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Bioactive glass material and its applications in dentistry

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Abstract
Bioactive glasses are silicate-based materials that can form a strong chemical bond with the tissues. Bioactive glass materials can bond to both soft an hard tissue and their bioactivity is related to the formation of a biologically active hydroxyapatite layer on the surface of the glasses. They have a wide range of applications in both medicine as well as in dentistry. This paper reviews the development, applications and different clinical studies of bioactive glass materials particularly in the field of dentistry.

Keywords: bioglass, hydroxyapatite, bioactive glass

1. Introduction
Bioactive glasses are novel dental materials that are used in dentistry. A material is considered to be bioactive, if it gives an appropriate biological response and results in the formation of a bond between material and the tissue. Bioactive glass is made of synthetic mineral containing sodium, calcium, phosphorous and silica (sodium calcium phosphosili cate), which are all elements naturally found in the body. Bioactive glass materials have been used in medicine and dentistry for years and are considered a breakthrough advance in remineralization technology [1, 2].

2. Development
The available implant materials in the late 1960's had many disadvantages as they initiated fibrous encapsulation after implantation, rather than forming a stable bond with the tissues. Hench (1969) introduced a material that could bond to the bone and survive the harsh environment of the human body. He discovered such glass with the composition of 46.1 mol. % SiO2, 24.4 mol.% Na2O, 26.9 mol.% Ca O and 2.6 mol.% P2O5 (later termed 45S5 and Bio dglass ®) which formed a tight bond with the bone that it could not be removed without breaking the bone.[1-3]

3. Mechanism of Remineralization
When in contact with saliva or water, bioactive glass first releases sodium ions. This elevates the pH into the range essential for HAP formation (7.5-8.5). The calcium and phosphate are released to supplement the normal levels found in saliva. This increase in ionic concentration, combined with an increase in pH, causes the ions to precipitate onto the tooth surface and form calcium hydroxycarbonate apatite (HCA) to remineralize the defect and to occlude open tubules. The standard for Bioactive glass; 45S5 particles have been shown to release ions and transform into HCA for up to 2 weeks. Ultimately, they will completely transform into HCA [4].

4. Mechanism of new bone formation
Bone bonding is attributed to the formation of an HCA layer, which interacts with collagen fibrils of damaged bone to form a bond. Bone bonding to the HCA layer is expected to involve protein adsorption, incorporation of collagen fibrils, attachment of bone progenitor cells, cell differentiation and the excretion of the bone extracellular matrix, followed by its mineralization. However, evidence for each of these steps is sparse [5].

5. Applications of bioactive glass and clinical trials
5.1 Monolithic medical devices
In 1986, bioactive glass was successfully used as middle ear prosthesis to repair conductive hearing loss and was marked as the first clinical application of such material.[6]
The first commercial Bioglass® device used in dentistry is the End osseous Ridge Maintenance Implant (ERMI®). They were inserted into fresh tooth sockets to repair the tooth roots and to provide a stable ridge for denture by preventing resorption of the alveolar bone. This product did not gain commercial success as their availability is limited to cones of fixed sizes and cannot be reshaped accordingly [7].

5.2 Bioactive glass particulates for bone regeneration
Bioactive glass as particles or granules is often preferred than monoliths, as they can be used easily to fill a defect. Perio-Glas® (Nova Bone Products LLC, Alachua, Florida) was one such material introduced for the repair of bony defects of the jaw and bone loss arising from periodontal disease. Particle size range of Periog lass ranges from 90–710 μm and can be used to regenerate bone around the root of a healthy tooth to save the tooth, or to repair bone in the jaw to improve the quality of bone for anchoring titanium implants [8].
Another application of Perio-Glas® is in "Guided tissue regeneration", which has been used with polymeric membranes [9].

Bioactive glass slurry prepared from Perio-Glas® has been used in root canal sterilization prior to insertion of implants. This slurry can raise the pH to bactericidal levels in addition to its bioactive properties [10].

A particulate for orthopaedic bone grafting of non-load-bearing sites was released in 1999, named Nova Bone (Nova Bone Products LLC). Nova bone is mixed with the blood from the defect site and worked into a putty-like consistency before the blood starts to clot, and is pushed into the defect. The particles have a similar distribution to Perio Glas so packing of the particles in the defect is random. Gaps between the particles are expected to increase the rate of bone ingrowth.

Biogran (BIOMET 3i, Palm Beach Gardens, FL) is another synthetic bone graft used in jaw bone defect regeneration. It has the Bioglass 45S5 composition but with a narrower (300–360 µm) particle size range. The significant bioactive glass research programme in Finland led to the commercialization of particulates of the S53P4 composition, now known as Bon Alive (Bon Alive Biomaterials, Turku, Finland).

Asmita *et al*. compared Nova Bone Dental Putty and Perio Glas in the treatment of mandibular Class II furcations and it was found that both the forms of bioactive glass effectively regenerated Class II furcation defects with an uneventful healing of the sites and in the treatment of horizontal defects Perio Glas showed better results [11].

