Tooth remineralization using bio-active glass - A novel approach

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Abstract:

Teeth go through a natural, continuous process of demineralization and re-mineralization. Demineralization occurs due to bacterial acids, foods and physiological process. Mineralization occurs from the calcium and phosphorus (normally present in saliva) precipitating into a crystalline form of calcium phosphate called Hydroxy Carbonate Apatite (HCA), which is the mineral component of all teeth and bones. Since natural re-mineralization is inadequate to maintain strong enamel, the natural re-mineralization process needs to be augmented. The discovery of Bioactive Glass pushed the boundaries of biomaterials capability and their function. In an era of bio-inert materials which can modify the tooth surface by getting impregnated in the tooth matrix, research is oriented to determine the critical steps for bioactive glass-ceramic interaction with the human body in order to bond. Various dentifrices have been formulated that have calcium-sodium-phosphosilicate as their prime constituent, which enhance tooth re-mineralization by providing calcium and phosphorus to the tooth surface. This paper is an attempt to highlight the unique re-mineralizing properties of Bio active glass.

Key words: Bio-active glass, Calcium Phosphate, Demineralization, Hydroxyapatite, Re-mineralization.

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Introduction:

Caries is just not a disease, but instead a disease process [1.] .The understanding of this basic fact has opened up newer avenues of interception of this disease process through re-mineralization. The current concept considers caries as a dynamic and reversible process and is the result of the interplay of a number of etiological factors [2,3]. Some or these factors cause demineralization whereas others promote re-mineralization of the tooth. When demineralization process continues, cavitation will eventually result. Caries can be arrested or even reversed at the pre-cavitated stage, provided a balance towards re-mineralization can be established[3].

The progressive increase in processed sugars and acidic foods and beverages in the human diet provide oral bacteria greater opportunity to produce acids that dissolve tooth mineral. Tooth mineral is composed mainly of calcium and phosphorous. Methods for providing these constituents of mineral to facilitate re-mineralization of teeth have been the backbone for newer re-mineralization strategies[1]. Recently, Bioactive glass materials have been introduced in many fields of dentistry [4].This unique material has numerous novel features, most important of which are its ability to act as a biomimetic mineralizer matching the body's own mineralizing traits while also affecting cell signals in a way that benefits the restoration of tissue structure and function [4]. Bioactive glass is considered to be a break through in re-mineralization technology. This is because the current standard treatment for tooth re-mineralization and prevention of decay is slow acting and is dependent on adequate saliva as a source of calcium and phosphorus [3,5]. When bioactive glass is incorporated into toothpaste formulations, the ions released from the amorphous calcium phosphate layer are believed to contribute to the re-mineralization process of the tooth surface [5] . The objective of this article is to highlight the unique re-mineralizing properties of Bio active glass

Fundamentals of the Tooth

Basic structure of teeth, like bone, is comprised of soft inner layers to provide nutrients, whereas outer layers are designed for structure and protection. In essence, if the tooth is generally viewed as "living" the prospect of it regenerating or re-mineralizing becomes no different than with any other biological tissue[6]. On a larger scale, it is advantageous to consider the oral cavity itself as a unique and independent ecosystem.

Hydroxyapatite

The formula for tooth mineral in enamel consists primarily of calcium hydroxyapatite, $Ca_{10}(PO_4)(OH)_2$. Enamel maintains a Ca:P ratio of nearly 1.63 as compared with the general hydroxyapatite (HA) ratio of 1.67 and that of bone is 1.71 [7.]

Featherstone describes newly mineralized bone and teeth as carbonated hydroxyapatite (CAP), which is essentially impure HA, represented by the formula $Ca_{l0-x}(Na_x)(PO_4)6\text{-}Y(C0_3)_z(OH)_{2\_u}(F)_u$ [2]
The biological apatite of tooth enamel varies due to crystal impurities and apatite combinations. At neutral pH, saliva is supersaturated with calcium and phosphate. This saturation is necessary to counter the recurrent acid challenge of dietary cycles and residual sugars which are used by oral bacteria to create acid via fermentation. These ions, among others, give saliva a buffering capacity in addition to a mineralization reservoir. Below the critical pH of human enamel (5.2 to 5.5) the dissolution of enamel mineral follows basic solubility laws for hydroxyapatite [8]

