A review of glass-ionomers: From conventional glass-ionomer to bioactive glass-ionomer

Maryam Khoroushi¹, Fateme Keshani²

¹Dental Materials Research Center, Department of Operative Dentistry, ²Torabinejad Dental Research Center and Department of Operative Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran

ABSTRACT

Materials used in the body, especially the materials used in various oral cavity regions should be stable and passive without any interactions with the body tissues or fluids. Dental amalgam, composite resins and dental cements are the materials of choice with such properties. The first attempts to produce active materials, which could interact with the human body tissues and fluids were prompted by the concept that fluoride-releasing materials exert useful effects in the body. The concept of using the “smart” materials in dentistry has attracted a lot of attention in recent years. Conventional glass-ionomer (GI) cements have a large number of applications in dentistry. They are biocompatible with the dental pulp to some extent. GI is predominantly used as cements in dentistry; however, they have some disadvantages, the most important of which is lack of adequate strength and toughness. In an attempt to improve the mechanical properties of the conventional GI, resin-modified glass-ionomers have been marketed, with hydrophilic monomers, such as hydroxyethyl methacrylated (HEMA). Some recent studies have evaluated GI with bioactive glass in its structure to validate the claims that such a combination will improve tooth bioactivity, regeneration capacity and restoration. There is ever-increasing interest in the application of bioactive materials in the dental field in an attempt to remineralize affected dentin. The aim of this review article is to evaluate these materials and their characteristics and applications.

Key Words: Bioactive materials, dental materials, glass-ionomer

INTRODUCTION

From the dawn of history the materials used in the human body, particularly those used in the oral cavity, should be stable, as well as passive, with no interactions with their surrounding environment. Amalgam, composite resins and cements generally have such characteristics. It is probable that the first sparks to produce active materials, with definite interactions with the human body, originated from the fact that materials capable of releasing fluoride can exert useful effects. The concept of producing “smart” materials in dentistry has gathered pace in the recent decade.¹,² The smart behavior of glass-ionomer (GI) cements was noted for the 1st time by Davidson.³ Glass-ionomer cements (GICs) are widely used in various branches of dentistry.³ One of the advantages of GI, compared to other restorative materials, is that they can be placed in cavities without any need for bonding agents;⁴ they also have good biocompatibility.³,⁴ Although GI are usually used as cements in dentistry, they have disadvantages, too. The most important disadvantage of conventional GI is lack of sufficient strength and toughness. In order to improve the mechanical properties of conventional GI, resin-modified glass-ionomers (RMGIs) have been introduced, which contain hydrophilic monomers and polymers like HEMA.³ A study showed that RMGIs
generally have much higher flexural strength compared to conventional GI (approximately, 71 MPa vs. 11 MPa).\[^5\]

In some recent studies,\[^1,2,5-8\] bioactive glass (BAG) has been added to GI structure to improve its bioactivity and tooth regeneration capacity. There is increasing attention to and interest in the use of bioactive materials in dentistry, particularly in an attempt to remineralize dentin. BAG contains silicon, sodium, calcium and phosphorus oxides with specific weight percentages, which was introduced by Larry Hench in 1969 as 45S5 Bioglass with the following weight percentages, which was introduced by Larry Hench in 1969 as 45S5 Bioglass with the following chemical composition and weight percentages: Na\(_2\)O, 24.5%; SiO\(_2\), 45%; P\(_2\)O\(_5\), 6%; and CaO, 24.5%.\[^9\]

Clinically, this material was initially used as a biomaterial to replace the lost osseous tissues in the human body. It produces a strong bond with bone through production of hydroxyapatite and formation of a strong bond between the collagen and the hydroxyapatite and is not rejected by the body.\[^9\]

