



The Use of Bioactive Glasses in Contemporary Dental Materials: A Literature Review

Luciano Bonatelli Bispo*

Clinical Practice by Department of Dentistry, University of São Paulo, Brazil

***Corresponding Author:** Luciano Bonatelli Bispo, Clinical Practice by Department of Dentistry, University of São Paulo, Brazil.

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Abstract

The new concepts have changed the paradigms of Dentistry. The minimally invasive procedures with conservation of the tooth structure and the advances in smart materials are a tendency. Thus, a better understanding of its biology and its use is essential to clinical employment. The bioactive glasses have been used to stimulate the remineralization process in cariogenic challenges because the feature of release ions to jeopardized structures like dentin and enamel. The increase of pH in the oral environment, hence, with antibacterial effect and long-term ions leaching are have been desired. Therefore, these materials have been used in luting cements, composite resins, dentin bonding agents, tooth bleaching agents and anti-hypersensitivity dentin products. The aim of this literature review was to do an explanation about the bioactive glass to promote a better understanding of its real advantages in clinical practice.

Keywords: Longevity; Materials Testing; Dental Caries

Introduction

The evolution of materials and restorative techniques developed new concepts. Nowadays that the beauty is highly valued and aesthetic surgeries have been enhanced the social-cultural patterns the search for new materials with great longevity have a responsibility to improve the quality of life. Materials in dentistry cannot be left out of this process. Therefore, the "smart materials" have been developed toward to stimulate the repair of tooth structure through the remineralization process leaching Ca^{2+} and PO_4^{3-} ions to the oral environment [1].

It is known that the dental caries formation take place in the following steps: 1) carbohydrates are fermented by acids from bacteria metabolism in the biofilm; 2) a decrease in pH causes demineralization of the tooth; 3) at first, white spots are formed, clinically, then cavitations of caries are formed [2].

Ancient civilizations, such as: Chinese, Egyptians and Indians had used biomaterials to build body parts and hide aesthetic defects [3]. However, just in 1969, Larry Hench [4], developed a bio-glass to be used clinically [5]. Hence, the Biovidro[®] 45S5 with 46.1 mol. % SiO_2 , 24.4 mol. % Na_2O , 26.9 mol. % CaO e 2.6 mol. % de P_2O_5 , has stimulated the hydroxyapatite formation $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$.

Furthermore, bioactive glasses have used for osseointegration to induce deposition of hydroxyl-carbonate apatite inducing natural mineralization of tissues. Antibacterial and acid neutralizing properties through the increase in pH have been studied [6].

In Dentistry, bioactive glasses have been applied for the augmentation of alveolar ridges [7], like a filler component of restorative dental materials (composite resins [8], dentin bonding agents [9]), for the treatment of hypersensitivity teeth [10], in the dental bleaching agents to remineralize the enamel [11], among others.

Aim of the Study

The goal of this literature review was to promote a better understanding of this new class of materials and elucidate clinicians and researchers about this new alternative in contemporary Dentistry.

Materials and Methods

The search of papers was done in the following databases: PubMed/MEDLINE, LILACS, BBO, SciELO and Google Scholar, with the indexing terms: bioactive glasses, dentin, dental enamel, testing materials, dentin bonding agents, micro-filler, degree of conversion, microtensile bond strength, biotechnology, restorative dentistry materials, airborne-particle abrasion, caries-affected dentin, den-

tin hypersensitivity, resin-dentin interfaces, ion release evaluation, bacterial penetration, MMPs activity (matrix metalloproteinases), bioactive properties, bio-active components, bioactive glass particulate filler composite, cytotoxicity, bonding performance, mechanical properties, shear bond strength and bonded-dentine interface.

It was considered eligible papers published between 2010 and 2019, preferably in English, that had a relationship with the goal of this literature review. A total of 83 articles were elected, 50 of which were excluded because they were not pertinent to the theme, or with materials other than the composition of bioglasses. Throughout the work, more references (4) were added because they are classical studies and relevant to the proposed subject.

