



Expanding applications for CPP-ACP technology: lessons from across the globe

By Laurence J. Walsh

Around the world, there has been increasing use of casein phosphopeptide amorphous calcium phosphate (CPP-ACP) technology in dentistry over the past decade, with the range of clinical applications now extending well beyond altering the demin/mineral balance for human enamel.¹ CPP-ACP complexes act as biological calcium phosphate delivery vehicles and are able to boost levels of bio-available calcium and phosphate in saliva and plaque fluid without causing indiscriminate precipitation of calcium salts. This makes this material particularly effective in the remineralization of early enamel lesions and in the treatment of other types of enamel opacities. This article summarizes the global research effort which underpins the current clinical applications of topical CPP-ACP crèmes (GC Tooth Mousse™ and GC Tooth Mousse Plus™), drawing particularly on refereed presentations at the International Association for Dental Research (IADR), the peak international body for dental research, over the period from January 2011 to August 2014 and covering the major areas of investigation into this technology across the globe.

White spot lesion reversal

Many recent studies have confirmed the usefulness of Tooth Mousse in reversing carious white spot lesions. In a 2011 laboratory study using naturally occurring enamel white spot lesions which had developed on third molar teeth during fixed orthodontic treatment, both Tooth Mousse and Tooth Mousse Plus gave mineral gain in the subsurface region up to 230 microns, as well as surface mineral deposition.²

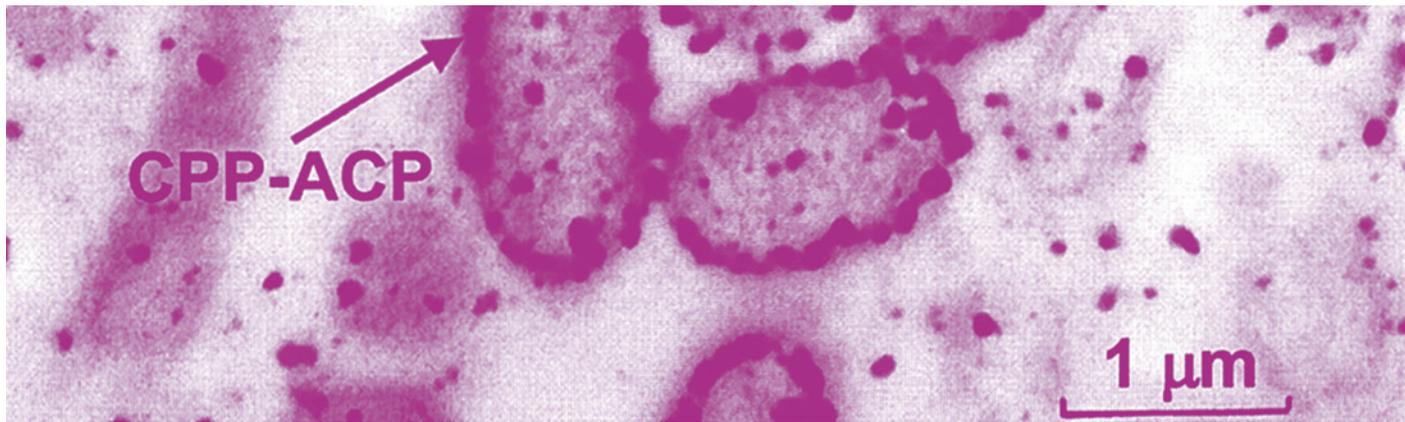
These results are consistent with other recent studies of reversal of white spot lesions created under laboratory conditions, in which the application of Tooth Mousse or Tooth Mousse Plus increased surface microhardness and longitudinal microhardness and caused mineral gain in the subsurface region of the lesion.^{3,4} Tooth Mousse has been shown to be more effective than fluoride varnish at treating experimental white spot enamel lesions.⁵ This extends the results of studies which compared Tooth Mousse or Tooth Mousse Plus with conventional fluoride dentifrices and showed the superiority of the CPP-ACP products.

