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Bioactive Glass: A Review

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Abstract: ***Bioactive glass (BAG) is one of the most recent biomaterials. Bioglass is one of the important bioceramics as a restorative material, and by managing the material's properties, it is feasible to design more effective formulations for restoration. Bioglass forms a rapid, strong, and stable bond with host tissues. It was discovered in the 1980s that bioactive glasses may be utilised in particle form to initiate osteogenesis, giving rise to the concept of tissue regeneration. Later, it was discovered that the dissolution of ions from the glasses behaved like growth factors, providing signals to the cells. Because of its bioactive qualities, BAG is suitable for a variety of clinical applications requiring the regeneration of hard tissues in medicine and dentistry. This review focuses on an overview of Bioactive glass. It also gives a detailed insight into its composition, preparation along with their properties and clinical applications.***

Keywords: Bioactive glass, inorganic/organic hybrids, sol–gel, scaffold, regenerative medicine, tissue engineering.

1. Introduction

One of the cornerstones to successful root canal therapy is sealing the root canal system. Root canal sealers' main purposes are to close off spaces between root canal walls and gutta - percha, embedding remaining bacteria and filling root canal irregularities like minor lateral canals and isthmuses.[3, 2]

Tissue tolerance, no shrinkage during setting, short setting time, adhesiveness, radiopacity, lack of staining, insolubility to oral and tissue fluids, bacteriostatic characteristics, and capacity to form a seal are the requirements for the optimal sealer. However, traditional root canal sealers composed of zinc oxide eugenol, calcium hydroxide, or resins may have issues with sealing because of solubility or polymerization shrinkage after setting, which can result in microleakage.[3]

Additionally, these conventional root canal sealers do not aid in tissue regeneration or even reduce inflammation of the periapical tissues.[3]

Due to its positive bioactivities, such as ensuring biocompatibility and accelerating periapical tissue regeneration, bioceramics, a type of biomaterial, have been introduced as promising endodontic materials for root canal filling.[3]

An additional benefit of bioceramic materials is that they encourage the production of hydroxyapatite (HA), which eventually makes it easier for the dentin and core material to fuse together after setting.[3]

Bioactive glass (BG), composed of silicon oxide, calcium oxide and phosphorus pentoxide has a greater potential for bioactivity, that explains its amorphous shape. Through a series of biochemical events at the interface, the ions exchange between the BG and body fluids after implantation can cause the synthesis of HA, building a strong chemical link with the bones and soft tissues and promoting tissue repair and regeneration. BG has recently been used in endodontic procedures.[2, 1]

1.1 Composition of Bioactive Glass

Bioactive glass includes the glass type of Na_2O - CaO - SiO_2 - P_2O_5 in a predetermined ratio, with a silica component of ≤ 50 mol%.1Bioactive glass (BAG) was initially marketed under the brand name Bioglass® 45S5, which was made out of 45% SiO_2, 24.5% Na_2O, 24.5% CaO, and 6% P_2O_5. The primary components of Class A BAGs were 40–52% SiO_2, 10–50% CaO, and 10–35% Na_2O. Additionally, the glass composition could include 0–25% CaF_2, 0–10% B_2O_3, or 2 - 8% P_2O_5. In addition, known biocompatible and bioactive minerals like fluorapatite (FAP), wollastonite, diopside, and tricalcium phosphate may also be present in BAG.[4, 5]

Sodium has been regarded as a crucial part of the bioactivity since it efficiently destroys the structure of the glass. To change the bioactivity and antibacterial characteristics, Si, P, Sr, Cu, Ag, Zn, and F ions may be added. When implanted in bone, Cobalt has been proven to improve angiogenesis. Ag may be able to produce improved antibacterial capabilities, although large doses have been shown to be cytotoxic.4 Antimicrobial properties are also present in Zn. Alkali - free BAG that had been doped with Zn also shown better apatite production. Cu, Mg, and Sr increase the BAG's bioactivity.[6]