At lower pH, the dissolution of apatite mineral continues until the oral pH returns to normal. Along with saliva's own buffering capacity, salivary bicarbonate in equilibrium with CO_2 from the respiratory process shifts the equilibrium to a more alkaline condition. The state of sub-saturation for calcium and phosphate at lower pH prevents re-mineralization. When oral pH again rises above "Critical" status, the calcium/phosphate saturation of the saliva again super cedes that of the enamel and mineral deposition begins. Due to the super-saturation condition of saliva at pH 7.0, one would expect that hydroxyapatite mineral would continue to form on the enamel surface [5,8]. As in many cases within the human body however, this microenvironment is equipped with its own checks and balances. The super-saturation of calcium and phosphate does not over mineralize teeth because of the protein rich film (tooth pellicle) on the enamel surface. It is thought that saliva proteins also play a part in maintaining this balance. Still the question remains, what if the salivary pH becomes severely alkaline? This increase in pH results in dental calculus, essentially calcium phosphate precipitate in the plaque fluid. A broader look at the demineralization and remineralization process is necessary, especially when topical fluoride is introduced into the system.[9, 10]

Demineralization and Re-mineralization Phenomena

Over the course of human life, enamel and dentin undergo unlimited cycles of de-mineralization and re-mineralization. A tip in the balance one way or the other will either lead to stronger healthier teeth or greater susceptible teeth. In order to promote general oral healthcare the use of fluoride toothpastes for daily promotion of re-mineralization has become a standard practice. The process of evaluating these tissues at different stages of the oral cycle and measuring the optical and mechanical properties is the key to determine a net increase or decrease in mineral flux.

The consumption of simple dietary sugars provides not only nourishment for our bodies but also a food source for oral bacteria[11]. As bacteria making up the normal oral flora adhere to the pellicle, a bacterial mass or film called plaque is formed [11] .The plaque bacteria, particularly Streptococcus mutans and lactobacilli, ingest sugars for glycolysis to produce weak organic acids (such as lactic, pyruvic, acetic acid). These acids lower the surface pH and diffuse through the plaque pH may have dropped to 4.0- 4.5 [12] .This mineral loss compromises the mechanical structure of the tooth and could lead to cavitation over a long period of time. The stages of caries progression are clear and in the interest of preventive maintenance, early carious lesions appear to be the best opportunity for countering this destructive-process[13]. The subsequent re-mineralization process is nearly the reverse. When oral pH returns to near neutral, Ca^{2+} and $P0_4$ ions in saliva incorporate themselves into the depleted mineral layers of enamel as new apatite. The de-mineralized zones in the crystal lattice act as nucleation sites for new mineral deposition. In the presence of fluoride (at high concentrations), the original CAP loses its remaining carbonate and is replaced with a hybrid of hydroxyapatite (HAP) and fluorapatite (FAP) [2]This cycle is fundamentally dependent upon enamel solubility and ion gradients. Essentially, the sudden drop in pH following meals produces an under saturation of those essential ions (Ca and PO) in the plaque fluid with respect to tooth mineral. This promotes the dissolution of the enamel. At elevated pH, the ionic super-saturation of plaque shifts the equilibrium the other way, causing a mineral deposition in the tooth[12,13].(Figure 1).

Despite advances in oral care and incorporation of fluoride into a large number of products, there are still a large number of cavities filled every year. A substantial number of these cavities result from inadequate saliva, without which fluoride is of limited value [14,15]. Bio-active glass could benefit many individuals who experience reduced calcium, phosphate and fluoride ions caused by hypo-salivation due to physiological and pathological processes. In addition, women are at increased caries risk due to inadequate salivary calcium levels at different points in their lives including ovulation, pregnancy and post-menopause, resulting in the same net effect as reduced saliva fluoride efficacy.[16]

Composition and mechanism of action:

Bioactive glass is made of synthetic mineral containing sodium, calcium, phosphorous and silica (sodium calcium phospho silicate) which are all elements naturally found in the body. When particles come in contact with saliva or water, they rapidly release sodium, calcium and phosphorous ions into the saliva which are available for re-mineralization of the tooth surface. Unlike other calcium phosphate technologies, the ions that bioactive glass release form hyaroxycarbonate apatite (HCA) directly, without the intermediate amorphous calcium phosphate phase [4,]. These particles also attach to the tooth surface and continue to release ions and re-mineralize the tooth surface after the initial application. These particles have been shown, in in-vitro studies, to release ions and transform into HCA for up to two weeks[16]. Ultimately these particles will completely transform into HCA which is the mineral our teeth and bones are made of and results in 80 % tubular occludance and desensitization.

