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Remineralising Agents: An Updated Review.

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ABSTRACT

Generally in the field of health, all the efforts aim at conservation of the human body and it's function. Likewise, the primary goal in dentistry is to preserve the natural tooth substance. Modern clinical dentistry focuses on managing the non-cavitated carious lesions non-invasively through the process of remineralisation. The present article highlights the different remineralising agents used in dentistry with their mechanism of action.

Keywords: remineralising, dentistry, lesions, dental caries.

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INTRODUCTION

Dental caries is a chronic multifactorial transmissible infection which results from an interaction between the bacterial biofilm, the environment and the tooth structure.[1] Its progress or reversal is determined by the balance between the pathological and the protective factors. The protective factors i.e salivary components, fluoride together with calcium and phosphate aid in remineralisation and pathological factors i.e, acid-producing bacteria, fermentable carbohydrates and reduced salivary function result in tooth demineralisation. (Fig 1) Hence, dental caries results from a shift in the balance between the two and the key factors are illustrated as part of the so-called ''caries balance''concept.[2]

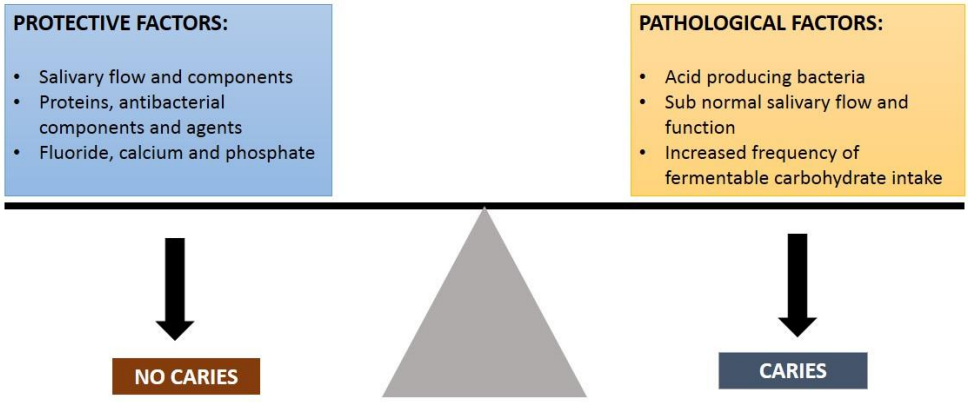

Figure 1: Illustration of Caries Balance Concept

In the management of dental decay, the conventional oral hygiene is simply not enough in many instances. Contemporary clinical practice focuses on the non-invasive management of non-cavitated lesions through remineralisation in an attempt to prevent the disease progress. Remineralisation is the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into crystal voids in demineralized enamel to produce net mineral gain. It acts a repair mechanism for sub-surface non cavitated carious lesions. [3] This article aims to review about the concept of remineralisation and the different non-fluoridated remineralising agents being currently used.

CONCEPT OF DEMINERALISATION-REMINERALISATION:

The oral cavity undergoes a continual cycle of remineralisation and demineralisation and the ratio between the two affects the toughness and the strength of the tooth structure. Demineralisation necessitates the presence of the fermentable carbohydrates and plaque on the tooth surface for a minimum interval of time. The time span has to be long enough so that these carbohydrates are retained in the mouth to be metabolised by oral microbes for the acid production. After this exposure of plaque to the carbohydrates , there is a rapid drop in the pH which is responsible for demineralisation. This is primarily due to the production of lactic acid and propionic acid being simultaneously lost from the plaque. However, the acidic nature of plaque remains only for some time and goes back to the normal within 30-60 minutes. This is due to the gradual diffusion of the acids out of the plaque and the buffering capacity of saliva which has a counteracting effect.[1]

