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Review Article

Tooth Remineralisation: Fluorides And Beyond

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Abstract
The goal of modern dentistry is to manage non-cavitated carious lesions non-invasively through remineralisation in an attempt to prevent disease progression, and to improve strength, esthetics, and function of teeth. The emphasis currently is being given to new technologies for enamel remineralisation which suggest the changes in the understanding of dental caries. The aim of this review article is to review the fluoridated and non-fluoridated systems available for remineralisation therapy and ideas for their implementation into clinical practice..

Introduction
Worldwide, dental caries is an endemic infection and a major public health problem. While caries rates decreased during the 20th century in the United States, they were relatively unchanged during the periods 1988-1994 and 1999-2002 based on NHANES surveys.[1]
Tooth decay or dental caries results from imbalance between the process of demineralisation and remineralisation.[2]The ratio between demineralisation and remineralisation is crucial, determining the hardness and strength of tooth structure.
Enamel remineralisation has been studied for over 100 years and it has been suggested that the non-invasive treatment of early carious lesions by remineralisation has the potential to be a major advancement in the clinical management of disease.[3]

Saliva In Remineralisation
The critical role played by salivary components in controlling the equilibrium between de and remineralisation is ably demonstrated when salivary output is compromised and patients suffer dramatic increases in risk for dental caries or dental erosion.[2,4]
In the context of remineralisation, an important component of saliva are its proteins, such as the glycoproteins which adsorb onto tooth structure to form the protective pellicle layer, and the phosphoproteins which regulate calcium saturation of the saliva.
Pellicle is known to reduce mineral loss from enamel under conditions of acid challenge, more so for enamel than for dentin. Moreover, the early pellicle glycoproteins, acidic proline rich proteins and statherin, are known to promote remineralisation of the enamel by attracting calcium ions.[1,3]

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Fluorides In Remineralisation
Fluorides play a pivotal role in the prevention of dental caries. It is the most effective and most extensively tested of current anti caries agents. Fluoride levels of about 3 parts per million (ppm) in the enamel are required to shift the balance from net demineralisation to net remineralisation.[4,5] Several mechanisms have been suggested to achieve the anticaries effects of fluoride, including the formation of fluorapatite, which is more acid-resistant than hydroxyapatite; the enhancement of remineralisation; interference of ionic bonding during pellicle and plaque formation; and the inhibition of microbial growth and metabolism.[3]

The labile fluoride depot
A thin layer of fine calcium fluoride crystals forms on the tooth surface due to the fluoride ions present in its environment.[1,2,5] This CaF_2 surface layer acts as a "labile" fluoride reservoir and releases the fluoride in therapeutically active quantities over a prolonged period in the form of a "slow releasing device". The pH of the environment has a crucial influence on the release kinetics of the fluoride ions. used in combination with sodium, tin or titanium.[6]

Newer Remineralising Agents
Bioactive Glass
A class of compounds called bioactive glass has been available since the late 1960s as materials designed to help repair damaged bone. Bioactive glass is a multicomponent inorganic compound made of elements (silicon, calcium, sodium and phosphorus) naturally found in the body. The key components - SiO_2, Na_2O, CaO and P_2O_5 are mixed to be highly reactive to aqueous media.[5,6]

Bioactive glasses in powder particulate form provide easy dispersion in dentrifice application and exploits the fact that fine glass powder particulates resorb much faster than bulk implants. Bioactive 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.[4,6]

Novamin is one of these bioactive ceramic materials which falls into a class of newer agents that provide calcium and phosphate upon reaction.[2]

The products containing NovaMin include a homecare toothpaste from Natural Health Organics (Oravive® Revitalizing Paste - 5 wt%, which does not contain fluoride), prescription pastes for hypersensitivity marketed by 3M/Omni (SootheRxTM) and European distributors (Denshield® - both with 7.5 wt%), and a prophyl paste promoted by Sunstar/Butler (NuCare® - 100 wt% and water).[4]

