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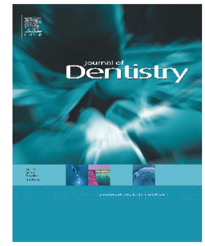

The remineralisation of enamel: a review of the literature

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KEYWORDS

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ABSTRACT

Objective: The purpose of this paper is to review current knowledge and technologies for tooth remineralisation.
Data sources: The literature was searched using the "Scopus" and "Web of Knowledge" database from the year 1971, with principal key words of *miner*, teeth and enamel. Language was restricted to English. Original studies and reviews were included. Conference papers and posters were excluded.
Conclusion: The importance of oral health for patients and consumers has seen a steady increase in the number of tooth remineralisation agents, products and procedures over recent years. Concomitantly, there has been continued publication of both *in vivo* and *in vitro* tooth remineralisation and demineralisation studies. It is clear that fluoride treatments are generally effective in helping to protect the dental enamel from demineralisation and enhancing remineralisation. Continued efforts to increase the efficacy of fluoride have been made, in particular, by the addition of calcium salts or calcium containing materials to oral care products which may enhance the delivery and retention of fluoride into the oral cavity. In addition, the calcium salts or materials may act as additional sources of calcium to promote enamel remineralisation or reduce demineralisation processes. Inspired by the concept of bioactive materials for bone repair and regeneration, bioglass and in particular calcium silicate type materials show potential for enamel health benefits and is a growing area of research.

1. Introduction

Tooth enamel is the hardest tissue in the human body.[1] Mature enamel is a crystalline structure, containing up to 96% hydroxyapatite (HAP, $Ca_{10}(PO_4)_6(OH)_2$) by weight.[1] The rest of the enamel is made up of around 3% water and 1% organic matter including proteins and lipids. The average size of the crystallites is about 50nm wide by 25nm thick and several microns long although size may vary with depth.[2] As the outer layer of teeth, enamel has to withstand a range of physical and chemical challenges. These include compressive forces (up to about 700N), abrasion, attrition and importantly acidic challenges from plaque and diet.[2,3]

The outermost region of tooth enamel is in intimate contact with saliva and plaque fluid, and the surfaces of the enamel HAP crystals are in dynamic equilibrium with these adjacent aqueous phases.[4] The rate and amount of dissolution depends not only on pH, but also on the concentration of calcium and phosphate ions in solution. The following equation describes the process in its simplest approximation.[5] At pH<5.5, HAP can dissolve in the process known as demineralisation.[6] Most commonly, tooth demineralisation is caused by acids excreted

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by bacteria as a product of their metabolism of carbohydrates or by ingestion of acidic foods. Oral health problems, such as caries and dental erosion, are associated with tooth mineral demineralisation. It has been suggested that clinical management of problems caused by tooth demineralisation should focus on early detection and prevention, such as tooth remineralisation, before a restorative approach is applied.[7,8]

$$Ca_{10}(PO_4)_6(OH)_{2\,(S)} + 8H^+_{(aq)} \rightleftharpoons 10\,Ca^{2+}_{(aq)} + 6HPO_4{}^{2-}_{(aq)} + 2\,H_2O$$

Saliva is rich in calcium and phosphate ions. It can act as a natural buffer to neutralise acid and restrict the dissolution process. At pH>5.5 together with the high concentration of calcium and phosphate ions, the equilibrium can be tipped the other way, calcium phosphate can be re-precipitated and demineralised tooth tissues remineralised.

The process of tooth remineralisation has been studied over many decades of research and has lead to the development of technologies that can promote enamel remineralisation or reduce enamel demineralisation thus giving potential oral health benefits. The purpose of the current review is to summarise the available literature concerning enamel remineralisation technologies and their modes of action. Only original studies and reviews reported in English language and listed in "Scopus" and "Web of Knowledge" databases were included in this review using the search terms of *miner*, teeth and enamel. Conference papers and posters were excluded from the review.

