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Different bioactive glass formulations in enamel remineralization: A review

Mai. M. Sleem[1*], El-sayed Gad Eid[1], Amr.M. Abdelghany[2], Dina. S Farahat[1]

[1]Department of Dental Biomaterials, Faculty of Dentistry, Mansoura University, Mansoura, Egypt

[2]Spectroscopy Department, Physics Research Institute, National Research Centre, Giza, Egypt

maisleem@mans.edu.eg,drgadclincc@gmail.com,a.m_abdelghany@yahoo.com

farahatdina4@gmail.com

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Abstract

Dental caries is a dynamic process characterized by alternating cycles of demineralization and remineralization, influenced by factors such as bacterial activity, dietary habits, and salivary composition. Current caries management focuses on early detection of carious lesions and enhancing remineralization to restore lost minerals and prevent lesion progression. Bioactive glass has emerged as a promising material for enamel remineralization, offering an effective alternative to conventional fluoride-based treatments. Its unique ability to release calcium and phosphate ions facilitates hydroxyapatite formation, enhancing enamel integrity and resistance to demineralization. This narrative review explores the role of bioactive glass in the management of white spot lesions, highlighting its mechanism of action and various delivery systems, including toothpaste, varnishes, air abrasion powders, bleaching agents, and orthodontic adhesives.

Keywords: Bioactive glass, Toothpaste, Varnish, Air abrasion, Bleaching, Orthodontic adhesives

Introduction

Dental caries is a dynamic process involving alternating cycles of demineralization and remineralization rather than a continuous loss of tooth minerals. Lesion progression or regression depends on the balance between demineralizing factors, such as cariogenic bacteria, fermentable carbohydrates, and

* **Author for correspondence: Email:** maisleem@mans.edu.eg

salivary dysfunction, and protective factors, including antibacterial agents, remineralizing ions, and adequate saliva. A cavity represents the advanced stage of enamel mineral loss, driven by biofilm activity and prolonged sugar exposure***(Philip, 2019)***. A white spot lesion (WSL) is a non-cavitated, early clinical manifestation of enamel demineralization that can be reversed through remineralization. If left untreated in its early stages, WSL may progress to a cavitated carious lesion ***(Richter et al., 2011)***. Based on the current understanding of caries process, minimum Intervention Dentistry (MID) is a contemporary approach in dentistry that prioritizes early caries detection, remineralization of initial lesions, and minimally invasive restorative treatments. It emphasizes preserving tooth structure and maintaining pulpal health, advocating for operative intervention only when cavitation occurs and the oral health balance is compromised***(de Moura et al., 2023)***.

Enamel remineralization serves as a clinically effective strategy for restoring the natural properties and structure of enamel while mitigating the limitations of restorative materials. This process involves replenishing minerals lost during the early stages of demineralization, thereby enhancing enamel hardness and integrity ***(Xu et al., 2022)***. Fluoride plays a key role in the non-invasive management of non-cavitated caries lesions by promoting remineralization. Its efficacy depends on the presence of sufficient calcium and phosphate ions in saliva or plaque, which are essential for the formation of fluorapatite ***(Cochrane et al., 2010)***. Therefore, remineralizing agents containing calcium and phosphate play a crucial role in the restoration of enamel integrity, both with and without fluoride supplementation. Bioactive glass is a reactive material primarily composed of calcium, sodium, phosphate, and silicate. Upon exposure to bodily fluids, it releases calcium and phosphate ions, which undergo a series of rapid reactions leading to the formation of hydroxyapatite crystals. Due to its bioactive properties, it has gained widespread use as both a bone graft material and a remineralizing agent ***(Agrawal and Patel, 2025)***. This review highlights the role of bioactive glass in the early treatment of enamel caries and explores various application methods to optimize its remineralizing efficacy on demineralized enamel surfaces.