Casein Phosphopeptides

Casein, a bovine milk phosphor-protein is known to interact with calcium and phosphate and is a natural food component. Its technical name is casein phosphorpeptides - amorphous calcium phosphate, or CPP-ACP. It was discovered by Prof. Eric Reynolds at the School of Dental Sciences at the University of Melbourne in Australia.[3,7]

Casein phosphopeptide calcium-phosphate complexes (CPP-ACP) have been found to increase the levels of calcium and phosphate in plaque up to five folds in humans in in situ caries models and short-term mouthwash studies. The proposed mechanism of their anticariogenicity is that they act as a calcium-phosphate reservoir, buffering the activities of free calcium and phosphate ions in the plaque fluid helping to maintain a state of supersaturation with respect to enamel minerals, thereby depressing enamel demineralisation and enhancing remineralisation.[5,7]

Clinical Applications Of CPP-ACP

The applications of CPP-ACP include-

1) Used for both primary and permanent teeth. Fluoride-free regular Tooth Mousse is a safe product to use in babies teeth especially young children under 2 years of age with early childhood caries.

2) Used for patients with special needs such as those with intellectual impairment, developmental and physical disabilities.

3) Used for high caries-risk patients in an attempt to remineralise early enamel lesions, early childhood caries, stabilize carious lesions awaiting treatment and root surface caries.

4) Used in cases of molar incisor hypomineralisation (MIH). This is done for remineralising hypoplastic molars and remineralisation of white spot lesions (enamel opacities and some cases of mild fluorosis).

5) Used in cases of erosion whereby it neutralizes acid challenges from internal and external acid sources.

6) Used in the prevention of tooth wear.

7) Used to reduce dentinal sensitivity by occluding patent tubules.

8) Used as a substitute for toothpaste in those allergic to commercial toothpastes.[6,7]

Amorphous Calcium Phosphate

Amorphous calcium phosphate (ACP) is the initial solid phase that precipitates from a highly supersaturated calcium phosphate solution, and can convert readily to stable crystalline phases such as octacalcium phosphate or apatite products. Its morphological form, structural model and X-ray diffraction patterns are typical for non crystalline substances with short-range periodic regularity.[8] ACP has been demonstrated to have better in vivo osteoconductivity than hydroxyapatite (HAP), better biodegradability than tricalcium phosphate, good bioactivity but no cytotoxicity. These excellent biological properties make ACP widely used in dentistry, orthopaedics and medicine.[6,7]

Tricalcium Phosphate

Tricalcium phosphate has the chemical formula $Ca_3(PO4)_2$, and exists in two forms, alpha and beta. Alpha TCP is formed when human enamel is heated to high temperatures. Beta TCP is less soluble than alpha TCP, and thus in an unmodified form is less likely to provide bio-available calcium.[9]

It is used in products such as Cerasorb®, Bio-Resorb® and Biovision®. TCP has also been considered as one possible means for enhancing levels of calcium in plaque and saliva.[8,9]

Xylitol

Xylitol was first derived from Birch trees in Finland in the 20th century and was first popularised in Europe as a safe sweetener for people with diabetes that would not impact insulin levels.

Xylitol does not simply protect teeth from caries, but creates a situation for remineralisation and repair of existing demineralised lesions.

"When remineralising solution containing xylitol is used, xylitol may act as Ca_2+ ion carrier and may maintain constant Ca_2+ ion content by introducing Ca_2+ ions from the surface layer to the middle and deep demineralised layers, thereby enhancing total remineralisation.[10]

Ozone

In cases of incipient caries, ozone can kill bacteria in the demineralized part and this demineralized tooth structure then, can be remineralised using a special remineralisation kit, containing Calcium, Fluorine, Phosphorus and Sodium, all in their ionic forms.[9,10]