Various studies have used different chemical compositions of Bioglass. Xie et al.\[^7\] used Vivoxid with the formula of S53P4 (wt% of: P\(_2\)O\(_5\), 4%; CaO, 20%; Na\(_2\)O, 23%; SiO\(_2\), 53%). Vollenweider et al.\[^10\] used NBG with the formula of 45S4 (wt% of: P\(_2\)O\(_5\), 4.9%; SiO\(_2\), 44.7%; Na\(_2\)O, 22.8%; CaO, 27.6%) and Perioglass (Nova Bone) with the formula of 45S5 and micron sizes. Marending et al.\[^11\] too, used 45S5 formula. In this context, some researchers evaluated the effect of these materials on tooth structure by studying their physical and chemical properties. Recent studies\[^8,12,13\] evaluated the effect of adding BAG on the setting and mechanical properties of RMGI. They reported that the compressive strength of the composition decrease a little, but it is much higher when it is compared with the conventional GIC containing BAG. They reported compressive strength values of 203.1 and 148.7 MPa for RMGIs (Fuji II LC) and its combination with 33 wt% of BAG, respectively. In a study carried out by Yli-Urpo et al.,\[^1\] too, BAG was added to (GIC). Then, the compressive strength, Young’s modulus and Vicker’s hardness of the composition were evaluated; it was reported that the experimental composition is biologically active under physiologic conditions and can mineralize human dentin in vitro. The material had also some antimicrobial activity.\[^1,14\] Xie\[^7\] used the polyacid he had invented to improve the mechanical properties of GI and BAG. He measured the compressive strength, diametral tensile strength, and hardness of the material and reported that its strength is comparable to that of commercially available Fuji II LC cement. However, only a limited number of studies have evaluated the effect of this material on the mechanical properties of tooth structures.\[^4,8\] Given the remineralization capacity of these materials in several studies, it is highly probable that these bioactive materials might be more effective in tooth restorations in open/close sandwich techniques or root surface restorations compared to RMGI or conventional GI, particularly in patients at a high-risk for caries. In addition, their use as a liner is highly contemplative.\[^14,15\]

In the current review, a short history of conventional and RMGIs will be presented and new conceptions regarding more “smart” materials, referred to as BAG -ionomers will be introduced.

**Smart materials in dentistry**

By definition, smart materials can change their behavior in response to various stimuli, which include stress, heat, moisture, pH, electricity, and magnetic fields. Of the smart materials used in dentistry, piezoelectric materials can be mentioned, which produce electric currents in response to pressure. These materials undergo changes in their shape or dimensions when electric currents are applied to them; in addition, when they undergo shape changes, they produce electricity. Another group of materials respond to heat, the examples of which are shape memory alloys. Yet another group consists of pH-sensitive polymers, which undergo increases or decreases in their volume or change color in response to changes in environment pH. Polymer gels, too, have smart behaviors. The majority of polymers, which have cross-linking networks and are water-soluble, belong to this group. The presence of water induces changes in the volume of the material in response to some environmental conditions like heat. The most notable of these gels include polyvinyl alcohol, polyacrylic acid, and polyacrylonitrile gels. Researchers are trying to adjust the smart behavior of each material with the conditions in its environment.\[^1,2]\n
Smart behavior was reported for the 1st time in GICs; these materials do not undergo great dimensional changes in a moist environment in response to heat or cold and it appears heating results only in water movement within the structure of the material. These materials exhibit noticeable shrinkage in a dry environment at temperatures higher than 50°C, which is similar to the behavior of dentin. The other aspect of the smart behavior of these materials is the fluoride release and recharge capacity.\[^1,2,5\]
History of GICs

One of the characteristic absolutely necessary for an ideal tooth restoration material is its adhesion to tooth structure, particularly to enamel and dentin, and the capacity to withstand pressures resulting from occlusion. Amalgam, gold and silicate cement all have long histories. From 1950s on, researchers became interested in producing new materials, including the composite resins and GICs. During 1950s, a small group of dental practitioners and researchers in the United Kingdom began research studies to produce a new restorative material so that the material would not be only a restorative material and would replace enamel and dentin. Their aim was to produce a material with thermal, mechanical, and optical properties comparable to those of tooth structure. They initially made attempts to improve the properties of silicate cement, which was available.[15,16]