Enamel structure

Enamel, the most highly mineralized tissue in the human body, exhibits exceptional mechanical properties. Its combination of high hardness, stiffness, and resilience enables it to withstand numerous masticatory cycles under significant biting forces ***(Beniash et al., 2019)***. Dental enamel consists of 96 wt% inorganic material, 4wt% organic material and water ***(Cui and Ge, 2007)***. The inorganic component consists mostly of hydroxyapatite crystals with trace amounts of fluoride, sodium, magnesium, zinc, and strontium. Enamel apatite consists of approximately 75% hydroxyapatite, 19% carbonate apatite, 4.4% chlorapatite, 0.66% fluorapatite, and 2% non-apatite phases ***(Kunin et al., 2015)***. Fluorapatite is formed when fluoride ions substitute hydroxyl groups within the hydroxyapatite structure, leading to enhanced mechanical strength compared to pure hydroxyapatite. The partial replacement of hydroxyl ions (–OH) by fluoride ions in enamel apatite increases crystal hardness and stability while also improving resistance to acidic conditions in the oral environment ***(Pajor et al., 2019)***. Hydroxyapatite aggregates into nanorods, which subsequently organize into enamel prisms. Most of these prisms are oriented with their long axes nearly perpendicular to the tooth surface ***(Xu et al., 2012)***. The crystals at the core of the prism are oriented parallel to its long axis and gradually fan outward toward the edges. Variations in crystal orientation at the prism interface create spaces that are filled with organic components and water, forming the interprismatic material known as the prism sheet.***(Yilmaz et al., 2015)***

Demineralization process

The processes of demineralization and remineralization occur continuously in a dynamic equilibrium within the oral cavity. Enamel demineralization results from acid exposure, either from dietary sources or as a byproduct of microbial carbohydrate metabolism ***(Abou Neel et al., 2016)***. An imbalance in this dynamic interaction, favoring demineralization, ultimately contributes to the development of carious lesions. Hydroxyapatite has a critical pH ranging from 5.3 to 5.5, below which enamel demineralization occurs, while remineralization takes place when the pH exceeds this range. In contrast, fluorapatite has a lower critical pH of approximately 4.5, making it more resistant to acidic conditions ***(Mitthra et al., 2020)***. On the other hand, carbonate apatite is more susceptible to demineralization under acid attack ***(West and Joiner, 2014)***. Demineralization is governed not only by pH but also by the concentration of calcium and phosphate ions in solution ***(Li et al., 2014)***. In its early stages, demineralization can be identified using an electron microscope. As the process advances through multiple phases, it becomes clinically observable as a white spot lesion (WSL), which may further progress to cavitation ***(Mitthra et al., 2020)***. White spot lesions (WSLs) present as opaque, chalky surfaces due to decreased water content and increased enamel porosity, which becomes filled with air. Dental enamel has a refractive index of 1.62, while air and water have refractive indices of 1.0 and 1.33, respectively. The greater refractive index contrast at the enamel-air interface compared to the enamel-water interface leads to increased light scattering, resulting in higher opacity ***(Malcangi et al., 2023)***.

Enamel remineralizing agent

Ameloblasts secrete enamel during formation but become non-functional once they reach full thickness. Thus, enamel cannot regenerate after development and is only altered through mineral gain and loss ***(Sa et al., 2014)***. Remineralization involves the replenishment of mineral ions lost during demineralization, facilitating the restoration of hydroxyapatite (HA) crystals. Saliva serves as a natural remineralizing agent by providing a continuous supply of calcium and phosphate ions, which contribute to buffering bacterial acids and maintaining enamel integrity. However, the remineralization capacity of saliva is limited due to the low ion concentration gradient between saliva and the demineralized lesion ***(Farooq and Bugshan, 2021)***.

Fluoride is considered the gold standard for arresting carious lesions, with its widespread incorporation into oral care products being a key factor in the significant reduction of caries prevalence rates ***(Philip, 2019)***. Fluoride contributes to the formation of intraoral reservoirs of calcium fluoride, which are protected from rapid dissolution by a phosphate-protein coating derived from saliva. This protective layer becomes more permeable under low pH conditions, ensuring fluoride availability when it is most needed ***(Peroš et al., 2013)***. Furthermore, fluoride exhibits antibacterial properties by inhibiting cellular enzymes, either independently or in combination with metal ions. Additionally, in the form of hydrogen fluoride (HF), it enhances proton permeability across bacterial cell membranes, further contributing to its antimicrobial activity ***(Koo, 2008)***.