Schepers E *et al*. evaluated bioactive glass granules Biogran and commercially available hydroxy lapatite (HA) granules as a filler for osseous lesions and found that bioactive glass granules are easier to handle and to pack into the bone defects than HA granules, and repair of the bone defects is enhanced in Bio gran by their osteoconductive and osteostimulatory properties [12].

5.3 Treatment of Hypersensitivity

Nova Min ® (Nova Min Technology, Glaxo Smith Kline, UK), is a fine Bioglass ® particulate with a particle size of 18 µm have been used as an active repair agent in toothpaste. The dentinal tubules that link to the pulp chamber contains sensory nerve endings and any change in fluid flow through the tubules like volume of fluid, ion concentration or temperature, can cause pain. Traditional toothpastes contains chemicals (e.g. potassium nitrate) that temporarily anaesthetize the nerves and prevent pain. Nova Min®, when exposed to water or body fluids, releases mineral ions that aid in the natural remineralization process in the mouth. It deposits hydroxycarbonate apatite and mineralises tiny holes in the dentin, reduces the possibility of reopening the dentinal tubules and thus reduces sensitivity.[13,14] Currently available Novamin containing products include Vantej, SHY NM, Sensodyne with 5% Novamin in each.

Salian S *et al*. compared the in vivo efficacy and safety of dentifrices containing either 5% Nova Min or 5% potassium nitrate, and a non-desensitizing dentifrice, on dentin hypersensitivity and found that the dentifrice containing 5% Nova Min occluded dentin tubules, and provided rapid and significantly more relief from hypersensitivity in four weeks compared to the others [15]. Novamin also showed better dentinal tubule occlusion when compared with Gluma desensitizer(hydroxyethyl methacrylate and glutaraldehyde) [16]

Kulal R *et al*. compared the efficacy of Nano Hydroxyapatite(15%), Novamin(5%) and Proargin (8%) Desensitizing Toothpaste and found that nano-hydroxyapatite toothpaste had greater efficacy in occluding of the dentinal tubules compared to the others.[17]

Pradeep AR *et al*. assessed the efficacy of three commercially available toothpastes - containing 5% potassium nitrate; 5% calcium sodium phosphosilicate with fused silica; 3.85% amine fluoride in the reduction of dentinal hypersensitivity and found that bioactive glass group showed a better reduction in the symptoms of dentinal hypersensitivity.[18]

Bleaching treatments of teeth with hydrogen peroxide can damage enamel by demineralization. In vitro trials indicate that Nova Min can repair the enamel though remineralization to pre-bleaching levels (5 min exposure and brushing).[19] The effects of Nova Min desensitising toothpaste mixed with 15% carbamide peroxide on tooth bleaching and tubule occlusion were evaluated and found that it occluded the dentinal tubules and that it did not affect the bleaching procedure.[20]

5.4 Bioactive glass coatings

Bioactive coatings are important for metallic implants such as hip prostheses and periodontal implants because the metals alone are bioinert, which means they are encapsulated with a fibrous tissue after implantation. Bioactive coatings improve the stability of implants by bonding them to the host bone. Bioactive glasses are by nature biodegradable, and therefore a highly bioactive coating may degrade over time, causing instability of the metallic implant in the long term. Bioactive glass coating applications may therefore be limited but can be used on titanium implants with screw threads [21].

5.5 Bioactive glass scaffolds

Bioactive glass particulate systems lack dimensional stability when first placed into the surgical site. A bone defect cavity may hold the particles in place until they are integrated with the host bone, but in some clinical cases, bone repair is needed. An ideal synthetic scaffold is expected to mimic porous cancellous bone in morphology, structure, and function to optimize integration with surrounding tissues. Even though Bioactive glass cannot fulfill all of the criteria, but porous bioactive glass scaffolds have the potential to improve on current market-leading commercial porous synthetic bone grafts such as Actifuse.[22]

The advantages of glasses as scaffold materials are ease in controlling their chemical composition and thus, the rate of degradation. Glass scaffolds can be designed with variable degradation rates to match the bone ingrowth and remodeling. In general, interconnected pores with a mean diameter (or width) of 100 µm or greater, and an open porosity of >50% are required to permit tissue ingrowth and function in porous scaffolds. Bioactive glass scaffolds can be fabricated by various methods, including sol-gel, thermally bonding of particles, fibers or spheres, polymer foam replication, freeze casting, and solid freeform fabrication.[23] The drawback in the use of bioactive glass scaffolds for the repair of defects in load-bearing bones has been their low strength [24]. Recent work has shown that by optimizing the composition, processing and sintering conditions, bioactive glass scaffolds can be created with predesigned pore architectures and with strength comparable to human trabecular and cortical bones [25, 26].

5.6 Bioactive glass composites

Tough conventional composites can be produced using a biodegradable polymer matrix with bioactive glass particles as the filler phase. Adding Bioglass 45S5 to polymers such as PLGA(Poly Lactic-co-Glycolic Acid) can increase the stiffness and compressive strength of the polymer [27].