By forming the much more acid - resistant fluorapatite rather than hydroxyapatite, fluoride is particularly important in increasing the bioactivity of dental treatments. Fluoride conjugated with BAG may also increase dentin remineralization and reduce the danger of dentin - matrix deterioration.[7]

When BG is implanted in a defect area near bone, reactions on the BG surface release essential concentrations of soluble Si, Ca, P, and Na ions, which induce favourable intracellular and extracellular reactions resulting in rapid bone formation. The formation of bone is then followed by the production of silica - rich gel on the surface. When ions from physiological fluids interact with silica - rich gel, hydroxyapatite (HAp) - like material is created on the surface of the BG.[1]

Additionally, BG can encourage osteoblasts to regenerate and repair themselves, greatly boosting the rate at which tissues heal. Osteoconductivity and osteoinductivity are the terms for these characteristics.[8]

1.2 Preparations of Bioactive Glass

Glasses have typically been made via melt quenching.4Powdered substances are heated to high temperatures—typically above 1300 °C—during the melt quenching process, and then they are quickly cooled to cause the atomic lattice to crystallize. However, this method has drawbacks such the difficulty to create porous scaffolds and decreased bioactivity at greater sintering temperatures.[9]

The production of crystalline phases together with the remaining glassy phases, which may have an impact on the mechanical
characteristics, is a possibility with silicate - based BAG, which leads to the release of tensions from the glass after heat treatment. Additionally, the glass particulates can be sintered into glass - ceramic scaffolds, however this limits the bioactivity and ion dissolution due to crystallisation.[4]

By using a sol - gel foaming procedure, Midha et al.[10]created scaffolds of bioactive glass (70S30C, 70% SiO_2, and 30% CaO) that are regarded as promising matrices for regeneration of bone tissue. Precursors are used in this method, which involves a number of condensation and hydrolysis reactions, followed by low heat treatment process. In comparison to melt - quenched glasses, which have the benefit of possessing greater mechanical qualities, sol - gel glasses have higher porosity, an enhanced capacity to create apatite, and an increased surface area.[1]

1.3 Properties of Bioactive Glass

A bioactive substance can communicate with the biological surrounding to cause a particular biological reaction, such as the development of a hydroxyapatite surface with the establishment of a link between the substance and the tissue. The glass that is the most bioactive has a greater surface area, a higher dissolution rate, and a faster rate of apatite formation. The mechanical properties of this composite for natural bones have also been proven to be improved, and they offer biomimetic nanostructures that improve cell adhesion. The makeup and structure of the glass, the manufacturing processes, and the speed of ionic solubility all have an impact on the bioactive qualities.[4]

1.4 Bioactivity of Bioactive glass

In general, conventional glasses are anticipated to have excellent durability and thus lower dissolving rates. For BAGs to be bioactive, certain dissolving rates are necessary. This is accomplished by adding network modifiers, like CaO and Na_2O, to increase the reactivity of the surface and silica network.4, [12]Bioactivity is a multi - step process from glass dissolution to hydroxyapatite production.

The interchange of H^+ ions within the solution and Na^+ and Ca^{2+} from the glass network causes BAGs to instantly experience ionic dissolution and glass deterioration when it comes in contact with body fluids (BF). The hydrolysis of the silica units during the ion exchange leads to the production of silanol groups (Si - O - H). The rise in the hydroxyl ion (OH) concentration causes the nearby environment to become more alkaline. As the pH increases, the silica network deteriorates even more, producing orthosilicic acid and negatively charged gel - like $Si(OH)_4$ on the surface. With precipitation sites, the gel layer serves as a matrix for hydroxyapatite. Over the bulk glass is a diminished alkaline surface layer that lies beneath the gel layer.

