OPEN ACCESS
Saudi Journal of Oral and Dental Research
Abbreviated Key Title: Saudi J Oral Dent Res
ISSN 2518-1300 (Print) | ISSN 2518-1297 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article | **Pediatric Dentistry**

The Role of Bioactive Glasses in Modern Dentistry: From Remineralization to Regeneration

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DOI: https://doi.org/10.36348/sjodr.2025.v10i02.001 | **Received:** 25.12.2024 | **Accepted:** 31.01.2025 | **Published:** 04.02.2025

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Abstract

Aim: This review explores the potential of bioactive glasses in dentistry, focusing on their applications in dental restorations, implants, and tissue regeneration. The aim is to assess the challenges and opportunities in their use, as well as the future directions for enhancing their performance. ***Materials and Methods***: A comprehensive review of recent literature was conducted to analyze the properties, applications, and limitations of bioactive glasses in dental materials. Studies on the composition, mechanical properties, biocompatibility, and long-term in vivo performance were included. Methods to enhance the mechanical strength of bioactive glasses, such as the formation of composites and advanced nano structuring, were also explored. ***Results***: Bioactive glasses have shown great promise in promoting remineralization, supporting tissue regeneration, and bonding with hard tissues. However, challenges such as mechanical brittleness, high costs, and limited long-term stability have been identified. Research on enhancing mechanical strength through composites, as well as developing more cost-effective production methods, is ongoing. ***Conclusion***: Bioactive glasses offer significant potential for improving dental treatments and advancing regenerative medicine. Future research should focus on enhancing their mechanical properties, developing personalized bioactive materials, and exploring their integration with stem cell therapies and growth factors. With continued development, bioactive glasses could revolutionize dental restorations, implants, and oral tissue regeneration, providing innovative solutions for oral healthcare.

Keywords: Bioactive, Remineralization, Regeneration, Composites, Biocompatibility.

INTRODUCTION

Bioactive glasses represent a class of advanced biomaterials that have significantly impacted fields such as dentistry and orthopedics. Their discovery over four decades ago marked a fundamental shift in the functionality of biomaterials, evolving from bioinert to bioactive. This transformation enabled bioactive glasses to stimulate positive biological responses, such as osteoproductivity [1], following implantation into the human body. The driving force behind ongoing research in biomaterials has always been the need to replace damaged body parts to restore their physiological functions [2].

The concept of biomaterials, initially focused on the idea of maximum inertness in contact with body fluids, was dramatically expanded with the discovery of 45S5 Bioglass® by Hench in 1969 [3]. This milestone introduced a novel material capable of forming strong bonds with living tissues and activated specific cell pathways to promote favorable biological responses. Before this breakthrough, materials like metals and polymers were designed to be bioinert, but they resulted in fibrous encapsulation rather than stable bonding with tissues. Hench's work, particularly the development of a high-calcium Na_2O-CaO-SiO_2-P_2O_5 glass, led to the creation of Bioglass® (45S5), which is renowned for its ability to bond to bone and stimulate bone growth[4]. This innovative material revolutionized the field of biomaterials and paved the way for the development of bioactive ceramics, including synthetic hydroxyapatite (HAp) and calcium phosphates [3-5].

The fabrication techniques for bioactive glasses encompass both traditional melting methods and sol-gel processes. Regardless of the technique used, the key feature shared by all bioactive glasses is their ability to interact with living tissues, forming strong bonds to bone and, in some cases, soft tissues. This bioreactivity is achieved through the formation of a calcium-deficient, carbonated apatite layer on the glass surface when it comes into contact with physiological fluids or during in vivo applications. This surface layer plays a critical role in establishing a bond with bone and is a defining characteristic of bioactive materials used in orthopedic implants, bone replacement, and tissue engineering scaffolds [6-8].

These materials initially found applications in small bone replacements, such as in middle ear surgery. Over time, their potential expanded into areas like periodontology, endodontics, and as coatings for metallic orthopedic implants. More recently, bioactive glasses have shown great promise in the field of tissue engineering, particularly for bone regeneration and scaffold development, with both micron-sized and nanoscale particles being considered. Furthermore, bioactive glasses have been explored for their hemostatic properties, with research demonstrating their ability to accelerate clotting time in laboratory tests, offering potential applications in wound healing and surgical procedures [4-9].