The plaque remains depressed if there is continuous repeated and frequent sugar consumption which results in demineralisation of the teeth. Robert Stephan first described a curve called Stephens curve which shows a fall in pH below the critical level of pH 5.5, following the intake of fermentable carbohydrates at which enamel demineralisation occurs. The amount of demineralisation is determined by the absolute pH decrease and the duration of time for which the pH remains below the critical level. The gradual return of pH occurs because of buffers present in plaque and saliva. This drop in pH can demineralise tooth structure depending on the absolute pH decrease as well as the length of time when pH remains below the critical level.[4] Caries occurs when the process of reminerlisation is slower than the deminerliasation and there is a net loss of mineral into the environment.[5]

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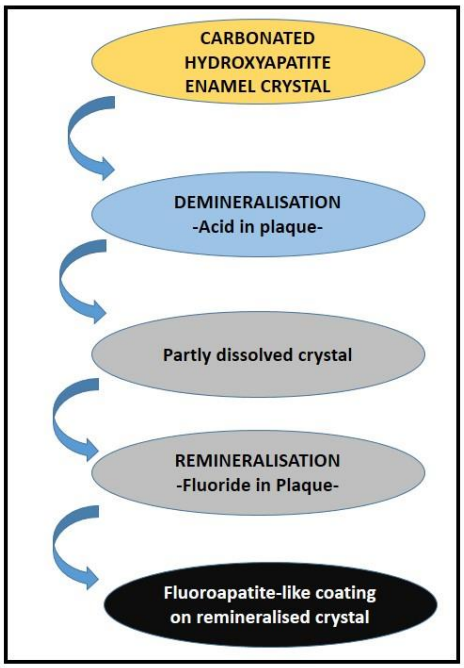

Figure 2: Demineralisation- Remineralisation Process

Tooth remineralisation can take place if pH of the environment adjacent to the tooth is high due to:

- Low cariogenic bacterial concentration
- Fluoride availability
- High salivary secretion rate
- Strong salivary buffering capacity
- Presence of inorganic ions in saliva
- Quick washing of retained food [5]

IDEAL REQUIREMENTS OFA REMINERALIZING AGENT

- Should deliver optimum calcium and phosphate into the sub-surface
- Should not favour calculus formation
- Should work at an acidic pH
- Should be able to work in xerostomic patients
- Should enhance the remineralizing properties of saliva
- Should show some benefits over fluoride [6]

Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) (GC Tooth Mousse, Recaldent)

It was introduced as a remineralizing agent in 1998. Casein phosphopeptides (CPPs) are produced from the tryptic digestion of a milk phosphor-protein, casein. There is an accumulation of the tryptic breakdown of casein and calcium phosphate which is then purified through ultrafiltration. The calcium and phosphate ions are stabilised by the small peptides released by casein. This promotes the formation of casein phosphopeptide-stabilized amorphous calcium phosphate complexes (CPP-ACP) and casein phosphopeptide-stabilized amorphous calcium fluoride phosphate complexes (CPP-ACFP). [6]

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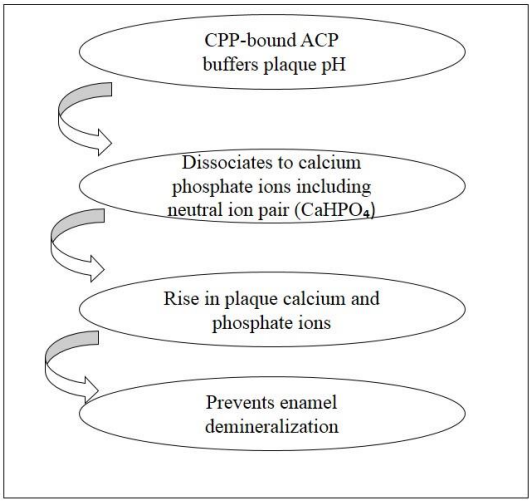

Figure 3: Mechanism of action of CPP-ACP

Casein Phosphopeptide-Amorphous Calcium Fluoride Phosphate(CPP-ACFP) (Tooth Mousse Plus™)