A coating of amorphous calcium phosphate develops over the gel layer.[15]

The incorporation of carbonate ions from the now supersaturated solution causes precipitation and subsequent mineralization, therefore the concentration of Ca - and Si - ions in solution—approximately 88–100 ppm and 17–20 ppm of the corresponding ions—is crucial. Growth factors can bind to the surface of newly generated hydroxyapatite, which also facilitates osteoprogenitor cell adhesion, proliferation, and differentiation by cytokines and extracellular matrix components represented by the over expression of numerous genes.1[5] The BAG begins to resorb as the hydroxyapatite develops inward, and is replaced by developing bone tissue.

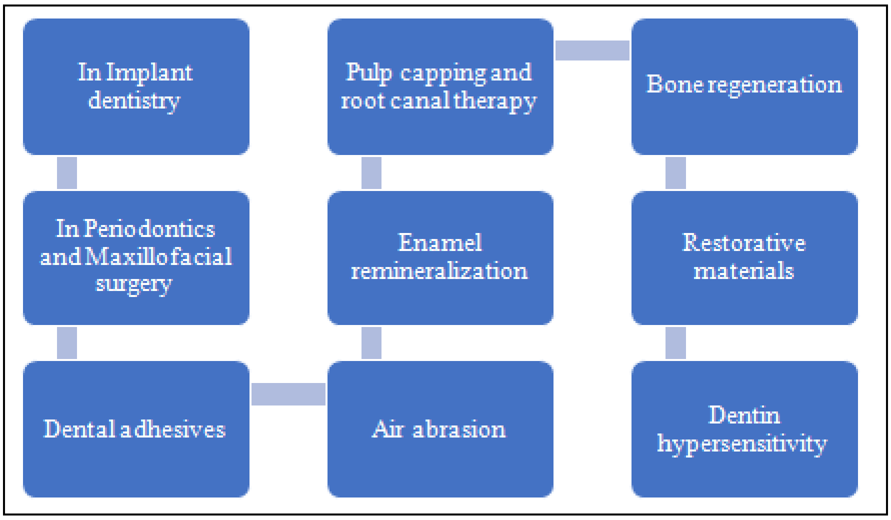
1.5 Antimicrobial properties

BAGs, in particular BAG - S53P4, have demonstrated to have broad - spectrum antimicrobial properties with no resistance to date being observed. One of the most frequent bacterial strains linked to PJIs and a significant biofilm contributor is S. aureus.[13]

The addition of antimicrobial compounds to the BAG also results in an enhanced antibiofilm action. Alkalinity is thought to be the main antibacterial action, making Bioglass® 45S5 more efficient. S53P4, on the other hand, exhibits a more sensitive equilibrium between osteogenicity, alkalinity with a pH of 7.9, and antibacterial characteristics. The antibacterial capabilities are also influenced by particle size; smaller particles have more surface area and have a stronger antimicrobial impact.

When made by melt quenching, alkali - free BAG doped with ZnO and SrO displayed antibacterial characteristics against strains of Staphylococcus aureus and Escherichia coli. The findings imply that even in the lack of alkalinity, BAGs can still offer antibacterial capabilities. BAG is likely the best bone substitute because of these characteristics.[4, 14]

Clinical Applications of Bioactive Glass in Dentistry



a) Dental adhesives:
Dental adhesives enable the substances or materials, like composites or orthodontic brackets, to adhere to the tooth surface.4
In comparison to the adhesive without BAG, the commercial adhesive containing niobophosphate BAG fillers produced higher microhardness and radiopacity. The mechanical qualities remained unchanged. Apatite development was also observed.[16]Using flowable resin, commercial orthodontic bonding agents were combined with BAG, Ag - or Zn - doped. After pH cycling and BAG addition, a demineralization - free zone was created up to 200 to 300 m distant from the bracket.

b) Enamel remineralization:
With routine plaque removal and fluoride, early caries lesions which have not yet cavitated, such as white spot lesions (WSLs), may be stopped and remineralized; operational treatment may then be prevented. Fluoride is a common ingredient in dentifrices, dental varnishes, and mouthwashes to prevent tooth decay and encourage remineralization.[4]

However, CPP - ACP and fluoride were used in conjunction to provide the best WSL remineralization. However, by applying BAG to WSLs, remineralization can occur.[17] FAP formed instead of fluorite, CaF2, in a BAG with fluoride and a high phosphate content that is commercially known as BiominF®. All the required ions for FAP, Ca5 (PO4) 3F, are delivered by the high phosphate concentration.[18]

c) Dentin hypersentivity:
Sharp, transient tooth pain brought on by a tactile, chemical, osmotic, evaporative, or thermal stimuli is known as dentin hypersensitivity (DH). DH may be brought on by exposed dentin as a result of periodontal disease, gingival recession, attrition, abfraction, abrasion, or erosion.