Zinc polyalkenoate cements

In 1968 Smith produced the first zinc polyalkenoate cement. Production of this family of materials resulted in the introduction of the first dental adhesive cement. Smith concentrated his attention on zinc oxide eugenol cement and decided to use polyalkenoic acid instead of eugenol as the liquid. He discovered that the resultant cement can bond to tooth structures to some extent. However, its physical properties were less than ideal.[15] These materials have been produced based on initial zinc phosphate cements and are formed through the acid-base reaction of the aqueous solution of polyacrylic acid and zinc oxide. During this reaction, the acid attacks zinc oxide, releasing metallic cations, which react with the polymer chains and produce cross-links. In comparison with zinc phosphate cement, zinc polyalkenoate cement is more stable in water, although it is inclined to absorb water and dissolve.[16] During the same period, Wilson and his group decided to use the polyalkenoic acid as a liquid for silicate cement powder, which was a surprising event and a basis for success.[15]

Glass polyalkenoate cements

The first GIC was produced in late 1960s by Alan Wilson and his group in a chemistry laboratory in London.[16] The aluminum-to-silica ratio in the powder of this cement has increased compared to silicate cement powder, which gives rise to an increase in the reactivity of glass hence that it reacts faster with polyacrylic acid because this acid is weaker than the phosphoric acid used in the silicate cement. In most cases, the glass used in polyalkenoic acid aluminosilicate cement (ASPA) is calcium-alumino-silicate glass system, which was introduced by Wilson and Kent and contains calcium oxide along with the fluoride, alumina, and silica.[16,18] In the initial GI, the liquid was an aqueous solution of 50% polyacrylic acid, which converted into gel form only after a few months because of the presence of inter-molecular hydrogen bonds. This gelation process decreases or is eliminated by the use of copolymers instead of homopolymers. At present, the liquid contains an aqueous acrylic acid or a copolymer of maleic acid/acrylic acid.[17,18]

The first ASPA cement had inappropriate setting and esthetic characteristics and it became evident in 1972 that incorporation of the positive isomer of tartaric acid can improve manipulation properties of cement and its setting time.[16] Wilson reported that it is possible to control deposition of aluminum with the tartaric acid and therefore, an efficacious clinical material, referred to as ASPA II (aluminosilicate polyacrylic acid) was produced and marketed.[15,19]

It should be pointed out that although aluminum is present within the GI structure, calcium is added as a flux, in the form of calcium fluoride, to the aluminosilicate powder, forming a superficial bond. Therefore, calcium is released faster than aluminum.[5] During glass production, fluoride flux is added to prevent oxidation. Then, fluoride is released after mixing of powder with the polyalkenoic acid and becomes available for absorption by the tooth structure.[15,20] Presence of fluoride decreases melting point, increases cement strength, improves manipulation properties of cement and finally has a cariostatic effect.[16]

During 1988 Purton and Rodda showed that the cement not only releases fluoride ions, but also it can release calcium and phosphate ions,[21] which was recently confirmed by Ngo et al.[15,22] This research group used a newer material (Fuji IX) in an in vitro study, in which strontium has replaced calcium in order to confer opacity to the material. Calcium and strontium can, to some extent, replace each other and these researchers reported a deep penetration of strontium into the demineralized dentin on the cavity floor. These studies showed the possibility of dentin remineralization by GI.[15,22]

Setting reaction

An acid-base reaction takes place between the polyacrylic acid as a proton donor and aluminosilicate glass as a proton recipient. The acid destroys the glass network and releases cations such as Al³⁺, Ca²⁺, Na⁺ etc.
These cations are trapped by the carboxylate polymer and chelated, finally producing cross-links in the polymer network and forming a hard polysalt matrix. In RMGIs, light-activated polymerization and free radicals of HEMA molecule, too, have a role in setting, in addition to ionic cross-links between polyacrylic chains.\[18\]