Casein phosphopeptides when further complexed with fluoride result in the formation of CPP-ACFP (casein phosphopeptides with amorphous calcium fluoride phosphate). CPPs improve the effectiveness of the fluoride as a remineralizing agent as they have been shown to keep fluoride ions in solution, thus leading to the formation of fluoroapatite [14]. Reynolds et l (2008) proved that in a 2% CPP ACP with 1100 ppm F dentrifice, the fluoride incorporation was much more than the one containing 1100 ppm F alone. Moreover, Jayarajan et al. in an in vitro study found that the efficacy of CPP-ACPF containing paste) was more than CPP-ACP containing paste (Tooth Mousse) paste in remineralization of artificial caries lesion. [7]

ACP TECHNOLOGY [ENAMELON, ENAMEL CARE]

The ACP technology was developed by Dr. Ming S. Tung. Tung. In 1999, ACP was incorporated into toothpaste called Enamelon and later reintroduced in 2004 as EnamelCare. It involves a two-phase delivery system which prevents any reaction between the calcium and phosphorous components before use. [8]

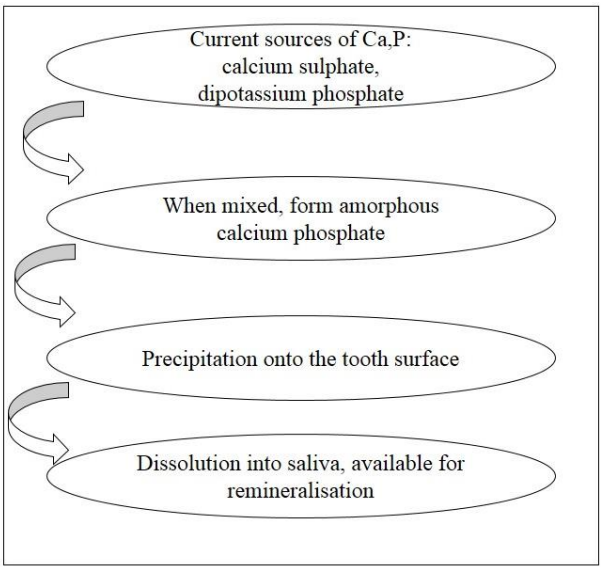

Figure 4: Mechanism of action of ACP

Regular application of ACP with fluoride increases levels of calcium and phosphate levels in biofilm and tooth structure. In fact on adding 2% ACP to as minute as 450 ppm can considerably facilitate the incorporation of fluoride ions into biofilm and coaggregate calcium and phosphate ions with fluoride ions at the tooth surface. In 1999, ACP was incorporated into toothpaste called Enamelon and later reintroduced in 2004 as EnamelCare toothpaste. However, an inherent practical concern with Enamelon™ is that calcium and phosphate are not stabilized,thus the two ions to combine into insoluble precipitates before they come into contact with saliva or enamel. This is unlike Recaldent™, which has the casein phosphoproteins to stabilize calcium and phosphate.[9]

Tri-Calcium Phosphate [Clinpro Tooth Crème]: A blend of beta tricalcium phosphate (ß-TCP) and sodium lauryl sulfate or fumaric acid made by a milling technique brings about the formation of a new hybrid material resulting in "functionalized" calcium and a "free" phosphate. Beta-TCP has an apatite like structure and retains unique calcium environments capable of reacting with fluoride and enamel.. The milling technique prevents the inactivation of both calcium and fluoride by protecting the active calcium sites prior to utilisation from premature reactions with fluoride .[10, 11, 12]