However, Excessive fluoride intake or treatment poses potential risks, including dental fluorosis resulting from prolonged low-level exposure and fluoride toxicity associated with high concentrations***(Grohe and Mittler, 2021)***. The penetration of fluoride into demineralized enamel is restricted due to its strong interaction with surface-bound calcium ions, resulting in predominant deposition on the outer layer and limited diffusion into deeper regions. Furthermore, effective fluoride-induced remineralization depends on the presence of calcium and phosphate ions ***(Shen et al., 2018)***. Consequently, an external supply of ions is required to enhance the remineralization process. Non-fluoride-based remineralizing agents comprise calcium, phosphate, or calcium-phosphate compounds that facilitate mineral deposition. Examples include nano-hydroxyapatite, amorphous calcium phosphate (ACP), casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), tricalcium phosphate (TCP), and calcium sodium phosphosilicate (bioactive glass). These agents serve as alternatives or adjuncts to fluoride, particularly beneficial for individuals with fluoride sensitivity or those opting for non-fluoride-based dental treatments ***(Jefferies, 2014)***.

Bioactive glass

Conventional glasses are bioinert amorphous solids primarily composed of silica networks. To impart bioactivity, network-modifying oxides such as CaO and Na_2O are introduced, which disrupt the silica network, enhancing its solubility in physiological fluids ***(Skallevold et al., 2019)***. Bioactive glasses exhibit biocompatibility, eliciting no toxicity, inflammation, or foreign-body response. Composed of an inorganic, amorphous calcium-sodium phosphosilicate matrix, they interact with aqueous solutions such as saliva, leading to the formation of a hydroxycarbonate apatite layer that chemically bonds to treated surfaces. Their ability to integrate with bone is facilitated by the deposition of hydroxyapatite, which closely resembles the mineral composition of natural hydroxyapatite ***(Aboayana et al., 2024)***.

Composition of bioactive glass

Bioglass® 45S5, the first bioactive glass, was developed by Hench and is composed of 45 wt% SiO_2, 24.4 wt% CaO, 24.5 wt% Na_2O, and 6 wt% P_2O_5. The designation 45S5 is derived from the silica content, which constitutes 45 weight percent as the network former, and the calcium-to-phosphorus molar ratio of 5:1 ***(Filip et al., 2022)***. Building upon this composition, Hench further developed and characterized an extensive series of glasses within the SiO_2-CaO-Na_2O-P_2O_5 quaternary system, all of which contain 6 wt% P_2O_5 ***(De Aza et al., 2007)***. The SiO_2 content and Ca/P ratio can be adjusted to enhance bioactivity. Numerous studies have been conducted to determine the optimal bioglass composition. Researchers have also explored the incorporation of various ions, including magnesium, calcium, cerium, zinc, aluminum, and strontium, to further improve the properties of bioglass ***(Pazarçeviren et al., 2018)***.

Manufacture of bioactive glass

Bioactive glass can be fabricated using either the melt-quenching or sol-gel method. The first bioactive glass, developed by Hench, was synthesized through the melt-quenching technique. In this process, various precursor oxides or carbonates are thoroughly mixed using a ball-milling procedure in an acetone medium. The resulting powder is then subjected to high-temperature melting in a high-resistance furnace. The molten glass is rapidly quenched in air using copper plates to form glass frits, followed by an annealing step at 500°C to eliminate internal stresses within the material ***(Kaur et al., 2014)***. The sol-gel method mainly involves the formation and assembly of silica nanoparticles at room temperature. This chemical synthesis approach relies on a solution of precursor compounds undergoing polymer-like reactions at ambient conditions to form a gel. The resulting gel is a wet inorganic silica network with covalent bonds, which can be dried and heated—typically up to 600°C—to convert it into glass***(Hench and West, 1990; Li et al., 1991)***.

Bioactive glass mechanism of action

Upon exposure to bodily fluids, sodium ions rapidly leach from the glass surface, followed by the release of calcium and phosphorus ions. This ion exchange leads to the degradation of the silica network, resulting in the formation of silanol (Si-OH) groups, which subsequently undergo re-polymerization to form a silica-rich surface layer. An amorphous calcium phosphate layer then precipitates on this silica-rich layer and gradually crystallizes into hydroxycarbonate apatite (HCA). The resulting HCA exhibits a chemical composition similar to that of dental apatite, enhancing its adhesion to enamel ***(Madan et al., 2011)***. HCA acts as a template for hydroxyapatite crystallization ***(Abbasi et al., 2015)***. Additionally, Bioactive glass-45S5 demonstrates bactericidal effects against *Streptococcus mutans* in oral biofilms, primarily due to the release of alkaline ions that elevate pH levels. Beyond fostering an alkaline environment, the addition of inorganic ions such as silver, magnesium, strontium, and zinc further enhances its antibacterial properties. Cation-doped bioactive glasses have shown significant bactericidal activity against *S. mutans* and *Lactobacillus casei*. Among these, silver-doped bioactive glass exhibited the most notable anticariogenic effect ***(Ramadoss et al., 2022)***.