It is of interest to note that the majority of silicate glasses are resistant to acid attacks due to the highly covalent characteristics of Si-O-Si-O-bond; however, the glass becomes more sensitive to acid attacks with an increase in the ionic properties of silicate. Silicates, which are attacked by acid, include different silicates, some chain silicates and aluminosilicate in which the ratio of Al: Si is sufficiently high. In fact, reactivity of aluminosilicate glasses depends on this ratio, which has an important effect on the formation of cement and its setting time.\[16\]

The setting reaction involves 4 stages:

1. Decomposition of the powder: The surfaces of glass particles are attacked by the acid, metallic cations are released into the solution and the silicate gel layer forms on the surface of the particles.

2. Gelation: With an increase in the concentration of cations, the pH value of the aqueous phase increases, which result in a greater ionization of carboxylic acid. At a specific point, the gel structure is formed through weak ionic cross-links and formation of hydrogen bonds. The gelation process of GI has been described as follows: As a result of an increase in ionization, the carboxylate groups of polymer chains become charged, repel each other, uncoil and probably take on a more linear configuration. The progression of the reaction of metallic cations with carboxylate groups results in an increase in viscosity. It appears the diffusion of these cations exerts the main effect on the gelation reaction of the cement.

3. Hardening: Formation of cross-links in the polymer chains as a result of release of metallic cations leads to the hardening of the cement. The final material consists of un-reacted glass particles surrounded by the polysalt matrix containing cross-links.

4. Maturation: The reaction continues after setting and bond strengths (inter-molecular forces) increase. Although much of strength is achieved after 24 h, increase in bond strength values along with an increase in Young’s modulus for a few months continues as a result of diffusion of cations toward acid locations.\[16\]

The role of tartaric acid

Addition of tartaric acid (+) increases the working time and improves the setting reaction of the cement, resulting in easier and better manipulation of the cement.\[16\] It assists in the dissolution of surfaces layers of glass particles because of higher and stronger acidity, resulting in a faster release of metallic cations, especially aluminum ions, and formation of complexes with them. Therefore, aluminum ions are not immediately available for reaction with the polyacid and the cement working time increases because the setting reaction is retarded.\[18\] The setting reaction progresses fast at a specific concentration of aqueous aluminum. It also aids in the formation of a complex between polyacid and three-valent aluminum ions. The two chelating groups of -COOH and one-OH group in this molecule help form a double bond with two metallic cations, which functions as a more effective agent in forming cross-links compared to one-COOH group, making the cement setting more noticeable.\[16,18\]

Mechanical properties

The liquid-to-powder ratio influences the mechanical cement microstructure: Based on the TEM evaluations and X-ray micro-analysis, the final structure of GIC is a composite material, which is composed of remaining glass particles made porous by the acid attack and surrounded by silica gel; it is surrounded by a polysalt matrix. Therefore, cohesive forces, which keep the matrix compressed are composed of ionic cross-links, convolutions, and interlocking of chains and hydrogen bridges. An important consideration is the fact that if the particle sizes are less than a critical point, it is possible for all the particles to be destroyed by the acid attack, after which un-reacted glass particles remain resulting in a decrease in the mechanical properties of the cement.\[16\]

Generally, properties of the cement mixed with a greater consistency sets faster and are stronger than cement with the lower consistency. In addition, based on the results of a study by Wilson, as the amount of powder increases the consistency of the cement increases, the setting reaction is accelerated and the cement becomes stronger. However, this situation has a critical point, beyond which the amount of the physical matrix will be insufficient to bind to the cement and hold the cement ingredients next to each other; therefore, the mechanical properties will significantly decrease.\[14,16\]
Aging
GIC are usually weak after setting and are not stable in water; however, they become stronger with the progression of reactions and become more resistant to moisture; the compressive strength of the cement increases from 200 MPa after 24 h to 400 MPa after a year. The concentration of Al\(^{3+}\) cation is effective in increasing the rigidity and stiffness of the matrix due to its ability to bind 3 chains to each other.\(^{[15,16]}\)