Bioactive glasses also exhibit antibacterial properties and can promote remineralization, especially when used in dental applications. They have been shown to occlude dentinal tubules, which may reduce dentine hypersensitivity. Additionally, bioactive glasses offer superior performance in air polishing for stain removal and can be employed for cavity preparation via air abrasion. These diverse applications underscore the versatility and transformative potential of bioactive glasses in medicine and dentistry [10, 11].

Chemical Structures and Variants of Bioactive Glasses

Bioactive glasses are classified into various types based on their chemical compositions, each of which offers unique properties for therapeutic and clinical applications [60]. Some bioactive glasses, including Bioglass 45S5 and S53P4, are FDA-approved for use in medical and dental treatments [61, 62]. These materials are highly biocompatible and exhibit similarity to bone hydroxyapatite in their calcium and phosphate content. Bioactive glasses facilitate bonding and integration with bone tissues by forming a silica gel layer that promotes osteoblast proliferation, differentiation, and organic bone matrix synthesis [63, 64]. As a result, bioactive glasses are extensively utilized in both medical and dental fields [65]. For instance, Bioglass 45S5 was first applied clinically to treat conductive hearing loss by reconstructing the middle ear's bony structures, and it has since been used in over 1.5 million cases globally [66].

There are three main categories of bioactive glasses: silicate-based (SiO_2), phosphate-based (P_2O_5), and borate-based (B_2O_3). The most commercially established formulation is Bioglass 45S5, composed of 45% SiO_2, 24.5% Na_2O, 24.5% CaO, and 6% P_2O_5 [67]. Additionally, bioactive glasses may incorporate biocompatible minerals such as fluorapatite, wollastonite, diopside, and tricalcium phosphate to enhance their properties. For example, the alkali-free (Na-free) bioactive glass known as FastOs BG contains 70% diopside, 10% fluorapatite, and 20% tricalcium phosphate [68, 69]. Research has focused on modifying the composition of Bioglass 45S5 by adding or removing specific ions to optimize its suitability for different clinical applications [71]. A recent development in this area is Biosilicate, a novel crystallized bioactive glass-ceramic with a composition of 48.5% SiO_2, 23.75% Na_2O, 23.75% CaO, and 4% P_2O_5, which has shown promising potential in various medical applications [70, 71].

Application of Bioactive Glasses in Dentistry

These materials provide several advantages, such as supporting the structure of biological tissues, acting as effective scaffolds, and inhibiting bacterial growth, which make them highly useful in various dental applications [12]. The diverse uses of bioactive glasses in dentistry are outlined below and summarized in (Figure 1).