In a clinical trial with 80 patients who had in total 967 teeth with white spot lesions which had developed during fixed orthodontic therapy, Tooth Mousse was more effective than neutral sodium fluoride gel when applied twice daily over six months, with greater reduction in the area of white spot lesions and in the frequency of persisting white spot lesions.⁶ Likewise, in a recent clinical trial with 60 children exhibiting at least one white spot lesion each, subjects were randomly divided into 2 groups to receive either Tooth Mousse or a fluoride containing toothpaste for a period of 3 months. Tooth Mousse gave a useful remineralization effect on the white spot lesions.⁷

Ecological effects on dental plaque

There is a growing awareness that daily application of CPP-ACP has substantial effects on the ecology of the oral microflora. A recent randomised trial conducted in the Logan-Baudest district in Queensland⁸ demonstrated that the daily application of Tooth Mousse lowered the levels of mutans streptococci (MS) in infants over the first two years of their life. In this study, subjects were randomized at a mean age of 11 days old to receive once-daily Tooth Mousse (102 subjects) or no product (89 subjects) from the time of first tooth eruption. All children underwent twice-daily tooth brushing using a low-dose fluoride dentifrice. At 24 months, there were fewer MS-positive children in the CPP-ACP group (26 percent) versus the comparison group (47 percent). A dose-response effect of CPP-ACP usage on MS was observed, where MS was present in eight percent of regular CPP-ACP users, 28 percent of irregular users and 47 percent of non-users. This emphasises the point that regular daily application of Tooth Mousse alters the oral microflora, whereas less frequent application produces more limited effects.

Parallel results have been seen in studies conducted in orthodontic patients with fixed appliances. In a recent clinical trial with 60 teenage orthodontic patients who already had white spot lesions, the daily application of Tooth Mousse suppressed the counts of mutans streptococci at 3 months, an effect not seen when an ordinary fluoride dentifrice was used.⁷



The ecological effects of CPP-ACP are underpinned by several mechanisms. The material is bound strongly into dental plaque biofilms, with particularly strong binding seen to individual *Streptococcus mutans* bacterial cells. This strong binding creates a reservoir effect, leading to elevated levels of calcium and phosphate ions in the plaque fluid.⁹ Of the existing commercial remineralization products, only CPP-ACP based products can give high levels of **water soluble** calcium and phosphate in dental plaque biofilms.⁹ Comparing the two different CPP-ACP products, greater effects are seen for Tooth Mousse Plus (which contains 900 ppm fluoride) than for Tooth Mousse (which is fluoride free) since the greater elevation of calcium and fluoride ion concentrations in the plaque fluid inhibits fermentation and helps establish a less aciduric environment. This difference between the two products was noted in a recent clinical study with 40 subjects, in which the application of either Tooth Mousse or Tooth Mousse Plus elevated plaque pH levels for the first 48 hours, but only Tooth Mousse Plus elevated plaque pH until 96 hours.¹⁰

Caries prevention

There have been many recent studies of caries prevention using topically applied CPP-ACP. Using a range of laboratory models of enamel or root surface caries, valuable preventive effects have been shown, with reduced lesion depths in both enamel and dentine.¹²

In an in vitro caries model, both Tooth Mousse and Tooth Mousse Plus gave a reduction of lesion depth in enamel and dentine and slowed lesion progression.¹² The first evidence of topical application of Tooth Mousse being able to arrest and reverse root surface caries was published in 2008,¹³ and since that time there have been many laboratory studies of root surface caries prevention, which show greater effects for Tooth Mousse and Tooth Mousse Plus compared to conventional fluoride dentifrices, a tricalcium phosphate and fluoride containing dentifrices, fluoride rinses and fluoride varnishes.¹⁴⁻¹⁹

An important caries prevention application relates to hypoplastic enamel, since enamel hypoplasia is a major risk factor for severe forms of early childhood caries. Application of Tooth Mousse improves the mechanical properties of enamel affected by Molar Incisor Hypomineralisation (MIH).²⁰ In a recent clinical study,²¹ Tooth Mousse Plus, when applied to newly erupted molars with MIH, gave elevated concentrations of calcium and

phosphate, with ratios of calcium to carbon similar to normal enamel. The treated surface had mineral crystals with a regular shape and that were better organized, with less porosity and inter-prismatic spaces. Tooth Mousse Plus accelerated the maturation of the hypoplastic enamel.

