

## Remineralization of the Tooth Structure - The Future of Dentistry

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**Abstract:** Tooth structure undergoes continuous remineralization and demineralization in the oral environment. When this balance is changed, demineralization will progress leading to a degradation of the tooth structure. Minimal intervention is the key phrase in today's dental practice. Minimal intervention dentistry focuses on the least invasive treatment options possible in order to minimize tissue loss and patient discomfort. In the last decade there has been a veritable explosion of interest in technologies which may have value for remineralization of enamel and dentine or desensitization of exposed dentine affected by dental erosion. The key element is the usage and application of remineralizing agents to tooth structure to control the demineralization/ remineralization activity. This article looks at the process of remineralization and the various agents that enhance and /or promote remineralization and discusses their clinical implications.

**Key words:** dental caries, remineralization, calcium phosphate, critical pH, CPP-ACP, bioactive glass.

### INTRODUCTION

The oral cavity is a battlefield of activities of both remineralization and demineralization. The ratio between demineralization and remineralization determines the hardness and strength of the tooth structure. Remineralization is the natural repair process of restoring minerals again in the form of mineral ions to the hydroxyapatite's latticework structure. Demineralization occurs at a low pH when the oral environment is under saturated with mineral ions, relative to a tooth's mineral content. The enamel crystal, which consists of carbonated apatite, is dissolved by organic acids (lactic and acetic) that are produced by the cellular action of plaque bacteria in the presence of dietary carbohydrates. Remineralization allows the subsequent loss of calcium, phosphate, and fluoride ions to be replaced by fluorapatite crystals. These crystals are more resistant to acid dissolution and are substantially larger than the original crystals, thereby providing a more favourable surface to volume ratio. Thus, larger apatite crystals in remineralized enamel are more resistant to enamel breakdown by the resident organic acids. This dissolution continues until the pH returns to the normal level.

Conversely, when the pH level rises the minerals, calcium, phosphate and fluoride ions in the form fluorapatite gets deposited back to the tooth structure resulting in newly formed crystals, these crystals fuse with each other to form large hexagonal crystals. Saliva and fluoride are two key players in remineralization. The best strategy for caries management is to recover the plaque pH level higher than the critical pH with the aid of remineralization agents. Commercially a variety of agents like fluorides, caesin calcium phosphopeptides, ozone, xylitol, etc. Minimal intervention dentistry is the order of the day and contemporary and future dentistry revolve around preservation and regeneration of the dental tissues. This article provides an overview of various available agents and their roles in remineralization and their clinical implications.

## MECHANISM OF REMINERALIZATION

Our bodies utilize carbon dioxide from our breath and water from our saliva to create a mild, unstable acid, carbonic acid. Carbonic acid is the heart of the natural remineralization process. Like all acids, carbonic acids can dissolve minerals in our saliva (present from our food); however, unlike strong stable acids, carbonic acid quickly and easily converts to carbon dioxide and water. When this happens, the mineral ions that are dissolved in it precipitate out as solid mineral ions again - but not necessarily as the original mineral molecules: If a particular mineral ion is near a demineralized portion of the hydroxyapatite crystal that requires that ion, the ion is incorporated into the dental enamel. Though natural remineralization is always taking place, the level of activity varies according to conditions in the mouth.

### Requirements of an ideal remineralizing material

- Diffuses into the substance or deliver calcium and phosphate into the subsurface.
- Does not deliver an excess of calcium.
- Does not favour calculus formation.
- Works at an acidic pH.
- Boosts the remineralization properties of saliva.
- Works in xerostomic patients.

## REMINERALIZING AGENTS

### Fluoride

Fluoride ions promote the formation of fluorapatite in enamel in the presence of calcium and phosphate ions produced during enamel demineralization by plaque bacterial organic acids. Fluoride ions can also drive the remineralization of previously demineralized enamel if enough salivary or plaque calcium and phosphate ions are available. Availability of calcium and phosphate ions can be the limiting factor for net enamel remineralization to occur this is highly exacerbated under xerostomic condition.