Adhesion
GI has the capacity to bond chemically to polar materials such as bone, enamel and dentin. These materials have a high surface energy, but are not able to react with the noble metals and porcelain.\(^{[16]}\) This kind of adhesion is divided into two stages:
1. The free-COOH groups form hydrogen bonds with the substrate.
2. With the progression of the reaction, the flexible hydrogen bonds are converted into stronger ionic bridges.

The carboxyl groups of the ionic polymers of polyalkenoic acid enter the structure of hydroxyapatite by replacing phosphate; they are the main agent with the hydroxyapatite component of tooth structure. Therefore, the bonding is permanent because all the adhesive groups are connected to each other with covalent bonds and all the bonds should fail simultaneously for the bonding to fail. It appears if one bond fails, it is possible for rebonding as long as other bonds have not failed.\(^{[15,18]}\)

Classification of GI
GI is classified as follows according to their application:
Type I: Luting cement for crowns, bridges, and orthodontic brackets
Type II a: Esthetic restorative cement
     b: Reinforced restorative cement
Type III: Liner and base.\(^{[23]}\)
There is another classification for GI as follows:

First generation
Reactivity of GI depends on alumina-to-silica ratio in the melted mixture used in their preparation. This ratio, the basic oxide-to-acidic oxide ratio, determines the alkalinity of the glass and since the reaction between the GI and the liquid is an acid-base reaction an increase in the alkalinity of the glass increases the setting reaction. The first GI, ASPA I (Detrey, Dentsply), was not very active, did not set fast, was very moist-sensitive and had low translucency. ASPA II contained tartaric acid, had better properties and was the first GI with practical applications.\(^{[23]}\)

Second generation
This generation consists of water-hardening GICs. In this group, polyacid has been incorporated into the powder; therefore, the cement sets by mixing the powder with water or an aqueous solution of tartaric acid. Its advantages include an increase in shelf life by prevention of gelation, a decrease in viscosity during mixing, and an increase in strength because the molecular weight of polyacid can be increased in this system. The commercial products of this group include Chemfil and Ketac-Cem.\(^{[23]}\)

Reinforced cements
Previous formulations had low shear strength values of 7-12 MPa and were not appropriate for high-stress areas. Therefore, the following methods were used to reinforce the cement:
1. Use of dispersed phases such as alumina, titanium oxide and zirconium oxide.
2. Fiber-reinforced glasses: Addition of alumina fibers or other fibers such as glass fibers, silica fibers and carbon fibers to increase flexural strength.
3. Glasses reinforced with metals: Mixing with amalgam powder, referred to as “Miracle Mix.”
4. Cermet ionomer, which was introduced by Melean and Gasser by sintering metal and glass powder, which resulted in a strong bond between them.
5. Conventional GI with a high viscosity: These materials are greatly used in atraumatic restorative treatment (ART) technique and include Fuji IX and Ketac-Molar. Fuji VIII is used for anterior teeth and is a resin-reinforced glass-ionomer. It has higher flexural strength and translucency and is appropriate for anterior regions. Flexural strength is necessary for anterior regions.
7. Amino acid-modified glass-ionomers.\(^{[21,23]}\)

RMGIs
RMGIs were produced by adding methacrylate to polyacrylic acid. Some of them are light-cured, which is supplementary to the basic acid-base reaction. In comparison, polyacid-modified composite resins consist of commonly used macromonomers in composite resins, which include Bisphenol A-Glycidyl dimethacrylate or urethane dimethacrylate along with small amounts of acidic monomers.\(^{[5,23]}\)

They have the same ion-releasing glass as filler particles used in conventional GI, but in small
sized. The initial setting reaction is triggered by the light, which is followed by acid-base reaction after absorption of water. A large number of researchers have reported that RMGIs can release fluoride at a rate comparable to that by conventional GI. However, this release is not only under the influence of formation of complex fluoride derivatives with their reaction with polyacrylic acid, but also it might be affected by the type and amount of the resin used in the light polymerization.