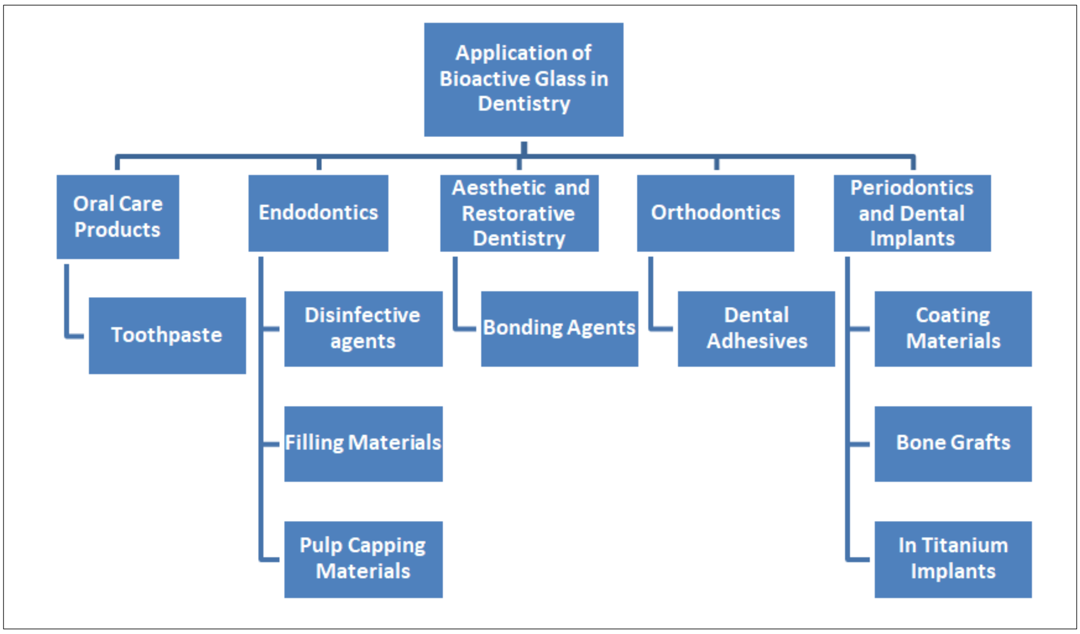

Figure 1: Application of bioactive glasses in dentistry

Although bioactive glasses are widely used in dentistry, there are still challenges to their broader adoption. One significant issue is the repair of bone defects in both orthopedic and dental surgeries. The mechanical limitations of current glass scaffolds, along with related challenges, require further investigation for improvement. Additionally, the evolving use of bioactive glasses in contact with soft tissues necessitates a reconsideration of biomechanical factors to ensure compatibility with the delicate collagen tissues [13].

Applications of Bioactive Glass in Oral Care Products

Bioactive glasses are increasingly being incorporated into dental products, particularly toothpaste [15], due to their beneficial properties [14]. These glasses are known to release antibacterial agents, promote remineralization, and help alleviate tooth sensitivity [16]. A well-known bioactive glass, NovaMin (calcium-sodium-phosphate silicate), is commonly used in toothpaste to enhance remineralization and reduce sensitivity. NovaMin works by releasing calcium and phosphate ions that raise the pH of the mouth, leading to the deposition of calcium phosphate, which eventually converts to hydroxyapatite [17]. Unlike other calcium-based products that release calcium in an initial burst, NovaMin provides a continuous release of these ions. Another bioactive glass product, BiominF, contains fluoride and phosphate and aids in the formation of fluorapatite (FAP) [18-20]. In 2021, the first toothpaste with both bioactive glass and fluoride received FDA approval. This toothpaste helps improve the acid resistance of fluorapatite on the tooth surface and within exposed dentin tubules by controlling the gradual release of calcium, phosphate, and fluoride ions over an extended period after brushing [21].

Application of Bioactive Glass in Endodontics

The use of biomaterials in dentistry is well-established and their significance is widely recognized. In the field of Endodontics, research often explores materials that have been rigorously tested both scientifically and clinically, alongside new innovations designed to improve treatment outcomes and success rates [22]. Bioactive glass (B-G) has emerged as a valuable material for promoting hard-tissue healing, particularly in endodontic treatments. Its chemical composition, which includes elements such as silicon, sodium, calcium, and phosphorus oxides, mirrors the mineral structure of human bone and dentine, making it especially suitable for dental applications [23, 24]. With over forty years of use, B-G's biocompatibility, regenerative abilities, and antimicrobial properties have made it an important material, although its dental applications remain relatively limited [24].

Application in Aesthetic and Restorative Dentistry

Dentin hypersensitivity is a condition marked by intense, short-term pain triggered by thermal, chemical, or tactile stimuli. The prevailing theory behind this pain is the hydrodynamic theory, which suggests that stimuli cause fluid movement within the dentinal tubules. This fluid movement stimulates mechanoreceptors near the pulp, activating nerve endings of Aδ fibers and resulting in sharp pain [25, 26]. According to this theory, reducing dentin hypersensitivity pain can be achieved by either sealing the dentinal tubules [27], or blocking the nerve endings [28]. Bioactive glasses can effectively alleviate pain associated with dentin hypersensitivity by interacting with collagen fibers and forming hydroxyapatite deposits, which block the dentinal tubules [29]. Products like PerioGlas are designed to seal the dentinal tubules and reduce pain by bonding securely to the collagen in dentin [30].

When preparing teeth for composite restorations, a smear layer is formed, containing both tooth tissue debris and bacteria. This smear layer can obstruct the dentinal tubules and hinder effective bonding of resin components. To optimize bonding, the smear layer is typically removed through acid-etching, which exposes the dentinal tubules. However, acid-etching can activate matrix metalloproteinases (MMPs), which break down the collagen network in dentin, potentially leading to microleakage [31-34]. Bonding systems that include bioactive glass, in contrast to those without it, can reduce microleakage by remineralizing the mineral-deficient areas and enhancing the modulus of elasticity and hardness at the dentin interface [35].