Ozone is produced naturally when there is photodissociation of molecular oxygen (O_2) into inactivated ions(O-) which in turn reacts with other oxygen molecules to form transient radical anion(O_3). Ozone eventually decomposes to the hydroxyl radical, a powerful oxidant. Ozone oxidizes biomolecules such as cysteine, methionine and histidine, disrupting microbial cell structures and metabolism. Ozone disrupts microbial cell walls in seconds leading to immediate cell lysis. Once the aciduric and acidogenic micro-organisms and the protected biofilm environment that hosted them have been destroyed by ozone application, remineralisation of tooth structures is not only theoretically possible but has been achieved and clinically proven in numerous clinical trials worldwide.[8.9]

Arginine Bicarbonate

Dr. Israel Kleinberg developed SensiStat at the Department of Oral Biology and Pathology at State University of New York at Stony Brook. This technology is made of arginine bicarbonate, an amino acid complex, and particles of calcium carbonate, a common abrasive in toothpaste. SensiStat was first marketed in 2003 in Ortek's Proclude desensitizing prophy paste, and later in Denclude.[10] a professionally dispensed sensitivity paste for home use launched in 2004. The arginine complex is responsible for adhering the calcium carbonate particles to the dentin or

enamel surface.[10,11] SensiStat does not increase calcium levels in saliva as significantly as the other calcium phosphate technologies do to enhance remineralisation. Proclude prophy paste and Denclude take-home product are more effective for desensitization than for remineralisation.[8,9]

Its mode of action is based upon the arginine deiminase pathway of non-pathogenic arginolytic bacteria. These bacteria break down arginine to ammonia to neutralize plaque acids and to preserve undisturbed plaque biofilm on the tooth surface in a healthy state. As the mechanisms of action of arginine and fluoride are highly complementary, the addition of the arginine to a calcium based 1450 ppm fluoride toothpaste enhances the anti-caries efficacy compared to the efficacy of fluoride dentifrices with the same level of fluoride alone.

Dairy Products

Evidence suggests that dairy products are beneficial for the prevention of dental caries. A high intake of yogurt may lower the prevalence of dental caries in young children. Consumption of dairy products, specifically cheese, during pregnancy has also been linked to reduced dental caries in early childhood.[10]

Consuming cheese on a regular basis can prevent demineralisation by stimulating saliva and increasing calcium and phosphorus concentration in dental biofilm. When consumed regularly, calcium and phosphate are readily available during acid attacks and can prevent dissolution of enamel.[11]

Dicalcium Phosphate Dihydrate

DCPD abrasive is unique for fluoride stability. A series of studies was conducted to clarify the role of DCPD in improving the effects of fluoride in the mouth.

Dicalcium phosphate dehydrate is an acidic calcium phosphate phase which can form from tooth mineral under caries like conditions. It has been proposed as a precursor to hydroxyapatite formation in bone and in calculus. In the absence of fluoride, DCPD has been proposed as essential in the development of subsurface enamel lesions. The role of DCPD with fluoride to form fluorapatite proceeds quite rapidly under appropriate conditions and can be a mechanism for incorporation of permanently bound fluoride.[12]

Green Tea

The protective effect of green tea could not be attributed to its fluoride content, since it was quite similar to that present in the negative control (water from the public supply). Additionally, its protective effect could not be attributed either to the temperature of the rinse, since the water rinse had the same temperature. One possible mechanism of action of green tea on the reduction of dentin erosion could be the inhibition of MMPs (matrix metalloproteinases). If it is true, the main responsible for this effect may be the polyphenols. Green tea polyphenols, especially epigallocatechin-3-gallate (EGCG), were found to have potent and distinct inhibitory activity against MMPs.[13]

Chlorhexidine

Chlorhexidine is effective against a wide variety of gram negative and gram positive organisms, aerobes, facultative anaerobes and yeast. Within dentistry, chlorhexidine is the gold standard for plaque and gingivitis control. For oral use, chlorhexidine is available as rinsing solutions, gels or dental varnishes at various concentrations.

The mechanism of action is two fold; at lower concentrations, chlorhexidine interferes with cell wall transportation and metabolic pathways, whereas higher concentrations cause precipitation of intracellular cytoplasm.[14]

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