Erosion prevention

In light of the increasing per capita consumption of soft drinks and other acidic beverages in the modern lifestyle, the applications of topical CPP-ACP cremes for both preventing erosion and

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for remineralizing tooth structure which has been exposed to an erosive challenge are of interest. The most common acid found in soft drinks is citric acid, an agent which is able to both etch exposed dentine and to sequester calcium ions to prevent subsequent remineralization. Both Tooth Mousse and Tooth Mousse Plus have been shown to reduce enamel surface loss in laboratory models of dental erosion using citric acid.²² Consistent with these findings, in a recent laboratory study of the surface microhardness of human enamel, a 5-minute application of Tooth Mousse protected the enamel surface and made it resistant to subsequent acid challenges and caused recovery of surface microhardness after acid exposure.²³ Likewise, in a laboratory study of dentine erosion, Tooth Mousse and Tooth Mousse Plus applied to dentine protected the surface when challenged with Coca Cola (pH 2.6) four times per day and provided an additive anti-erosion effect over a regular fluoride dentifrice.^{24,25}

Of direct relevance to gastric reflux is the ability of topical CPP-ACP to protect tooth structure from hydrochloric acid. A recent laboratory investigation demonstrated that both Tooth Mousse and Tooth Mousse Plus increased the hardness of enamel that had been softened by exposure to hydrochloric acid for 10 minutes, using conditions which mimicked regurgitated stomach acid. Tooth Mousse Plus restored the enamel surface microhardness within one hour to the baseline value, whereas recovery of the surface microhardness of enamel was minimal with saliva alone.²⁶

While providing a degree of protection from dental erosion, CPP-ACP does not adversely affect adhesion or bonding to tooth structure. In fact, there is evidence for the converse, which relates to how the substrate for bonding is improved. For example, application of Tooth Mousse before bonding to enamel has been shown to increase the micro-tensile bond strength of sealants bonded with either etch-and-rinse and self-etching adhesives without additional enamel acid etching.²⁷ Similarly, application of Tooth Mousse to enamel was shown to improve the micro-tensile bond strength for Optibond all-in-one when used to bond composite resin restorations.²⁸

Cosmetic dentistry

The final topic of discussion is the various ways in which the application of topical CPP-ACP can augment aesthetic dentistry. A common question is whether patients who have been using topical CPP-ACP can still undergo bleaching in the normal manner. The answer to this question is yes because there is direct evidence that the application of Tooth Mousse to enamel prior to in-office bleaching does not affect the colour change caused by the bleaching procedure.^{29,30} In fact, the use of Tooth Mousse prior to bleaching can be of considerable benefit since it will improve the quality of the enamel and help prevent any reduction in surface microhardness caused by exposure to hydrogen peroxide from bleaching gels.²⁹

Following at home or in-office bleaching, the development of external stains on teeth from lifestyle factors such as cigarette smoking and consumption of beverages with tannins compromises the overall improvement to tooth shade gained by the bleaching treatment. Two recent studies show how CPP-ACP treatment of freshly bleached enamel can reduce the propensity for this surface to be stained by smoking and the consumption of tea. In a laboratory model of extrinsic tooth staining occurring after in-office bleaching, both Tooth Mousse and Tooth Mousse prevented staining of freshly bleached enamel by black tea.³¹ Using a similar methodology, in a laboratory study of cigarette smoke staining of freshly bleached enamel, treatment of bleached enamel with neutral fluoride increased staining of the enamel due to cigarette smoke, while Tooth Mousse Plus did not.³²

About the author

Professor Laurence J. Walsh is the technology editor of Australasian Dental Practice. He is also a noted commentator on and user of new technologies and the former Head of The University of Queensland School of Dentistry.

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