Biosilicate, another form of bioactive glass, has also shown promise in treating dentin hypersensitivity. A clinical study confirmed the effectiveness of Biosilicate over a six-month period. The particles of Biosilicate, when in contact with dentin, react with the tissue inside the dentinal tubules, leading to tubule occlusion through the formation of hydroxyapatite, which creates a stronger bond. Additionally, other research has demonstrated that using a suspension of Biosilicate microparticles on dentin increases the bond strength of adhesive systems, further enhancing the restorative potential of bioactive glasses in dental care [36, 37].

Application in Orthodontics

In orthodontics, dental adhesives are crucial for bonding materials, such as attaching orthodontic brackets or composite resins to natural tooth surfaces [38]. While composite resins are hydrophobic and tooth surfaces are hydrophilic, the adhesive functions as an interface that facilitates bonding between the two materials. However, the presence of orthodontic brackets can create favorable conditions for bacterial growth, which may lead to tooth demineralization and the formation of white spot lesions (WSLs). To mitigate such risks, maintaining good oral hygiene, regular brushing, and using fluoride toothpaste and mouthwashes are recommended. Bioactive glasses have the ability to remineralize these white spot lesions, offering a promising solution [38].

Studies conducted in laboratory settings have shown that bioactive glasses can promote enamel remineralization more effectively and rapidly than traditional treatments like topical fluoride and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) [39]. However, further clinical trials are needed to verify these findings. One study revealed that orthodontic adhesives incorporating bioactive glass and fluoride could strengthen the apatite structure, potentially preventing the formation of WSLs. Another investigation demonstrated that orthodontic bonding agents containing bioactive glasses enriched with silver or zinc ions exhibited enhanced antimicrobial and remineralizing effects compared to conventional adhesives, helping to prevent demineralization up to 200 to 300 μm away from the brackets during pH cycling [40, 41].

One of the primary concerns in orthodontics is the enamel damage caused by the removal of residual orthodontic adhesive after treatment. Typically, slow-speed tungsten carbide burs are used for this task. A novel bioactive glass called QMAT3 has been evaluated in a study, comparing it with Bioglass 45S5 and tungsten carbide burs in terms of enamel damage during adhesive removal. The results showed that QMAT3 caused minimal enamel damage, making it a promising option for a more conservative approach to orthodontic adhesive removal [42].

Application in Periodontics and Dental Implants

Periodontitis is a prevalent chronic inflammatory disease that affects the periodontium, leading to clinical attachment loss, alveolar bone resorption, periodontal pockets, and gingival bleeding. If left untreated, it can result in tooth mobility and loss of periodontal tissue support [43]. In dental implantology, periodontitis may cause inflammation around the implant site, increasing the risk of implant failure due to compromised osseointegration and detachment. Therefore, the reconstruction of bone defects is crucial for enhancing the prognosis of dental implants [44].

Studies on animal models, particularly dogs, have demonstrated that bioactive glass particles can effectively promote bone mineralization and treat periodontal defects [45]. One such bioactive material, PerioGlas, has a composition similar to Bioglass 45S5 and is commonly used in bone grafts to regenerate osseous defects in periodontal treatments. PerioGlas particles, ranging from 90 to 710 μm, have the ability to penetrate bone defects and stimulate bone regeneration during periodontal surgeries [46-49]. Clinical outcomes have shown that using PerioGlas granules as graft material in tooth extraction sites leads to new bone formation and successful implant loading, ensuring long-term implant stability. Additionally, the application of PerioGlas in periodontal intrabony defects has been shown to significantly reduce probing depth and improve clinical attachment levels (CAL), with a similar clinical attachment gain to autogenous bone grafts in cases of moderate to severe chronic periodontitis [50].

The Role of Complementary Ions in Enhancing the Efficacy of Bioactive Glasses in Dentistry

Bioactive glasses are known for their strong mechanical properties, such as high stiffness and hardness. However, like many glass materials, they are inherently brittle and not suitable for load-bearing applications. To enhance their performance and broaden their clinical utility, complementary ions such as strontium, zinc, phosphorus, fluoride, cobalt, and silver are often incorporated into bioactive glasses. These ions can modify various properties, improving their functionality in dental applications [51-53].