Glass ionomer cement (GIC), dentin bonding agents, and toothpastes are among of the over - the - counter items used for the conservative management of DH. These goods might also contain glass particles. BAG compositions block the dentinal tubules by attaching to collagen fibres and depositing hydroxyapatite to provide therapeutic relief.[19] Novamin®, PerioGlas®, FAP - forming BioMin - F®, the crystallized BAG, Biosilicate® have been successful in treating dentin hypersensitivity.

d) Air abrasion:
The hardness of Novamin®, or Bioative glass in general, is 7 GPa, something that is greater than the hardness of enamel (3.5 GPa). The abrasiveness increases as particle size decreases. Due to enamel deterioration, the cement - enamel interface is vulnerable to DH.

As a result, it is recommended to use less abrasive dentifrices on the outer enamel layer which is prone to wear. Dentifrices ought to have fluoride or strontium since they can make BAG less brittle. Due to its abrasive qualities, Novamin® has been utilised for tooth whitening. Ceramic particles under high - pressure airflow can be used to remove surface stains. Patients who used airflow with Novamin® particles instead of standard sodium bicarbonate particles reported subjectively lower DH levels and brighter teeth.[4, 20]

The removal of the remaining orthodontic adhesive after the procedure is complete causes the most substantial enamel damage as a result of orthodontic therapy. Thus, it appears that QMAT3, a bioactive glass with a hardness lesser than enamel, offers a cautious method for removing orthodontic adhesive.[4, 21]

e) Restorative materials:
The currently available restorative materials can resemble teeth in terms of look, structure, and functionality, but they lack bioactive characteristics. BAG was initially inserted into a resin composite in the non - silanated formulation at weight percentages of 5, 10, and 15 with 72% filler. After being exposed to bacterial invasion and aqueous conditions for two months, it had stronger mechanical characteristics than the control, 0 weight% BAG. Comparing the BAG composites to commercially available resin composites, the latter demonstrated cytotoxicity caused by the discharge of unreacted monomers. Without weakening the connection, flowable resin composite materials have been shown to slow the growth of oral microorganisms like S. mutans and E. coli.[4, 22]

A GIC based on BAG and polyacrylic acid demonstrated a setting reaction combining glass particles and polyacrylic acid that was similar to that of a traditional GIC. Additionally, rmGIC is associated with enhanced water absorption, which accounts for the stronger bioactivity of BAG - rmGIC than GIC.[4]

f) Pulp capping and root canal therapy:

The selection of a pulp - capping material is significant when treating an exposed dental pulp that requires partial pulpotomy or pulp capping, among other variables. A biocompatible, antimicrobial, and manageable pulp capping substance should be able to create a tight seal. In order to protect the pulp, it should also encourage the development of a dentin bridge. Although tunnel - like defects prevent calcium hydroxide (CH) from completing the dentin bridge, it has been employed in a number of endodontic procedures, including pulp capping.[4]

BAG's potential dentinogenesis property has led to research into pulp capping. When utilized for direct pulp capping, BAG made from sol - gel encouraged the growth of a thick dentin bridge. BAGs have also been incorporated into the materials used for endodontic root filling.