Different delivery systems of bioactive glass

Bioactive glass has been widely integrated into various anticaries oral care formulations, primarily in toothpaste. Additionally, it has been incorporated into prophylactic powders and dental materials to aid in the treatment of enamel demineralization ***(Taha et al., 2017)***.

Bioactive glass in toothpaste

Toothpaste formulations have advanced from basic abrasives to complex compositions specifically designed for remineralization and antibacterial protection ***(Prasad et al., 2024)***. Bioactive glass-based toothpaste helps prevent dental caries by releasing calcium and phosphate ions, promoting enamel restoration and enhancing acid resistance. Additionally, bioactive glass aids in dentin hypersensitivity by occluding exposed dentinal tubules with hydroxyapatite-like deposits, reducing nerve exposure ***(da Cruz et al., 2018)***. NovaMin, the commercial name for bioactive glass, has been incorporated in many toothpastes ***(Hsu et al., 2021)***. Golpayegani et al. ***(2012)***found that NovaMin toothpaste significantly enhanced the surface hardness of artificially induced enamel lesions compared to fluoride-containing toothpaste. Gjorgievska et al. ***(2011)*** recommended the use of NovaMin-containing toothpaste following bleaching procedures to aid in the restoration of mineral tissue integrity. Prabhakaran et al. ***(2010)*** and Salian et al. ***(2010)*** agreed in their studies that dentifrice containing NovaMin significantly reduced dentin hypersensitivity compared to potassium nitrate toothpaste, attributed to its ability to form hydroxyapatite crystals and effectively occlude dentinal tubules. Pradeep et al. ***(2012)*** reported a significant reduction in dentin hypersensitivity after treatment with bioactive glass-containing tooth paste compared to potassium nitrate. Tai et al.***(2006)*** Reported that NovaMin-containing toothpaste exhibited anti-plaque properties and effectively reduced gingivitis, despite the absence of fluoride or antibiotics in its formulation.

BioMin F is a commercially available bioactive glass incorporating fluoride, designed to facilitate the formation of fluorapatite (FAP)***(Jafari et al., 2022)***. Eldeeb et al. ***(2024)*** concluded that BioMin F toothpaste shows potential in restoring white spot lesions on demineralized enamel surfaces. Farooq et al.***(2021)*** reported that BioMin F toothpaste exhibited superior surface microhardness, lower surface roughness, and enhanced enamel remineralization compared to fluoride toothpaste. Ergucu et al. ***(2023)*** reported that BioMin F toothpaste resulted in higher calcium and phosphate deposition on bleached enamel compared to fluoride and NovaMin-containing toothpastes. Poopirom et al. ***(2025)*** proposed BioMin F toothpaste as a viable alternative for promoting remineralization in children while minimizing the risk of fluoride toxicity and dental fluorosis.

Bioactive glass varnishes

The film-forming capability of dental varnish prolongs its contact with the tooth surface, enhancing its remineralizing efficacy and reducing the required frequency of application, making it particularly beneficial for uncooperative patients ***(Virupaxi et al., 2016)***. Kim et al.***(2021)*** developed a light-cured bioactive glass varnish and demonstrated the formation of hydroxyapatite crystals along with an enhancement in surface microhardness following 14 days of application. Cengiz et al.***(2025)*** suggested that fluoridated bioactive glass varnish could be a better alternative to fluoride varnish. Durmuş et al. ***(2023)*** reported that bioactive glass varnish exhibited a remineralizing effect on demineralized enamel comparable to that of fluoride varnish, suggesting its potential as a less toxic alternative to fluoride-based treatments. Hardikar et al. ***(2023)*** observed that the incorporation of bioactive glass into commercial fluoride varnish enhanced mineral content and surface hardness and reduced lesion depth.