The inclusion of cobalt, for example, has been shown to promote angiogenesis, particularly in bone grafting procedures, facilitating improved tissue healing. Additionally, the presence of silver in bioactive glasses contributes antimicrobial properties, enhancing the material's ability to resist bacterial colonization, which is essential in preventing infections and promoting healing [52].

Fluoride is one of the most beneficial ions to incorporate into bioactive glasses, offering several advantages in dental health. Fluoride helps prevent tooth decay by reducing enamel and dentin demineralization, enhancing remineralization, and inhibiting bacterial enzymes. It can also form fluorapatite (FAP) instead of carbonated hydroxyapatite, and fluorapatite is more resistant to acidic conditions. Thus, fluoride-modified bioactive glasses not only provide restorative benefits but also improve oral health by increasing the resistance of tooth structures to decay [54, 55].

Phosphate ions, typically present in bioactive glasses as orthophosphate, also play a key role in enhancing the material's properties. Increasing the concentration of P2O5 (phosphorus pentoxide) and other cations in fluoride-containing bioactive glasses helps preserve the integrity of the glass network and supports the formation of fluorapatite, making these bioactive glasses even more suitable for dental applications [56, 57].

Strontium, a bone-seeking agent similar to calcium, has been shown to enhance osteoblast proliferation and reduce osteoclast activity in cell cultures. This effect makes strontium-containing bioactive glasses particularly beneficial in bone regeneration applications, such as in periodontal treatments or bone grafts, as they promote bone formation while inhibiting resorption [57].

Lastly, zinc is another essential ion that can improve the bond between bioactive glass and bone tissue, further enhancing the material's performance in dental restorative applications [58].

Incorporating these complementary ions into bioactive glasses not only improves their physical properties but also enhances their biological activity, making them more effective in promoting tissue healing, remineralization, and overall oral health. These modified bioactive glasses have significant potential for clinical applications in restorative and periodontal dentistry [58, 59].

Challenges and Limitations

Despite their promising applications, bioactive glasses still face certain challenges. One of the most significant limitations is their brittleness, which can affect their durability, especially in load-bearing applications. To address this, researchers have focused on developing composites that combine bioactive glasses with other materials, such as polymers and ceramics, to improve their mechanical strength and toughness [37]. However, more research is needed to optimize these composites for clinical use.

Another challenge is the cost of bioactive glass materials, which can be higher than that of traditional materials like composite resins and ceramics. The production process for bioactive glasses, particularly those incorporating advanced nanotechnology, can be expensive, limiting their widespread adoption in clinical settings [38]. Moreover, the long-term performance and stability of bioactive glasses, particularly in vivo, are still areas that require further investigation.

Future Directions

The future of bioactive glasses in dentistry lies in overcoming their mechanical limitations and enhancing their clinical applicability. Advances in nanostructured bioactive glasses, composite materials, and improved processing techniques are likely to improve the mechanical properties of these materials while maintaining their bioactivity. Future research may also focus on the development of personalized bioactive glasses tailored to individual patient needs, such as those with specific oral health conditions or genetic predispositions [28].

Another exciting area of research is the use of bioactive glasses in regenerative therapies. Combining bioactive glasses with stem cells or growth factors could further enhance tissue regeneration and healing. Additionally, bioactive glasses may play a pivotal role in the development of new bioactive implants, scaffolds, and delivery systems for oral and craniofacial tissue engineering [26]. As our understanding of these materials grows, it is likely that their use will expand to new and innovative applications in dentistry and beyond.

CONCLUSIONS

Bioactive glasses have diverse applications across various dental disciplines, making the identification of affordable and accessible sources of bioactive glass crucial. Recent research has highlighted marine sponges, particularly those found in the Persian Gulf, as a promising resource for bioactive glass production. These sponges contain minerals within their structural skeletons, primarily composed of biosilica, which can be leveraged to create bioactive glass. As such, marine sponges present both a scientifically viable and economically advantageous option for bioactive glass extraction. Continued exploration of novel methods and sources for bioactive glass could significantly expand their use in dentistry, potentially improving the effectiveness and availability of dental treatments.

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