### Fluoride mechanisms

When fluoride is applied to the tooth substrate, for every two fluoride ions, 10 calcium ions and six phosphate ions are required to form one unit cell of fluorapatite ( $\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$ ). Free fluoride ion combines with  $\text{H}^+$  to produce hydrogen fluoride, which migrates throughout acidified plaque. This ionized form is lipophilic and can readily penetrate bacterial membranes. Bacterial cytoplasm is relatively alkaline, which forces the dissociation of  $\text{H}^+$  and  $\text{F}^-$ . Fluoride ion inhibits various cellular enzymes (enolase, proton extruding ATPase) key to sugar metabolism. Hydrogen ions simultaneously acidify the cytoplasm, thus slowing cellular activities and inhibiting bacterial function.

The fluoride integrated in the enamel surface (as fluorapatite, FAP) makes enamel more resistant to demineralization than HAP during acid challenge. Fluorapatite is less soluble due to incorporation of fluoride and washing out of carbonate. Fluoridated saliva not only decreases critical pH, but also further inhibits demineralization of the deposited Calcium fluoride at the tooth surface (1).

Since the 1980's fluoride has been the most commonly used remineralizing agents (2). It is known to control caries predominantly through its topical effect. Fluoride inhibits demineralization, enhances remineralization, inhibits bacterial activity. When the acid attacks the enamel surface, the pH begins to rise and fluoride present in the microenvironment causes enamel dissolution to stop. It acts by creating calcium and phosphate phases and thereby increases the surface fluoride content in the enamel (3,4) The other contributing factors for fluoride is its antimicrobial property, reduction in bacterial adherence and increases the plaque pH (5)

Fluoride acts as a catalyst for remineralization. It may be enhanced by providing low levels of calcium and phosphate, in conjunction with minimal amounts of fluoride. It is truly remarkable the difference that a very small amount of fluoride (<1 ppm) has upon demineralization and remineralization (3). Fluoride influences the

reaction rates with dissolution and transformation of various calcium phosphate mineral phases within tooth structure and resident within plaque adjacent to tooth surfaces. When the pH rises to 5.5 and above the saliva which is supersaturated with calcium and phosphate, forces mineral back into the tooth. Fluoride makes the surface more acid resistant by bringing the calcium and the phosphate ions together and incorporates into the remineralized surface (6). Low level of F - transformation of DCPD, OCP, TCP to HAP, FHAP, FAP and high level of F - CaF is formed (3,4).

One aspect of fluoride reactivity that has raised considerable controversy is the benefits of "firmly" and "loosely" bound fluoride. Ogaard et al. proved that structurally bound fluoride is not so important for remineralization but loosely bound fluoride are important (7,8,9). Fluoride is retained in intraoral reservoirs after the application of a fluoride treatment such as toothpaste, varnish or restorative material and is then released into the saliva over time (10,11).

Fluoride release/recharge property of a material is also very important property to be considered for their long term inhibition of caries. The releasing and recharge ability of the material fully depends on the glass particle, particularly the amount of hydrogel layer over glass filler. In case of glass ionomer cement, the powder liquid reaction is acid base reaction and the reaction results in more well defined amount of hydrogel matrix over the glass particle. So that glass ionomer releases large amount of fluoride initially (hydrogel matrix) and release reduces with time, at the same time the released fluoride is recharged with external fluoride source such as fluoride solution, fluoride varnish, fluoride tooth paste, fluoride mouthrinse. The initial "burst" effect is only seen in glass ionomer, compomer and giomer does on exhibit initial "burst" (12).

The critical pH of FA is 4.5. The Ksp of fluorapatite is greater than the Ksp of hydroxyapatite. Fluoride activity is known to produce 4000 times that of OH in carious plaque. In cariogenic plaque, FA is 6 times supersaturated. The amount of fluoride needed for remineralization is F level in saliva / plaque - 0.03 to 0.08 ppm. F in saliva is retained at 0.03 to 1 ppm for 2 to 6 hours following fluoridated dentifrices, low dose fluoride mouthrinse, topical home use F agents, is reported to give very good results (13).

## **Xylitol**

Xylitol is believed to be a "tooth-friendly", non-fermentable sugar alcohol. The main properties of this sweetener is that it is not fermented to acids, less formation of plaque and reduced number of Mutans streptococci in saliva (14). It is suggested to have non-cariogenic and cariostatic properties (13).