In a clinical trial on tooth hypersensitivity a bioactive glass containing toothpaste was shown to decrease sensitivity significantly greater than a strontium chloride toothpaste. They have also been shown to have significant anti microbial properties and can kill up to 99.99% of oral pathogens associated with periodontal disease and caries [4,16]

Bio active glass

The discovery of bioactive glasses pushed the boundaries of biomaterials capability and function. Bio active glass is a multi-component inorganic compound made of elements (silicon, calcium, sodium and phosphorous) naturally found in the body.[1] Bioactive glasses in powder particulate form provide easy dispersion in dentifrice application and exploits the fact that fine glass powder particulates resorb much faster than bulk implants [17.] Bio active glass in aqueous environment immediately begins surface reaction in three phases, leaching and exchange of cations, network dissolution of SiO^2, and precipitation of calcium and phosphate to form an apatite layer. The 5 critical stages for glass surface reactions are detailed below [18] (Table 1),

The initial Na and H /H_3O ion exchange and de-alkinization of the glass surface layer is quite rapid, within minutes of implantation and exposure to body fluids. The net negative charge on the surface and loss of sodium causes localized breakdown of the silica network with the resultant formation of (silanol) Si(OH) groups, which then re-polymerize into a silica rich surface layer. This stage involves the base catalyzed hydrolysis or Si-O-Si bonds of the glass structure.

This mechanism is based on previously well documented corrosion studies of alkali silicate glasses as well as infrared spectroscopy studies that appear to show the formation of non-bridging oxygen species following 8i-0-8i bond breakage[18] .The subsequent stages (4 and 5) involve the development of silica rich and amorphous calcium phosphate layers respectively. These stages incorporate the noticeable of biological moieties such as blood proteins, growth factors and collagen. Within 3-6 hrs, in vitro, the calcium phosphate layer will crystallize into (CAP) layer, which is essentially the bonding layer. Chemically and structurally, this apatite is identical to bone and tooth mineral, thus allowing the body to attach directly to it. These Bioactive glass surface reactions from implantation to 100-150 um CAP layer formation takes12 to 24 hours[19].

The standard for Bioactive glass formulation is commonly known as 45S5 which has been used extensively in research studies. It contains 45 wt% SiO_2, 24.5 wt% Na_2O and Ca, O and 6-wt% P_2O_5. Bioactive glasses have traditionally kept the P_2O_5 fraction constant while varying the Si-O_2 content. In fact, the network breakdown of silica by OH was found to be time dependant upon the concentration of SiO_2. It is now understood that keeping the silica below 60-w% and maintaining a high CaO/P_2O_5 ratio guarantees a highly reactive surface. A bioactive glass was developed by Dr. Len Litkowski and Dr. Gary Hack at the Department of compositions Restorative Dentistry at the University of Maryland and by Dr. David Greenspan at NovaMin® Technologies Inc [16] .When bioactive glass is incorporated into toothpaste formulations, the ions released from the amorphous calcium phosphate layer are believed to contribute to the re-mineralization process of the tooth surface [5,10] . Recently, it has been demonstrated that fine particulate bioactive glasses (<90um) incorporated into an aqueous dentifrice have the ability to clinically reduce the tooth hypersensitivity through the occlusion of dentinal tubules by the formation of the CAP layer . Investigators using bioactive glass have

demonstrated a significant anti-microbial effect against caries pathogens (S. mutans, S.sanguis) upon exposure to bioactive glass powders as well as solution and extracts.[10,20,21]