Release of fluoride from various RMGIs during the first 24 h is maximum with 5-35 μg/cm² depending on the storage environment. Daily fluoride release begins from 8 ppm to 15 ppm on the 1st day and decreases to 1-2 ppm on the 7th day and stabilizes in 10 days to 3 weeks.

Factors influencing fluoride release from restorative materials

Release of fluoride is under the influence of some internal variables such as matrix formulation, filler, and fluoride content. In addition, some experimental factors such as the storage environment, number and frequency of changing the preserving solution, composition and pH of saliva, formation of plaque and pellicle, powder-to-liquid ratio, mixing, curing time and the exposed surface. Release of fluoride in the laboratory depends on the exposed surface rather than on the specimen bulk. Generally, the highest and the lowest fluoride release have been recorded in the demineralizing-remineralizing regimens and saliva, respectively. Demineralizing-remineralizing regimens are selected to simulate the cycle of pH variations during caries attack. However, release of fluoride increases in the human saliva, which is the result of enzymatic activity of the saliva. It has been demonstrated that release of fluoride from RMGI in artificial saliva containing esterase is higher than that in artificial saliva without the enzyme. Bleaching and brushing have no effect on fluoride release. Removal of the outer layer of compomer by air-polishing or finishing results in an increase in fluoride release. Covering of the surface of these restorative materials with an adhesive or surface covering agents to prevent contamination with moisture and dehydration during initial stages, results in a decrease of fluoride release up to 1.4-4 folds. evaluated the amount of fluoride released by four brands of GI (Fuji II LC, Fuji IX Extra, Fuji VII, and Fuji IX), one compomer (Dyraect Extra) and giomer (Beautifil) and reported a noticeable difference in the release of fluoride based on the type of the material and time. According to the results, GI release more fluoride compared to compomer and giomer under study. They, too, emphasized the key role of the bulk of GI matrix in the fluoride release capacity of this material.

Clinical applications

GIC-based fissure sealants

Review studies have reported less retention for GIC-based fissure sealants compared to resin bases. However, when absence of carious lesions in permanent teeth protected by these two materials is compared, it becomes evident that GICs are as effective as resin bases which are considered the gold standard. Although the clinical appearance shows relative or complete loss of the GIC-based fissure sealant, the entrances to fissures remain sealed. It is hypothesized that the effect of GI is due to deprivation of bacteria of food and substrates and simultaneous release of fluoride. In contrast, resin-based sealants lose almost all of their protective effects after losing their retention.

Tooth restorations, liners, bases

GIC is the material of choice for ART because it has been demonstrated that it has a mineralizing effect on tooth hard tissues.

Biomaterials and bioactive glasses

Biomaterials are synthetic materials, which are in contact with the human body tissues and their presence does not induce a toxic response in the body. When a material is placed in living tissues, different tissue responses are induced depending on the material, which gives rise to the classification of materials as follows:

Toxicity

The placed material releases components, which are able to destroy or irritate the surrounding cells.

Nearly biological inert

As a protective mechanism, fibroblasts form a fibrotic capsule around the material to isolate it from the host. In such cases, if the material is porous, the tissue grows into it and biological fixation takes place.

Bioresorbability

The material is gradually resorbed or destroyed though hydrolysis or enzymatic processes and replaced by newly formed tissue. It is important that degradation and disintegration rate of the material be controlled and be in harmony with the growth rate of
surrounding tissues. Some of the materials exhibiting such behavior include resorbable sutures or tricalcium phosphate ceramics.