BAG filler particles are used in the endodontic obturation thermoplastic polymer called as ResilonTM. In place of traditional gutta - percha (GP), Bio - Gutta, a mixture of GP and Bioglass® 45S5, has become popular since it can adhere to dentin and doesn't need any sealant.[4, 23]

g) Bone regeneration:

Age - related bone abnormalities and the associated demand for artificial bone graft alternatives are predicted to rise along with the ageing population. Trauma, congenital or developmental conditions, deformities, malignancy, post - operative complications, periodontitis, or osteomyelitis can all result in bony abnormalities. Synthetic bone grafts (BG) are becoming more popular as a result of rising BG demand. This gives a synthetic BG with BAG an edge because it may be specially produced to have the best characteristics of a bone - grafting material.[4]

h) In Periodontics:

Deepened soft tissue pockets between the gingiva and tooth roots, the resorption of alveolar bone, the lack of clinical attachment level, and eventually the loosening of teeth are all signs of periodontitis, a chronic inflammatory disease of the periodontium that affects a large percentage of the population.

BAG is a top - notch bone graft material that has been extensively used in clinical settings to regenerate periodontal bone deficiencies as PerioGlas®. PerioGlas® and Bioglass® 45S5 share a similar formulation. In intraosseous periodontal defects in RCTs and treatment of grade II furcation involvement, regenerative attachment gain with PerioGlas® and autogenic bone graft was comparable.[4, 24]

i) In Implant dentistry:

Endosseous implants, commonly known as dental implants (DI), are screw - shaped medical devices that are placed in the alveolar bone to anchor prosthodontic constructs that enhance function and beauty. To be properly integrated, DIs must be mechanically robust enough to survive repeated chewing stresses, not trigger inflammatory responses, and support osseointegration by promoting bone apposition. BAG may assist implants attach aggressively to the bone, provide antibacterial protection, and shorten the length of treatment, which would promote the bioinert nature of Ti - DIs.[4]

j) In Maxillofacial surgery:

BAG stimulates bone production at a higher amount, higher quality, and faster rate than other calcium phosphate - based chemicals used in osseous repair, such as hydroxyapatite and tricalcium phosphate. Biogran® is one of the commercially available products mostly utilised for fixing flaws in maxillofacial applications. Blood from the defect can be combined with NovaBone®, another Bioglass® 45S5 - based formulation, to create a putty that can be used to fill the site. Using BonAlive®, an S53P4 particle, large defects as mandibular advances, mastoid or orbital floor fractures can be treated.[5]

Granular BAG combined with tiny amounts of autogenous bone can also successfully cure large bone lesions while significantly reducing donor site morbidity. Additionally, StronBone®, a BAG that contains SrO, is offered clinically to lessen bone resorption. Both long - and short - term clinical investigations using BAG indicate good bone healing and decreased donor site morbidity.[4, 25] Future therapy options could include electrospun andmesoporous BAG scaffolds, with the capacity to modify not only the scaffold's form but also to incorporate stem cells, certain medications, and growth hormones to enhance the patients' unique treatment regimens.

2. Future Direction

Based on its fundamental characteristics, bioglass can be said to be among the most bioactive of all bioceramics; yet, its mechanical stability is constrained.

Better materials for restoration can be created by manufacturing stable bioglass with hard polymer composite or by replacing strong metal ions in the glass network with stronger metal ions in the bioglass lattice. Such materials must be thoroughly analyzed in future with regard to their structural, mechanical, and in vitro/in vivo compatibility qualities.[26]

3. Conclusion

The extensive literature on BGs published to date attests to their amazing versatility, which is essentially due to the flexibility of their composition. BAG's chemistry mimics the make - up of natural hard tissues and plays a bioactive part in regeneration. To improve bioactivity and antibacterial characteristics, several elements such as silicon, phosphorus, strontium, copper, silver, zinc, and fluoride are added. The structure and composition of the glass, manufacturing procedures, and the rate of ionic dissolution all have an impact on bioactivity. Bioactive glasses are being used more frequently in several areas of dentistry, such as dental restorations, sealers and obturating materials in root canal therapy, toothpaste, desensitising and mineralizing agents, pulp capping, and air abrasion. Dentin remineralization was accelerated in resin composites containing BAG and fluoride.

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