Bioactive glass prophylactic air abrasion powder

Air abrasion is a minimally invasive dental technique utilized for the removal of extrinsic stains, as well as sound and carious enamel and dentin. It is commonly employed for various purposes, including esthetic enhancement, remineralization, caries removal, and the creation of microroughness to improve adhesion prior to restorative procedures. This technique is well-accepted by patients due to its absence of vibration, lack of heat generation, and reduced need for local anesthesia ***(Banerjee et al., 2011)***. Alumina is the most commonly utilized abrasive powder in air abrasion procedures due to its non-toxic nature, chemical stability, colorlessness, cost-effectiveness, and widespread availability. Other abrasive materials, including sodium bicarbonate, glycine, erythritol, and bioactive glass, are also employed. Among these, bioactive glass is unique in its ability to induce remineralization and contribute to caries prevention ***(Eram et al., 2024)***.

Dionysopoulos et al. ***(2020)*** demonstrated that air abrasion using Bioglass 45S5 has the potential to protect enamel from erosion associated with poor dietary habits. Karaoulani et al. ***(2022)*** demonstrated that both bioactive glass and fluoridated bioactive glass powders facilitated apatite crystal formation on enamel under acidic conditions, providing protection against erosive challenges. Banerjee et al. ***(2010)*** reported that air abrasion using bioactive glass powder provided a more prolonged desensitizing effect and demonstrated superior whitening efficacy compared to sodium bicarbonate. King et al. ***(2016)*** found that bioactive glass powder was less invasive than alumina powder, indicating more safe controlled enamel cleaning. Furthermore, bioactive glass ,with hardness lower than enamel, could be used to effectively remove orthodontic adhesive without damaging sound enamel as reported by Taha et al. ***(2018)***.

Bioactive glass in bleaching

Tooth bleaching is a widely requested esthetic procedure for enhancing smile aesthetics. However, it is considered an erosive process, affecting the organic protein components and altering the mineral phase, leading to noticeable morphological changes on the tooth surface ***(Coceska et al., 2016)***. Borges et al. ***(2009)*** observed that a 35% hydrogen peroxide bleaching agent led to a decrease in both surface and subsurface enamel microhardness. Remineralizing agents are utilized before, during, or after bleaching treatments to minimize enamel damage and alleviate dental sensitivity, helping to counteract the adverse effects associated with the bleaching process ***(Kutuk et al., 2018)***.

Yang et al. ***(2022)*** reported that the addition of 45S5 bioactive glass to 30% hydrogen peroxide increased the pH from 3.5 to 5.5, preventing enamel demineralization and preserving surface morphology. Dascanio et al. ***(2023)*** demonstrated that the addition of 10% 45S5 bioactive glass to 35% hydrogen peroxide reduced surface hardness loss while maintaining the whitening efficacy. Yezdani et al. ***(2024)*** demonstrated in their study that the integration of strontium fluorophosphate bioactive glass into hydrogen peroxide enhanced both tooth color and surface hardness. Kavoor et al. ***(2024)*** found that the addition of bioactive glass to carbamide peroxide significantly improved surface microhardness. Kakodkar et al. ***(2013)*** concluded that incorporating NovaMin into carbamide peroxide effectively reduced dental sensitivity without compromising tooth color.

Bioactive glass in orthodontic adhesive systems

White spot lesions (WSLs) commonly develop during orthodontic treatment with fixed appliances, primarily on the gingival and buccal surfaces, and may progress to cavitated caries if left untreated. Consequently, various strategies have been explored to enhance the remineralization and antibacterial properties of orthodontic adhesives ***(Patano et al., 2023)***. Choi et al. ***(2021)*** reported that incorporating 1% and 3% mesoporous bioactive glass nanoparticles enhanced shear bond strength while improving antibacterial and remineralizing effects. Chaichana et al. ***(2022)*** reported that orthodontic adhesives incorporating Sr-bioactive glass nanoparticles enhanced ion release, facilitated calcium phosphate precipitation, and inhibited cariogenic bacteria, potentially reducing white spot lesion formation. Kim et al. ***(2023)*** reported that incorporating Zn-bioactive glass into orthodontic adhesives preserved immediate bonding performance while promoting remineralization through calcium-phosphate deposition on demineralized enamel surfaces. Mohammed et al. reported that incorporating 1% bioactive glass into self-adhesive resin enhanced surface microhardness while preserving acceptable shear bond strength.

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