**Bioactivity**

When a bioactive material is placed in living tissues, certain biochemical reactions take place at the material-tissue interface and bioactive fixation is initiated. Therefore, a bioactive material has an intermediate behavior between a bioabsorbable material and an almost neutral material and can create an environment, which can promote a proper bond between living tissues and the material.[40]

Therefore, the terms biocompatibility and bioactivity are different from each other. Biocompatibility refers to those materials, which do not induce any negative response. The components released by biocompatible materials are not toxic, they do not induce any inflammatory reactions and they are not rejected by surrounding tissues. However, by definition, bioactive materials induce a specific biologic response at the tissue-material interface.[43] Generally, bioactive materials interact with the tissues through a positive reaction. For example, the reaction at the tissue-implant interface and formation of new osseous tissue at this interface is a parameter, which characterizes a bioactive material. Hench introduced some criteria for the evaluation of bioactivity of a material. However, a new classification was proposed in 1994, according to which bioactive materials are divided into 2 groups:

**Group A**

This group consists of materials, which induce both intracellular and extracellular responses. They are not only able to bond to bone, but also they can bind to soft-tissues. These materials are osteoconductive, too. The surfaces of these materials are colonized by osteogenic stem cells after they are placed in the body.

**Group B**

These materials are osteoconductive and induce only extracellular responses.[9]

Of all the commercially available bioactive materials, only a limited number of them, such as 45S5 Bioglass, induce both osteoproducive and osteoconductive responses.[9]

**BAG**

In 1969, Larry Hench from the University of Florida discovered glass materials, which had the capacity to chemically bond to bone. He named these glasses BAG. They are commonly used in the reconstruction of damaged hard tissues like bone.[9]

The advantage of this material is the possibility of designing a glass with a special purpose such as achieving a controlled level of disintegration and binding to tissues. Rapid surface reaction results in rapid binding to the living tissues; however, due to the two-dimensional structure of glass structure, it has relatively low mechanical properties. Any minor changes in the composition might result in completely different properties so that the bioglass can be used in contact with the different tissues and different properties can be adjusted and regulated based on the tissue the glass is to be placed in.[9]

When BAG is immersed in aqueous solutions such as body fluids, simulated body fluid, (SBF) or tris buffer solution, (TBS) three main processes take place:[9,44,45]

**Leaching and formation of silanols**

The glass network releases alkaline agents; in other words, alkaline agents replace H+ or H3O+ cations, which results in an increase in pH at the interface to values higher than 7.4.

**Dissolution of the glass network**

The activity of hydroxyl groups results in the breakdown of Si-O-Si-O-Si-bonds. Disruption of silica networks results in the local release of [Si(OH)]. If silica content is more than 60% the amount of disruption and its rate decrease because the number of oxygen bridges in the structure of the glass increases. This process results in the formation of aqueous silica (SiOH) on the surface and a silica-rich gel is formed by concentration and compaction of adjacent silanols.[9]

**Precipitation**

Calcium and phosphate ions released from the glass, along with those present in the solution, form a layer rich in calcium and phosphate on the surface. This layer is amorphous at first; then it crystallizes into hydroxyl carbonate apatite (HCA). The process is mediated by incorporation of carbonate anions from the solution into the amorphous calcium phosphate phase. It appears the mechanism of nucleation and maturation of HCA is the same in vivo and in vitro and is accelerated in the presence of aqueous silica. These steps, which occur on the surface of the material do not require the presence of tissue and can happen in distilled water, SBF or TBS. During these steps, dissolved ions are released, aqueous silica is
formed at high concentrations, and polycrystalline HCA is formed on the glass surface.[9,24]

The following additional steps are necessary to bind to the tissue:
• Absorption of biological moieties in the SiO$_2$-HCA layer: This process improves the reactive layer, and deep and superficial absorption of growth factors.
• Action of macrophages: This process prepares the macrophages in the placement area for tissue repair.
• Differentiation of stem cells.
• Production of matrix.
• Mineralization of matrix.