Literature Review

Deng, *et al.* [11] (2013), indicated the benefits of bioactive glasses to form a protective layer on the enamel surface during hydrogen peroxide use for dental bleaching. The bleaching agent increased porosities, depressions and pits because the lost mineral from enamel. The dissolution of organic and inorganic dental matrices was induced by oxide-reduction reaction up to the point that only water and carbon dioxide remain. Thus, pre or post-bleaching use of bioactive glasses possessed much milder mineral loss and morphological changes. However, using bioactive glasses during hydrogen peroxide process showed the optimal way to reduce the microhardness loss of enamel while retaining the dental surface integrity. A quarter of the adult population is affected by dentine hypersensitivity and its consequences.

Cruz and Tuñas [12] (2018), studied treatment options for dentine hypersensitivity through over-the-counter (in the house of the patients) and professionally-applied (in office) products, with a focus on the role of bioactive glass-based toothpastes. Ideally, a desensitizing agent should have as properties: rapid action, long-term effects, be non-irritating to pulp, easy to apply, non-staining tooth structures and painless. Hence, incorporating bioactive glasses in toothpastes should be an easy and economical solution for desensitizing in-home treatments. The findings of that work promote the use of bioactive glass-based toothpastes because of its low cost, evidence that occlude the dentinal tubules, easy of employment and scientific based-evidence in the published literature. Three types of bioactive glasses (BAGs) are approved for clinical applications by the FDA and have been widely used as bone graft materials: 45S5, 45S5F and S53P4 [1,13]. So, Yang, *et al.* [1] (2016) used a commercially available orthodontic adhesive with the three BAGs approved by FDA (Food and Drug Administration) in the acid neutralizing property and shear bond strength. The highest value

in the bond strength was from 45S5F, followed by S53P4 and 45S5. The acid neutralizing ability indicated by the pH change of the acid solution was shown to be the best for the 45S5. Sinhoreti, *et al.* [14] (2015), evaluated the influence of air-abrasion with Bioglass 45S5 on the microtensile bond strength with total and self-etching techniques. Despite the teeth were stored only for 24 hours after bioglass 45S5 air-abrasion, very short period to make changes in this material to induce the dentin remineralization process by calcium precipitation. The bioglass 45S5 air-abrasion didn't promote improvements on microtensile bond strength rates in self-etching groups. Also, the bioglass 45S5 didn't increase the microtensile bond strength values for total-etching groups. Sauro, *et al.* [15] (2012), have shown the incorporation of bioglass into experimental adhesive systems did not prevent the reduction in bond strength values after 3 months of storage.

Bauer, *et al.* [9] (2016), have proposed that addition of niobium to the composition of the bioglass could be advantageous. The niobium incorporation results in higher chemical durability, improved biocompatibility, mechanical properties and increased radiopacity. The effect of adding micro-filler of niobium-phosphate bioactive glass to experimental bond agent has shown an increased degree of conversion that could have made the adhesive less prone to hydrolytic degradation during storage. Although the niobium-phosphate bioactive glass has some anti-biofilm activity, it is impossible to determine the effects of niobium on enzymes such as MMPs (matrix metalloproteinases) and cathepsins. MMPs and cathepsins are enzymes involved in collagen degradation exposed by lack of interdiffusion of resinous monomers of dentin bonding agents in the hybrid layer formation [16]. Many researchers are looking for an adhesive which is able to re-mineralize hybrid layers and restore the mechanical properties of mineral-depleted dental collagen structures within resin-bonded interfaces by biomimetic apatite formation.

The greatest challenge is to insert demineralized bioactive glasses smaller than 40 nanometers between collagen fibrils, according Sauro and Pashley [17] (2016) and Carneiro, *et al.* [18] (2016). Consonant Carneiro, *et al.* [18] (2016), the presence of niobium phosphate bioactive glass into commercial adhesives at 40% concentration maintained the degree of conversion values unaltered. However, it was unable to prevent, after 6 months of storage, a decrease in the microtensile bond strength rates. Profeta, *et al.* [19] (2012) had shown maintenance of microtensile bond strength values after 6 months of storage, but with an adhesive that was added 45S5 and with a solution to rewet the dentine with 45S5 in the composition too. It was hypothesized that bioactive micro-filler

particles may have reacted with water to release calcium hydroxide that increase the alkalinity of the environment and may have slowed the activity of MMPs.