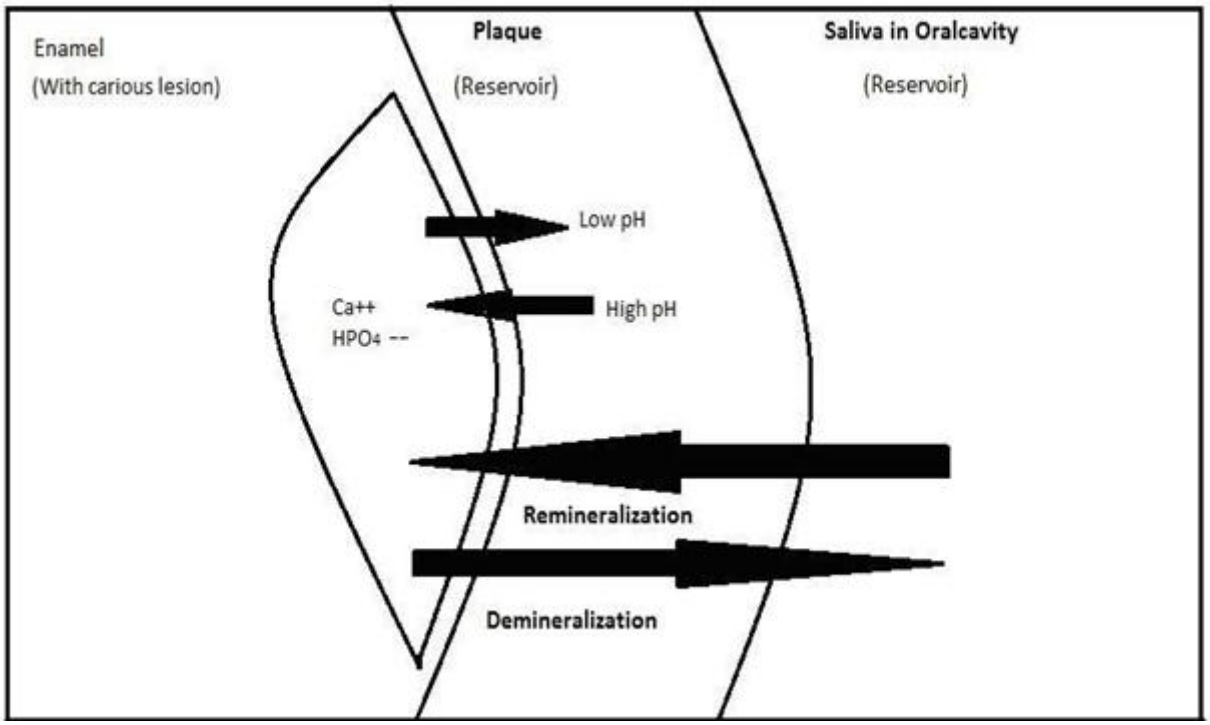


Figure 1: Cycle of demineralization and remineralization in enamel

Table 1: Stages for glass surface reactions

STAGES

1. **Exchange of Na^+ or K^+ with H^+ or H_3O^+ from the solution**

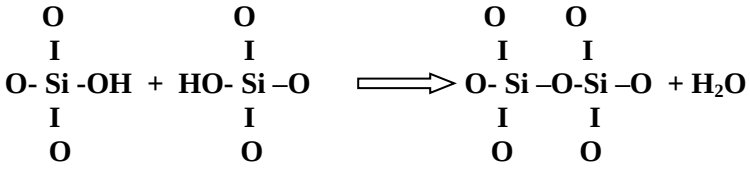
$$Si\text{-}O\text{-}Na^+ + H^+ + OH^- \Longrightarrow Si\text{-}OH^+ + Na^+ \text{(solution)} + OH^-$$

Diffusion controls this stage and exhibits a time dependent pattern

2. **Soluble silica is lost in form of $Si(OH)_4$ into the solution. This occurs because of breaking of Si-O-Si bonds and formation of Si-OH bonds at the glass solution interface.**

$$Si\text{-}O\text{-}Si + H_2O \Longrightarrow Si\text{-}OH + OH\text{-}Si$$

3. **The depleted layer in alkaline and alkaline-earth cations is repolymerised and condensed with SiO_2 rich layer.**



4. **Migration of Ca^{2+} and $PO^{3+}{}_4$ groups to the surface through the SiO_2 rich layer forming a $CaO\text{-}P_2O_5$ rich film on top of the SiO_2 rich layer, followed by growth of the amorphous $CaO\text{-}P_2O_5$ rich film by incorporation of soluble calcium and phosphates from the solution.**

5. **Crystallization of the amorphous $CaO\text{-}P_2O_5$ film by incorporation of OH^+, $CO^2{}_3$ or F^+ anions from solution to form a mixed hydroxyl, carbonate, florapatite layer.**

The bioactive glass available through bioerodible gel systems have shown significant remineralization properties[9,13.]The noninvasive treatment of early caries lesions by remineralization has the potential to be a major advancement in the clinical management of the disease. Casein phosphopeptides stabilized amorphous calcium phosphate, unstabilized amorphous calcium phosphate and bioactive glass are found to have anticariogenic efficacy.[22]

Hence, the calcium phosphate based remineralization technologies show promise as an adjunctive treatment to fluoride therapy in the noninvasive management of early carious lesions. Research is directed in search of effective biomaterials which may prove to effective and economical for tooth remineralization.

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