It was believed until 1981 that only calcified tissues bind to bioactive materials. Wilson et al. showed that if the tissue-material interface is immovable, soft-tissue, too, can bind to 45S5 bioglass.[9,19] It became evident in 1990 that only glass components with a high reaction potential bind to soft tissues. When the glass composition has a wt% of more than 52% of SiO$_2$, the glass binds to bone, but does not bind to soft-tissues. Materials with SiO$_2$ content of more than 60% become bioinert and do not form bonds because they have low reactivity. These findings formed a foundation for the clinical application of bioglass in bone replacements and placement of implants to preserve the alveolar ridge in edentulous patients. Generally, the higher the solubility rate is and the higher concentrations of the ions are, the more effective the bioactive materials are. If these factors are low the concentration to induce cellular proliferation and differentiation will be insufficient. Another interesting characteristic of these glasses is the fact that it appears if these glasses break during placement and the fractured surfaces remain in contact with each other, it is possible that they will be able to join together through the surface layer of apatite via self-repair capacity.[9]

**New generation of biomaterials (third generation)**

The aim is tissue regeneration and use of the biomaterial in the form of a powder or solution is to induce local tissue repair. These bioactive materials release chemical agents in the form of dissolved ions or growth factors such as bone morphogenic protein, which stimulate and activate cells. The cells produce more growth factors, which induce cell proliferation and regeneration.[9,35]

Some third generation BAG materials include Nova Bone, Nova Min and Nova Thera. The first special Nova Bone material marketed in the United States was Perio Glass in 1993. In 1995, it was marketed in Europe, too.[9,46]

**A review of clinical products of bioactive glasses**

The first clinical product of these materials was a tool for the treatment of conductive hearing deficiency by replacing middle-ear ossicles. It was called bioglass ossicular reconstruction prosthesis with a trade name of MEP, which was applied clinically in 1985. The second bioglass instrument, Endoosseous Ridge Maintenance Implant, with the trade name of EMRI, was marketed in 1988. Subsequent products were Nova Bone, Nova Min and Nova Thera, all of which have tissue regeneration and local tissue repair induction properties. All these products have the principal 45S5 bioglass structure. Perio Glass was the first special Nova Bone material marketed in 1993. The initial indication of this material was reconstruction of bone loss as a result of periodontal diseases in infrabony defects.[9] Recently, bioglass has been used in the treatment of dentinal hypersensitivity; bioglass fine particles have been incorporated into toothpastes or they are applied to tooth surfaces with an aqueous vector. Bioglass particles attach to dentin surfaces and rapidly form a hydroxyapatite layer, sealing the tubules and relieving pain. Recent studies have shown that bioglass has a better function compared to other commonly used treatment modalities.[45,46] In addition, the Orative commercial product, which contains Nova Min particles with the chemical composition of calcium sodium phosphosilicate decreases dentin hypersensitivity by precipitating calcium phosphate.[46]

**CONCLUSION**

In recent decade there has been increasing attention to the use of “smart” bioactive materials in dentistry, especially with the aim of remineralizing dentin. In some recent studies, BAG has been incorporated into GI composition to improve bioactivity and tooth regeneration and reconstruction capacity. It appears researchers all over the world should pay more attention to improve the characteristics of these materials, particularly in an attempt to control the prevalence of primary and recurrent caries.

**REFERENCES**

2. McCabe JF, Yan Z, Al Naimi OT, Mahmoud G, Rolland SL.

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Source of Support: Vice Chancellor for research at Isfahan University of Medical Sciences. Conflict of Interest: The authors declare that they have no individual, financial, or personal interests of any nature or kind in any commercial product and/or company that is presented in this article.