Degrazia, *et al.* [20] (2016) did an experimental composite resin blend prepared using halloysite nanotubes doped with or without triclosan. Triclosan is a typical agent used in several toothpastes, mouth-rinse solutions and detergents. It is particularly active against *Streptococcus mutans*; one of the main pathogens of caries, along with *S. aureus*, *Lactobacillus spp.* and *Actinomyces spp.* Fillers were incorporated into the resin blend at different concentrations (5, 10 and 20 wt%). This study has assessed the degree of conversion, microhardness, solvent degradation, among others. The triclosan-encapsulated halloysite nanotubes up to 20 wt% into a composite promoted mineral deposition, with obvious benefits in remineralization processes. Because of the variable employment and the multiple outcomes found in research involving bioactive glasses, it is necessary to standardize the real findings and better understand their mechanism of action.

Discussion

Orthodontic adhesives containing bioactive glass

To the BAG-containing adhesives tested, the one with 61.25% of BAG resulted a significant increase of pH compared with the others including smaller amounts of BAGs [1]. The acid neutralizing effect was ranked in the following order: 45S5, S53P4 and 45S5F. These outcomes would be explained due to an increased release of ions with superior ability to raise the pH and a higher bioactivity rate. This would be speculated by constant releasing of F^- and OH^- ions at the glass surface. The F^- ions in the solution could react with the OH^- ions making the solution with a less pronounced pH rise. Thus, larger amounts of fluoride ions result in a buffering effect on the alkaline ions released. The 45S5 bioglass has a higher alkalization capacity by releasing smaller amounts of fluoride ions that can react with hydroxyl ions. With greater release of hydroxyl ions without reacting more alkaline is the environment. Even more, the debonded surfaces of BAG-containing groups showed an undamaged state after shear bonding test. Therefore, this is important clinically to improve the maintenance and minimizing the amount of tooth destruction mainly after removal of orthodontic brackets [1].

Bioactive glasses and human osteoblast cells

The most common behaviour observed in bioglass is the formation of a calcium-phosphate-rich layer when inside the body fluids independent of its composition [7]. Studies [21] have observed

that AP40 and RKKP exchange ions far slower than the original composition of the Hench's glass (45S5) [4,5]. Small amounts of La_2O_3 and Ta_2O_5 (RKKP) were added to furnish a possible nucleus for the deposition of ions involved in bone formation [7]. Hence, the slower leaching of ions of RKKP promotes the formation of silicate chain networks. These networks have demonstrated great packing density of the molecular chains. The adhesion of cells to bioactive materials like RKKP might not require an adhesive protein, thus, osteoblast cells can adhere directly or through a gel-like layer of bioglass to bioactive material [7]. This is very important in the phenomenon of osseointegration and as a graft material in increasing bone ridge.

Bioactive glass as a treatment option for dentin hypersensitivity

Studies of scanning electron microscopy have shown that the number of tubules in sensitive dentine is eight times higher than in non-sensitive dentine [12]. This is a relevant problem in public health around the world. It is known that bioglasses in contact with biological fluids react. Three process may occur in following the steps: releasing and formation of silanols, dissolution of the glass network and precipitation for occluding dentinal tubules [12]. Addition of bioactive glasses in hypersensitivity agents, like toothpastes, is responsible to the formation of a layer composed of calcium and phosphate induced by release of ions from the glass occluding the dentine tubules and lower the permeability levels of the teeth [12]. So, this layer crystallized into hydroxyapatite and the presence of silica accelerate the maturation of hydroxyapatite. All of this is promoted by bioactive glass triggers an osteoblast cell cycle, leading to rapid cell differentiation and proliferation [12]. The mesoporous silica nanoparticles with 100 - 350 nm in diameter were reported to able to fill-up 3 - 4 μm deeper than other dentinal hypersensitivity materials and protocols [10]. However, more studies could be conducted to promote the use of bioactive glass-based toothpastes to minimize the dentinal hypersensitivity.