5.7 Antibacterial effects

In addition to remineralization, bioactive glass can kill microbes due to the pH rise caused by cation release during dissolution. S53P4 was shown to kill pathogens connected with enamel caries (Streptococcus mutans), root caries (Actinomyces naes lundi, S. mutans) and periodontitis (e.g. Actinobacillus action my cetemcomitas) in vitro [28]. Nanoparticles of 45S5 have been shown to kill Enterococcus faecalis, a micro-organism associated with failed root canal treatments [29].

5.8 Vehicle for drug delivery

Bioglass materials have been tried to be used as a vehicle for drug delivery. Vancomycin on bioglass carrier has been tested for treating osteomyelitis with success [30]. Indomethacin was tried with self-setting bioactive cement based on $CaO\text{-}SiO_2$ - P_2O_5 glass. This mixture hardened and formed hydroxyapatite in about 5 minutes with volume shrinkage of 5% in simulated body fluid.[31]

5.9 Fluoride containing bio active glass

Fluoride is an important mineral for the hard tissues in the body and is beneficial to both bone and tooth integrity. Brauer *et al*. incorporated fluoride into bioactive glasses and found that the effects on the hard tissue were improved [32].

Bio Min™ is a fine particulate bioactive glass material which slowly dissolves in saliva in up to 12 hours. The particles of Bio Min™ are designed to be small enough to enter any exposed dentine tubules and are able to precipitate onto the tooth surfaces as the glass dissolves in saliva. Bio Min™ F and Bio Min™ C additives are from the same family of bioactive glass materials, developed to reduce tooth sensitivity, replace lost mineral from tooth surfaces and protect against acid erosion.

Bio Min™ F contains Fluoride in the glass mixture along with Calcium and Phosphate. As the glass starts to dissolve in saliva these three ions combine to precipitate fluorapatite on the tooth surface which is more resistant to acid attack than hydroxyapatite by a factor of 10.The Fluoride content of the toothpaste is below 600ppm and is slowly released in a controlled manner as saliva dissolves the fine glass particles while traditional Fluoride toothpastes normally contains 1450ppm of soluble Fluoride. BioMin™ C is comparatively a more reactive glass and develops apatite formation rapidly, even though it does not provide the enhanced acid resistance of Bio Min™ F

Ashwini S *et al*. conducted a two-months randomized clinical trial to compare the desensitizing efficacy of dentifrice containing 5% fluoro calcium phosphosilicate and 5% calcium sodium phosphosilicate in participants with sensitive teeth and found that greater reduction in sensitivity was found with the fluoro calcium phosphosilicate [33].

Pereira R *et al*. evaluated the in vitro effectiveness of Biomin ®,Novamin® and a fluoride containing dentifrice on dentinal tubule occlusion an found that Biomin ® and Novamin® gave better dentinal tubule occlusion than the fluoridated dentifrice and there was no significant difference between Biomin ® and Novamin® in tubule occlusion [34].

The fluoride containing bioactive glass was also found to be an effective remineralization agent in white spot lesions around the orthodontic brackets as they promote apatite formation.[35,36]

When fluoride containing bioactive glass composite was used as an orthodontic adhesives it was found that unlike glass ionomer resins, favourable ions F, Ca and PO_4 releases were maintained over a long time period especially in acidic condition. It also showed that the resin has the potential to prevent formation and progression of early caries lesions.[37]

Fluoride-containing BG, also have the ability to release fluoride locally at an implant site, affect osteoblast cells *in vitro*, promoting osteoblast differentiation and stimulates markers for bone formation which make them good candidates for a range of bone regeneration applications.[38]

Milly H *et al*. evaluated the effect of pre-conditioning enamel white spot lesion surfaces using bioactive glass (BAG) air-abrasion prior to remineralization therapy and found that with air-abrasion the lesion surface was modified physically with enhanced remineralisation [39].

Mehta AB *et al*. compared the remineralization potential of bioactive-Glass and CPP-ACP containing dentifrice and concluded that; application of BAG more effectively remineralized the carious lesion when compared with CPP-ACP [40].

Prabhakar AR *et al*. found that incorporation of bioactive glass into glass ionomer cement enhanced their remineralization property but it compromised the mechanical properties of the materials to some extent. So, their clinical use has to be restricted to those areas where their bioactivity can be made beneficial, such as root surface fillings, base and liner materials in deep cavities, and in the treatment of hypersensitive dentin.[41]

Mousavinasab SM *et al*. compared the flexural strength of a resin-modified glass-ionomer containing bioactive glass (RMGI-BAG) with resin-modified glass-ionomer (RMGI) and it was found that the addition of bioactive glass reduced the flexural strength of Resin modified glass ionomer cement [42].

6. Conclusion

The objective of all biomaterials research is to produce improved products for clinical use. Bioglass medical and dental products have a wide range of applications and are hence a promising biomaterial in dentistry.

Conflicts of Interest: Nil

7. References

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