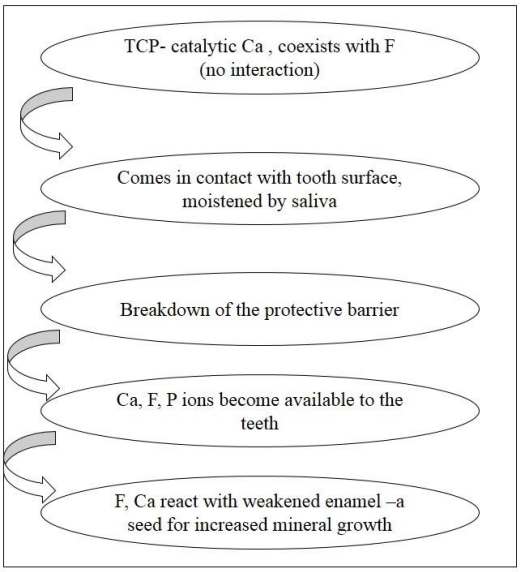

Figure 5: Mechanism of action of TCP

Products available with TCP include a 5000 ppm sodium fluoride dentifrice and a 5% sodium fluoride varnish..[35Clinpro 5000 toothpaste is TCP -Ca oxides, Ca phosphate and free phosphate ions , 5000 ppm of fluoride which makes it an effective reminerlising agents. Studies have also concluded that TCP provided superior surface and sub-surface remineralization compared with a 5000 ppm fluoride and CPP-ACP. TCP with 950 ppm enhances the microhardness of eroded enamel by chlorinated water and also results in an strength of the tooth structure.[13]

Bioglass® *(NovaMin)*

Bioglass was first introduced by Dr Larry Hench in 1960s. It has the property of biomimetic remineralisation which equals the body's mineralising traits and simultaneously controls the cell signals that aids in the restoration of tissue structure and function. [14]

NovaMin is the brand name of a particulate bioactive glass. It is technically described as an inorganic amorphous calcium sodium phosphosilicate (CSPS) material constituting of SiO2 (45%),Na2O (24.5%), CaO (24.5%) and P2O5 (6%) [26]. It is shown to release calcium and phosphate ions intraorally which repairs the weakened enamel. Although being used as a desensitizing agent , it is seen that the chemical reactions that promote apatite formation may contribute to remineralization as well .[15]

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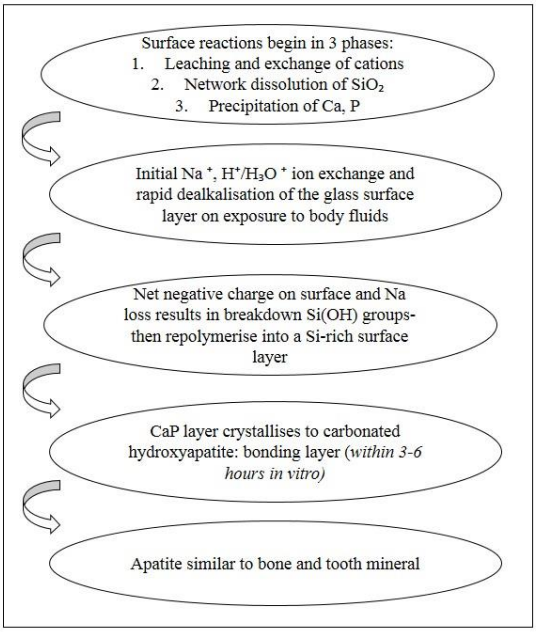

Figure 6: Mechanism of action of Bioglass

A novel study evaluated the potential remineralisation effect of topical NovaMin and sodium fluoride gel on caries-like lesions in permanent teeth. It was observed that NovaMin dentifrice had a better effect on remineralization than a fiuoride-containing dentifrice (Topex" Take Home Care' 1.1% neutral sodium fluoride gel containing 0.5% fluoride)

Pritam Mohanty 2014 evaluated the remineralization potential of Novamin by analyzing the Ca/P ratio of enamel samples around the orthodontic brackets for time periods of 0, 2 and 10 days . On comparison with a control group Novamin was suggested as a potential novel remineralizing agent.16

