dental implant	https://patents.google.com/patent/KR101603474B1/en
Bioglass granular material and preparation technique thereof	https://patents.google.com/patent/CN104724922A/en
System and kit for delivering collagen Bioglass composite bone grafting materials for regenerating hard tissues	https://patents.google.com/patent/US20150105748A1/en
Development, production and use of generic Bioglass, and its crystallized version, using nAPO3 as the exclusive source of phosphorus	https://patents.google.com/patent/BRPI0900608A2/en
Degradable mechanically enhanced Bioglass-based porous composite material and preparation method thereof	https://patents.google.com/patent/CN101288780B/en
Silver-containing, sol-gel derived Bioglass compositions	https://patents.google.com/patent/WO2000076486A1/en
Fluoride-containing Bioglass compositions	https://patents.google.com/patent/US4775646A/en

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