Effect of bioglass air-abrasion on dentin bonding

Bioglass 45S4 [14] and niobium phosphate bioactive glass [22] have been tried to air-abrasion on the bonding performance of dentin bonding agents. The difficulty of adhesion in deep dentin is the large calibre of dentinal tubules and the high permeability of dentinal fluids that affect resin materials by hydrolytic degradation. Furthermore, the kinetic energy of airborne-particle abrasion with microparticles of 45S4 or niobium in deep dentin could have sealed the entrance to the dentinal tubules avoiding the passage of water through the entrance of the dentinal tubules. However, these

microparticles may have served as a link with the restorative material, which makes the strong union between organic and inorganic matrix, promoting higher bond strength values.

The presence of abundant minerals would be responsible to the highest bond strength rates obtained in healthy dentin [22]. Air-abrasion is commonly used to remove the affected tissue by caries and to cavities preparation in clinical practice. However, the purpose of applying BAGs on caries-affected dentin have been to contribute to remineralization, increase of pH and to prevent the bacterial growth, as well as minimizing the enzymes that degrade collagen, such as: MMPs and cathepsins. The results are contradictory in the consulted literature to air-abrasion, once papers have purposed the quality improvement of the hybrid layer but did not increase the microtensile bond strength values [14].

Dentin pretreatment with bioactive glass

In adhesive systems, the incorporation of BAGs is much complex [23]. Despite the incorporation of bioactive particles into resin materials to be frequent [9], the presence of acid monomers may lead to reactivity with the glass surface particles [24]. The bioactive glasses in an aqueous suspension on the dentin before the adhesive application seem to present more satisfactory outcomes [19].

While the adhesive systems can have protocols challenging, BAGs dispersed in water are capable of diffusing into the demineralized dentin, providing an efficient contact between the glass and the bottom of the hybrid layer. It has been required for inducing mineralization [23]. The 45S5 and 20% niobophosphate bioactive glass rewetting suspensions were able to maintain the microtensile bond strength values after three months of storage [23]. There was an increase in the hardness rates after three months of storage too [23].

It was postulated that a layer formed by niobium-oxygen bonds is less permeable due to more strong chemical bonds and the elevation of pH affected the integrity of the bacterial cytoplasmic membrane, guiding to cellular destruction. Therefore, calcium hydroxide has a widely known antimicrobial activity, so the dissociation of hydroxyl ions has generated an increase in the environment alkalinity [23].

BAGs on the enamel surface during dental bleaching products action

45S5 bioglass consists of 45% SiO₂, 24.5% Na₂O, 24.5% CaO and 6% P₂O₅ in weight [4,5]. It's a biocompatible material, with osteo-

conductivity, osteoinductivity and slow biodegradability [25]. The hydrogen peroxide is the most common bleaching agent used in office or in products over-the-counter. In tooth whitening the enamel is reached at a depth of up to 100 micrometers.

The evidence of morphological alteration has observed on enamel surfaces, such as: eroded enamel prisms, porosities and demolished interprismatic structures. The tooth whitening is achieved by decomposing hydrogen peroxide into oxygen radicals, which can destroy the double bonds or oxidize other chemical radicals in the conjugated chain of chromophore [11]. The major findings suggest that the use of hydrogen peroxide conjugated with BAGs have potentiated the enamel surface integrity, protective effect, reduce the mineral loss and minimizes all the possible morphological changes.

When the hydrogen peroxide and BAGs are employment at same time during the bleaching process compared to pre or post-bleaching use [11]. New formulations must be tested as well as pH incompatibilities with products on the market in order to confirm these findings [3,6].

Composite resins with bioactive glass

Restorative composite resins are named as materials in which the composition is: organic matrix (monomers), inorganic matrix (filler particles) and a silane to join the matrices. Recently, dicalcium phosphate dihydrate (DPCD) nanoparticles were functionalized with triethylene glycol dimethacrylate (TEGDMA) - a common monomer in Dentistry. DPCD (CaHPO₄·2H₂O) presents high solubility that is suitable like ion source with less soluble phases, such as hydroxyapatite. Notwithstanding, increasing TEGDMA content in resin blend was shown to increase the degree of conversion. The TEGDMA has a small size and flexible monomeric structure. The higher TEGDMA content in composites with a higher fraction of functionalized nanoparticles leading to the formation of a more heterogeneous network, with great facilitation of water sorption. Hence, the high hydrophilicity of TEGDMA would lead to increased composite degradation [26]. Silanization of calcium phosphate particles has demonstrated to negatively affect ion release due to the hydrophobic nature of silane coating. The phosphate tetrahedral structure inhibits the leaching of hydrogen phosphate that following the patterns of calcium ion. Therefore, it is in agreement with other studies [27].