Xylitol

Xylitol, a well known non-acidogenic sweetener, interfers with plaque formation and its adhesion to the tooth surface. It neutralizes the plaque pH by decreasing the lactic acid formation.When used as a chewing gum, since the stimulated saliva contains higher concentration of bicarbonate and phosphate ,it enhances the salivary flow rate and the other protective properties of saliva Also it reduces the levels of S.mutans and inhibits its metabolism hence assists in remineralization of the tooth structure.[17]

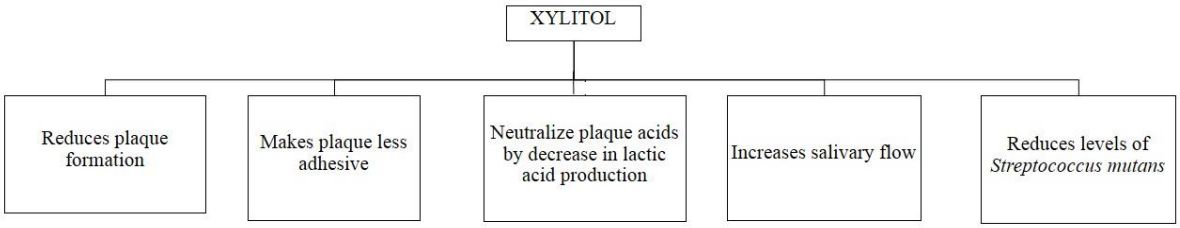

Figure 7: Mechanism of action of Xylitol

Studies have shown xylitol causes the net reduction in caries is by 83-99%. . Manton et al. showed that remineralization can occur with the use of sugar-free gum containing xylitol [17]

Grape seed extract : It contains polyanthocyanidin which is an antioxidant, reacts with microbial cell membrane proteins, and lipids resulting in breakdown of cell membrane thus causing arrest of root caries. PA facilitates the conversion of soluble collagen to insoluble collagen during development and enhances collagen synthesis.

It inhibits the glucosyltransferase, F-ATPase and amylase produced by S. mutans resulting in inhibition of dental Caries. It's potent substitute for fluorides for the prevention of root caries in elderly patients. [18,19,20]

OZONE: It is a chemical compound which is a potent oxidizing agent. Ozone acts by attacking thiol groups of cysteine amino acid and destroys the cellular membrane of carious bacteria.Ozone can shift microbial flora from acidogenic and aciduric micro-organisms to normal commensals allowing remineralization to occur. Presently HealOzone (KaVo GmbH , Germany) remineralizing solution consisting of xylitol, fluoride, calcium, phosphate and zinc is approved for treatment of caries. It can be used as 2100 ppm of ozone ± 5% at a flow rate of 615 cc/min for 40 seconds. [21]

SILVER DIAMINE FLUORIDE: It was first tested in Japan in 1960's .A chemical that is claimed to be more stable than silver fluoride and that can be kept in a constant concentration but is not as alkaine.

Studies show that it is more effective as a dentine caries arresting reagent than NaF and has many implications for pediatric dentistry. There is a reduced treatment cost associated with SDF/Fluoride varnish use. The ease of application can result in greater delivery of the reagent to a larger population of children with untreated caries. The main reported disadvantage being the non-aesthetic black colouring of carious lesions after SDF application, however the additional use of potassium iodide has been reported to reduce the discolouration [22,23]

CONCLUSION

The focus of contemporary dentistry lies in managing non-cavitated caries lesions non-invasively through remineralization to prevent disease progression and improve aesthetics, strength, and function. Evidence suggests that initial non cavitated lesion can be remineralised using appropriate technologies and even the non fluoride remineralisation strategies will be benefit to many. A favourable relationip can be established with a better understanding of the application of these remineralizing agents, It is important for dental professionals to be aware that it takes significant time to establish the bonafides of a new technology.

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