2. Fluoride for enamel remineralisation

Fluoride has long been known to be effective in protecting the dental enamel from caries by reducing enamel dissolution and enhancing enamel remineralisation processes. Indeed, regular brushing of the teeth with a fluoride containing toothpaste can reduce the incidence of dental caries and convey an essential oral health benefit.[9-11]

Early insights into the possible mechanisms of action of fluoride for enamel protection and repair indicated that fluoride can reduce the acid solubility of enamel and dentine.[12] It was shown that fluoride can induce fluorapatite (FA) or fluoridated hydroxyapatite (FHA) formation through reaction with HAP directly or promote the transformation of other calcium phosphate phases (such as octacalcium phosphate (OCP) and dicalcium phosphate dihydrate (DCPD)) to FA or FHA.[13] The formation of FA or FHA can reduce the solubility of HAP. In comparison with pure HAP, the inorganic components of enamel are more reactive due to their non-stoichiometry and the inclusion of impurities, such as carbonate groups.[6] Therefore, it is relatively easy to form FA or FHA on the enamel surface. Moreno *et al.*[14] studied the solubility behavior of HAP at various levels of fluoride substitution. It was found that the maximum effect was obtained when only 50% of the hydroxyl groups were replaced with fluoride corresponding to the greatest lattice stability and reflecting a low lattice free energy. Under these circumstances, there is a reduced tendency for lattice ions to dissolve and, conversely a greater tendency for such ions to join the lattice. Ingram and Nash studied the Ca:P ratio change of three calcium-deficient HAP materials with different Ca:P ratios during incubation in remineralisation solutions containing 1, 2.5 or 5 ppm fluoride. It was found that the formed FHA offered a thermodynamically more receptive location for the dissolved calcium ions to re-enter the crystal lattice vacancies created by the earlier acid attack.[15] However, the fluoride concentrations typically found in enamel are unable to confer a significant protection from caries.[16] The highest fluoride levels are found near the surface and are typically around 2000ppm in non-fluoridated and 3000ppm in fluoridated water areas. This equates to about 6 and 8% replacement of OH^- by F^- in HAP, respectively. The concentration of fluoride falls rapidly after the outer first 10-20 microns and calculations have shown that these levels are far below those able to confer an expressive reduction on the solubility of HAP.[16] During the 1980s it was established that fluoride controls caries lesion development primarily through a topical effect on de- and remineralisation processes occurring at the interface between the tooth surface and the oral fluids.[17,18] Low levels of fluoride in solution can not only prevent enamel demineralisation *in vitro* and *in situ*[19-22] but also enhance enamel surface remineralisation through enhancing apatite precipitation.[23-30] For example, the deposition of apatite mineral from mineralisation solutions into surface softened enamel was sharply increased with fluoride concentrations up to 4ppm, at which concentration the accelerating effect leveled off.[27,28]

During brushing with a fluoride containing toothpaste, the fluoride can be delivered to many parts of oral cavity including the tooth surface, saliva, soft tissues and remaining plaque biofilm. Fluoride can be deposited onto the tooth surface by formation of a CaF_2-like material. This deposit can act as a fluoride reservoir serving to protect the underlying mineral from subsequent acid challenges. At low pH, free fluoride can be released from the CaF_2-like deposit and subsequently suppress demineralisation in the local microenvironment. As the pH increases, the presence of free fluoride serves to drive mineral formation, thus fluoride acts as an inhibitor of acid-mediated demineralisation and also a promoter of remineralisation.[31,32]

The fluoride levels in saliva will be highest during brushing followed by rapid decrease post brushing due to oral clearance. However, the fluoride concentrations in saliva can be elevated compared to baseline for some considerable time and hence have the potential to reduce demineralisation and promote remineralisation.[33] Fluoride can be delivered and retained in the remaining biofilm[33] where it can be held by bacteria or bacterial fragments *via* calcium-fluoride bonds. These deposits can become involved in the re- and demineralisation processes right at the site where it is most likely needed and hence is considered the most important reservoir for fluoride in the protection of teeth from caries.[35] Indeed, clinical studies have demonstrated an inverse relationship between the fluoride concentrations in plaque and the prevalence of dental caries.[32,36]

Fluoride can also provide some protection against acid erosion processes,[37] in particular, high-concentrated fluoride applications have been demonstrated to increase abrasion resistance and to decrease the development of erosion in enamel.[37-39] In addition, there has been growing *in* vitro and *in situ* evidence that demonstrates the application of fluoride containing toothpastes and mouthrinses can help reduce the formation and progression of dental erosion compared to placebo controls.[40-55] For example, Fowler *et al*[40] found that toothpaste formulations containing 1426ppm F as sodium fluoride or 1400ppm F as amine fluoride gave significant protection of enamel from erosive acid challenges *in vitro*