The perception of sweetness obtained from consuming xylitol initiates the body to secrete saliva that acts as a buffer system against the acidic environment created by the microorganisms in the dental plaque. Increase in salivary pH can raise the falling pH to its neutral pH within few minutes of xylitol consumption (15). This indicates that xylitol can induce remineralization of deeper layers of demineralized enamel by facilitating Ca<sup>2+</sup> movement and accessibility (16).

Chewing xylitol gums shows a good report of reduction in the caries incidence upto 5 years even after the therapy is discontinued. The dental literature suggests that a minimum of 5-6 grams and three exposures per day (from chewing gum and/or candies) is required for clinical effect (17, 18). An exposure of three times a day and 5-6 gms of xylitol gums or candies are proven to give clinical effects (19).

A novel method of delivering remineralizing ions (calcium and phosphate) in combination with xylitol has been developed using a NaF varnish (Embrace Varnish, Pulpdent). The xylitol coating prevents early reaction and produces a sustained release of the remineralizing ions. Saliva exposure dissolves the xylitol and frees the calcium and phosphate ions. They then react with the fluoride in the varnish to form protective fluorapatite on the teeth (20).

## **Casein Phospho Peptide - Amorphous Calcium Phosphate (CPP-ACP)**

Recaldent, with the technical name casein phosphopeptide - amorphous calcium phosphate or CPP-ACP, is a milk-derived product that strengthens and remineralizes teeth and helps prevent dental caries (21). ACP technology was developed by Dr. Ming S. Tung. It was first incorporated into a consumer toothpaste product called Enamelon in 1999. The technology was reintroduced in the Enamel Care Toothpaste brand by Church &

Dwight (the Arm & Hammer folks) in mid 2004. a dual compartment tube has also been suggested to be sources of calcium and phosphate ions in the form of calcium sulfate and dipotassium phosphate.

CPP-ACP system is essentially a two phase system which when mixed together reacts to form ACP material that precipitates on to the tooth structure. It is available in solutions, gums, lozenges and creams. Reynolds et al. suggested that CPP binds to the plaque, soft tissue and dentin. The reservoir of calcium and phosphate gets accumulated on the saliva and enamel and changes the pH to acidic, thus enabling the remineralizing action (21,22). The CPP in milk stabilizes the calcium and phosphate ions through the formation of complexes which are more readily absorbed by the intestine. The same concept has been applied to Recaldent. The bioavailable complexes of calcium and phosphate are created in the appropriate form for optimal remineralization of subsurface lesions in enamel, not just on the enamel surface. CPP also localizes the ACP in the dental plaque biofilm. This initiates remineralization in the enamel and thus reduces the caries incidence (23). This paste has been claimed to fight demineralization while improving saliva flow, boosting fluoride uptake and soothing sensitive surfaces. It restores minerals that strengthen tooth enamel, reduces sensitivity from post-whitening procedures, reduces high oral acid levels from excessive soft drinks, relieves dry mouth caused by certain medications and buffers plaque and bacteria acid. The latest product available commercially is the GC Tooth Mousse. It is a water based, sugar free crème containing Recaldent® CPP-ACP. It helps to neutralize an acidic oral environment. Additional professional applications are GC can be immediately used following bleaching, ultrasonic, hand scaling or root planing.

### Bioactive glass

Bioglass one of the most important formulations, is composed of SiO<sub>2</sub>, Na<sub>2</sub>O, CaO and P<sub>2</sub>O<sub>5</sub>. Professor Larry Hench developed Bioglass at the University of Florida in the late 1960s. (24). Brauer et al. performed a study to understand the effect of addition of fluoride in the properties of bioactive glasses. CaF<sub>2</sub> concentration was increased in SiO<sub>2</sub>-CaO-P<sub>2</sub>O<sub>5</sub>-Na<sub>2</sub>O system. The incorporation of fluorine made it more bioactive (25). LitKowski et al. conducted an in vitro study on dentinal surfaces of teeth and demonstrated increased occlusion of dentinal tubules. Thereby proposed that it should also decrease dentine hypersensitivity in vivo (26). In addition to remineralization, bioactive glasses have antibacterial effects, as they can raise the pH of aqueous solution. (27, 28)