The incorporation of triclosan-encapsulated halloysite nanotubes up to 20 wt% into a dental methacrylate-based material promoted mineral deposition constituting a real alternative in terms of remineralizing option in the oral challenges [20]. The decreas-

ing solubility in the silanized glass filler can be attributed to the protection of the glass structure by the silane based polysiloxane network [28]. Biostable glass is known by having a tetrahedron structure resistant to reactions. Meantime, bioactive glass is more open to reactions with cations which disrupt the Si-O-Si links with formation of non-bridging oxygen ions. The higher the number of non-bridging oxygen ion the, higher the bioactivity of bioactive glass [28].

A stronger bond between the substrate and filler could be done by saturating the particles by viscous acrylate using silane coupling agents [28]. Fibers of higher ratio have better reinforcing against stress transfer interruption capabilities than particulate fillers [28]. Notwithstanding, there are an inverse correlation between the quantity of extractable monomers and the cell viability [8]. Moreover, the cytotoxicity of composite resins must be attributed to the release of residual monomers, regardless if the composite with or without BAGs. The relatively short term of exposure to fluids will guide to extraction of unreacted monomers with all its undesirable features [8]. However, the exact mechanism of the antimicrobial effect of BAG remains unclear. It would be related to a local rise in pH, principally in the gap [29].

The hypothesis is that composites with BAG have some potential to slow down penetration into and demineralization within marginal gaps. These findings have been accorded with 15 wt% additions of bioactive glass fillers to composite resin demonstrated a significant antimicrobial effect to disorganizing the dental biofilm [29]. This is very important to prevent secondary caries, marginal infiltration, percolation and loss of the restoration. Resin fits the role of minimizing the infiltration of the margins at the level of the cavosurface angle, but it is impossible to postpone polymerization shrinkage (inherent in resinous materials). The ideal solution will be an anti-bacterial dental bonding agent used in conjunction with an anti-bacterial composite resin [29]. It is important to note that the true restorative material is the dentin bonding agent because its interaction is directly on the dentine.

BAGs and dentin bonding agents

The decline in bond strengths values in terms of percentage with etch-and-rinse adhesives system is higher than the self-etch adhesives with 1-ethyl-3 (3-dimethylaminopropyl) carbodiimide (EDC)-containing primer. This could be explained by the loss of integrity of resinous components within the hybrid layer due to polymer swelling and resin leaching that occur after water fluid sorption, which is more pronounced for simplified (two-step) etch-and-rinse adhesives than unsimplified systems (three-step)

[30]. Although, 2-step self-etch adhesive is considered as the most durable bond. This can be due to the fact that the self-etch adhesives do not completely expose the dentin collagen matrix. Self-etch adhesives maintain more residual hydroxyapatite crystal in their hybrid layers which minimizes activation of dentin MMPs (matrix metalloproteinases).

The microtensile bond strength values can be revealed that bonded dentin interfaces created with EDC pretreatment improves the durability of the resin-dentin bonds [30]. Also, previous results suggest that resin encapsulation of acid-etched collagen fibrils is more complete in the top half of the hybrid layer, but not in the bottom half [31]. These hydrophilic resin monomers are adhesives formulations cause high sorption of water by the resin systems and generate a hybrid layer that behaves as a permeable membrane after polymerization, permitting water movement throughout the bonded interface [31].

The water movement produces a diffusion mechanism, with the creation of water-filled channels degrading its hydrophilic phase [31]. Tay and Pashley [32] (2008) had showed that Portland cement in a phosphoprotein analogous-containing fluid can form a meta-stable amorphous calcium-phosphate, which can deposit inside the collagen organic network in the form of apatite crystallites. From a clinical point of view, it seems that long-term bonding stability of an adhesive is more desirable than achieving higher initial bond strengths [16,33].

Bonding to dentin is considered a more challenging scenario, due to the composition on this substrate. The outcomes can conclude that the bond strength to dentin was affected by the bonding strategy and the pH of the adhesive used [16]. So, the high zinc-content of the bioglass-Zn (20 wt%) may have a role in protecting the collagen fibrils from MMPs, which are responsible for the degradation process in carious dentine and within the hybrid layer. Hence, the creation of a moderate alkaline environment within the bonded-dentine interface due to the exchange between Na^+ and $\text{H}^+/\text{H}_3\text{O}^+$ ions and the rapid release of Ca^{2+} and PO_4^{-3} species from the bioactive glasses may also have contributed in the inhibition of pH-dependent MMPs [15].

Nowadays it is known that a specific formulation of resin bonding systems containing bioactive fillers such as with Zn may offer the possibility of increasing the nano-mechanical properties of hybrid layer and reduce the micropermeability along the dentine-bonded interface [15]. All this by therapeutic remineralisation of imperfect mineral-depleted areas [15].

Nanosized bioactive glass particles or methacryl-functionalized polyhedral oligomeric silsesquioxanes (POSS) have been tried in dentin bonding agents [34]. The effect of the multifunctional POSS particles on the degree of conversion, sol fraction and water sorption indicate an improved cross-link density of the filled dentin bonding agent while keeping the viscosity low [34]. It's possible to integrate bactericidal effects with bioactivity in dentin bonding agents [35].

Dental adhesives containing crystalline titanium nanoparticles (NPs) were analysed³⁵. All the tested NP adhesives showed bioactive behaviour; accumulation of hydroxyapatite crystals on the adhesion surface with your intrinsic benefits [35]. MDPB (a novel dental resin monomer - 12-methacryloyloxydodecylpyridinium bromide) at 5% (concentration of commercial adhesive) achieved 89% inhibition of soluble MMP-9 and approximately 90% inhibition of matrix-bound MMPs. Compared with chlorhexidine or benzalkonium chloride, which may leach out from bonded interfaces over time, polymerizable MMP-inhibitors are advantageous as they can be retained in the hybrid layers for years by copolymerization, producing a more durable interface than conventional dentin bonding agents [36].

More recently, sodium-calcium-aluminum-magnesium silicate hydroxide (HOPC), aluminium-magnesium-carbonate hydroxide hydrates (HCPMM) and titanium oxide (HPCTO) were mixed with a type-I ordinary Portland cement to create three bioactive micro-fillers [37]. Beyond observation of minerals precipitants within the adhesive interface, there was a contribution to seal the dentinal tubules due to the small-scale volume of the forming gels, increased with a slight expansion of the silicate-based materials in solution. There were the prevention hygroscopic effects and hydrolytic degradation of the polymer chains. However, the metallic ions on phyllosilicate were released by cations present in the surrounding solutions and acted as effective antibacterial substances in the long term [37].

Adhesives doped with bioactive niobophosphate micro-filler [18] at 40% concentration into commercial adhesives showed the degree of conversion values unaltered and unable to prevent a reduction in bonding strength after 6 months. Meantime, the presence of the niobophosphate micro-filler next to the collagen network may provide ions like Ca^{2+} and PO_4^{-3} to inhibit enzymatic degradation, bacterial growth and remineralize collagen. Contrary, Bauer, *et al.* [9] (2016), presented outcomes that reveal the inclusion of micro-filler of niobium phosphate bioactive glass like beneficial in produce an adhesive system with higher radiopacity,

degree of conversion and Knoop hardness and with no decreasing of the bond strength after 6 months in water storage (statistically no significant decreasing when compared to the control-without BAGs).

Conclusion

It can be observed in the consulted literature that bioglasses have enormous capacity to be incorporated in dental materials. Mainly by the ionic release of calcium and phosphate that contribute to the remineralization of dental hard tissues lost through caries. Also by the alkalization of the acid medium promoted by the release of enzymes by the aciduric and acidogenic bacteria in the oral environment. This inhibits bacterial colonization and prevents biofilm formation.

Depending on the formulation of the bioglass used, they may also reinforce resins and prevent or delay hydrolytic degradation. Further studies are needed to determine if bioglass also acts against the harmful effects of MMPs.

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