The mechanism is as follows: There is a rapid exchange of Na<sup>+</sup> or K<sup>+</sup> or H<sub>3</sub>O<sup>+</sup> from solution. This stage is usually controlled by diffusion and exhibits a t<sup>-1/2</sup> dependence. There is loss of soluble silica in the form of Si(OH<sub>4</sub>) to the solution, resulting from breakage of Si-O-Si bonds and formation of Si-OH (silanols) at the glass solution interface. This stage is usually controlled by interfacial reaction and exhibits a t<sup>1.0</sup> dependence. Condensation and repolymerization of a SiO<sub>2</sub> rich surface is depelted in alkalis and alkaline-earth cations. Migration of Ca<sup>2+</sup> and PO<sub>4</sub><sup>3-</sup> groups to the surface through the SiO<sub>2</sub> rich layer forming a CaO-P<sub>2</sub>O<sub>5</sub> rich film on top, followed by growth of amorphous CaO-P<sub>2</sub>O<sub>5</sub> rich film by incorporation of soluble calcium and phosphates from solution. Crystallization of this film forms a mixed hydroxyl, carbonate, fluorapatite layer.

The commercially available material is NovaMin. The main ingredient including , Calcium Sodium Phosphosilicate. Ions that NovaMin release form hydroxycarbonate apatite (HCA) directly. These particles release ions and transform into HCA for up to two weeks. NovaMine is significant for its anti microbial property that can kill up to 99.999% of oral pathogens associated with periodontal diseases and caries (29, 30, 31).

### Tricalcium phosphate (TCP)

TCP is a bioactive formulation of tri-calcium phosphate and simple organic ingredients. It works synergistically with fluoride to produce superior remineralization of enamel subsurface lesions when compared to using fluoride alone (32, 33). When it is used in toothpaste formulations, a protective barrier is created around the calcium, allowing it to coexist with the fluoride ions. During tooth brushing, TCP comes into contact with saliva, causing the barrier to dissolve and releasing calcium, phosphate and fluoride.

Functionalized tri-calcium phosphate, is a smart calcium phosphate system that controls the delivery of calcium and phosphate ions to the teeth, works synergistically with fluoride to improve performance. Since the structure of TCP is similar to HA, once the functionalized calcium ions are released, they readily interact

with the tooth surface and subsurface. While other calcium phosphates additives may require an acidic pH, TCP can offer optimal benefits when delivered in a neutral pH environment. This TCP ingredient can enhance mineralization and help build a high quality, acid-resistant mineral without the need for high levels of calcium (34).

TCP protects against lesion initiation and progression, prevents mineral loss, decreases hypersensitivity, sustains fluoride availability, prevents early lesions and also TCP is used in water fluoride systems (35, 36) .

### Ozone

Ozone (O<sub>3</sub>) is a powerful oxidizing agent which neutralizes acids and affects on cell structures, metabolism of micro-organisms (37, 38). O<sub>3</sub> attacks many biomolecules - cysteine, methionine, histidine residues of proteins and change the surface ecology of the carious lesion. Ozone plays an important role in caries reversal by shifting the microbial flora in carious lesion to one containing normal oral commensals. Reversal of primary root caries lesions by remineralizing plus reduction in acidogenic and aciduric micro-organisms (39). Some proteins, which are natural inhibitors to remineralization are reduced. Bioavailable minerals - patient's supersaturated saliva, aided by the remineralizing rinses, sprays and toothpastes. Currently only one device that has approval for the treatment of caries in the mouth - HealOzone (KaVo GmbH, Germany). 2100 ppm of ozone  $\pm 5\%$  at a flow rate of 615 cc/minute for 40s is regularly used. Heal Ozone remineralizing solution contains xylitol, fluoride, calcium, phosphate and zinc. (40)

### CONCLUSION

Minimal intervention dentistry is not a strategy, it is a philosophy. The future of dentistry will rely on regeneration of tooth structure. Understanding the remineralization process allows dentist to treat the lesion before cavitation. More clinical trials are necessary to know efficacy of these newer remineralizing agents.

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