Role of CPP-ACP in preventing white spot lesions – A Short Review
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Introduction
White spot lesions are a problem commonly found in patients who use orthodontic devices. While it takes at least 6 months for caries to develop in a patient not submitted to orthodontic treatment, it takes around 1 month (1,2) to develop in an orthodontic patient, because of the difficulty these patients have with performing oral hygiene (3). Although there are many methods for the effective control of this caries disease, prevention of white spot lesions is a great challenge to orthodontists (4).

Formation of White Spots in Orthodontic Patients
Accumulation of plaque and cariogenic microorganism around orthodontic appliances has been reported to increase significantly during orthodontic treatment. Enamel demineralization (white spot) develops around orthodontic brackets, ligatures, and bands because these appliances make it difficult to perform cleaning, and potentiate bacterial biofilm accumulation on tooth surfaces (5). This occurs due to an imbalance between the demineralization and remineralization processes performed by saliva (6). These reactions occur in the oral cavity all the time.

Removal of fixed orthodontic appliances results in substantial reduction of the levels of cariogenic challenge and facilitates subsequent remineralization of white spot lesions. The mineral content of dental enamel is in equilibrium with its environment, and saliva contains all the necessary elements for hydroxyapatite crystal growth. In the natural state, demineralization and remineralization take place continuously; this equilibrium is restored following the completion of fixed orthodontic treatment.

Prevention of White Spot Lesions
Deminerlization area is a common problem after orthodontic treatment has been performed. Nowadays, there are various materials available, promising to minimize this problem (6). Different forms of treatment for the prevention of these lesions have been indicated, especially for orthodontic patients, because after the conclusion of treatment, many of these lesions may remain, and this is cause for concern to patients. In addition to oral health promotion and education of the patient, these methods include the adoption of measures such as the application of appropriate preventive medications (7).

Good oral hygiene with a standard fluoridated dentifrice, used daily, is prescribed for the prevention of white spot lesions. The additional use of sodium fluoride rinses (twice daily) can be effective in remineralizing the demineralized enamel. In order to achieve a balance between demineralization and remineralization, fluoride is used. Fluoride strengthens these lesions may remain, and this is cause for concern to patients. In addition to oral health promotion and education of the patient, these methods include the adoption of measures such as the application of appropriate preventive medications (7).

Good oral hygiene with a standard fluoridated dentifrice, used daily, is prescribed for the prevention of white spot lesions. The additional use of sodium fluoride rinses (twice daily) can be effective in remineralizing the demineralized enamel. In order to achieve a balance between demineralization and remineralization, fluoride is used. Fluoride strengthens the enamel structure and makes it less susceptible to demineralization. The use of fluoride releasing materials (adhesives, elastics) or even topical application of this ion (varnishes, sealants, gels, dentifrices and mouth washes) are important adjuvants in clinical practice, suggested as a method for the prevention of demineralization, particularly when the patient’s level of cooperation is not ideal (2,4).

Many researches have suggested that topical fluoride in the form of dentifrices, gels, mouth washes, and varnishes may reduce or eliminate tooth enamel decalcification around orthodontic brackets; however, due to the wide diversity of materials on the market, it is difficult for the clinician to determine which product is the most effective. Reynolds (8) reported that CPP-ACP, which is derived from milk casein, was capable of being absorbed through the enamel surface and could affect the demineralization-remineralization processes.
Effect of CPP-ACP in Treatment of White Spot Lesions

Over the last few years, agents have been developed which, under cariogenic conditions, release substances that help in the remineralization of enamel and dentin. There are new products that have casein phosphopeptide (CPP) and amorphous calcium phosphate (ACP) in their composition, a protein derived from milk, which acts on reducing remineralization and promotes remineralization of caries lesions when they are incorporated into the tooth surface of dental biofilm.

In 1995, researchers demonstrated the remineralizing potential of CPP–ACP in cariogenic studies with animals, and only in 2009 was it used for the treatment of white spot lesions. CPP–ACP is a product derived from milk, which strengthens and remineralizes the tooth structure and also has anti-cariogenic properties. CPP–ACP greatly diminishes the depth of caries lesions and increases the mineral concentration of enamel, acting as a reservoir of calcium and phosphate. These minerals form nanocomplexes in the biofilm and on the tooth surface, creating a barrier that is highly resistant to changes in pH arising from tooth enamel remineralization(9). Moreover, the enamel remineralized by CPP–ACP is more resistant to changes in pH, due to hydroxyapatite with high concentrations of calcium and phosphate ions.

Mechanism of action of CPP-ACP

CPP-ACP is a nanocluster that binds calcium and phosphate ions in an amorphous form. CPP-ACP has been shown to adhere to the bacterial wall of microorganisms and tooth surfaces. When an intraoral acid attack occurs, the calcium and phosphate ions are released to produce a supersaturated concentration of ions in the saliva, which then precipitates a calcium-phosphate compound onto the exposed tooth surface.

In Sheffield, clinical experience has been developed using the mousse (GC Tooth Mousse; Recaldent, Newport Pagnell, UK) to treat postorthodontic lesions using thermoplastic retainers as the delivery method. Patient wears a thermoplastic retainer in which a pea sized amount of CPP-ACP mousse has been spread evenly. The patient places the mousse at night and wears the retainer throughout sleep.

Use of Casein Phosphopeptide Amorphous Calcium Phosphate (CPP-ACP)

Enamel demineralization might be prevented by the application of products containing Casein Phosphopeptides Amorphous Calcium Phosphate (CPP-ACP). For many years, it has been known that milk and its derivatives have a tooth protective effect. Reynolds reported that CPP-ACP, which is derived from milk casein, was capable of being absorbed through the enamel surface and could affect the remineralization-remineralization processes. Recently, research has shown that this activity is due to a part of the casein protein called CPP, which carries calcium and phosphate ions ‘stuck’ to it, in the form of APP. This complex of CPP-ACP is an ideal delivery system for bio-available calcium and phosphate ions. The proposed anticariogenic mechanism of CPP-ACP involves the incorporation of the nanocomplexes into dental plaque and onto the tooth surface, thereby acting as a calcium and phosphate reservoir.

CPP-ACP has been shown to adhere to the bacterial wall of microorganisms and tooth surfaces. When an intraoral acid attack occurs, the calcium and phosphate ions are released to produce a supersaturated concentration of ions in the saliva, which then precipitates a calcium-phosphate compound onto the exposed tooth surface. Few studies showed that daily applications of the remineralizing cream could reverse the severity and visual appearance of postorthodontic WSL more effective than or at least as good as, fluoride toothpaste. The use of CPP-ACP can be more beneficial than fluoride rinse for postorthodontic remineralization.

Uysal et al. displayed reduced demineralization when ACP was incorporated in the orthodontic composite.

CPP-ACP products

A number of different media have been produced to deliver the CPP-ACP, including a water-based mousse, a topical cream, chewing gum, mouth rinses, and sugar-free lozenges. The material is marketed under the trade name “Recaldent, MI Paste Plus and GC Tooth Mousse.”

Recaldent (CPP-ACP) is available in several forms (gum, solution, MI Paste and MI Paste Plus [GC America, Alsip, IL, USA]), has been shown to reduce dentin hypersensitivity, reduce demineralization of enamel, and enhance remineralization in laboratory studies. An in-vitro study have reported that enamel lesions remineralized with topical exposure to CPP-ACP gum were more resistant to subsequent acid challenges compared with normal remineralized enamel. However, MI Paste and MI Paste Plus have not yet been used specifically in extensive caries clinical trials, and there is insufficient clinical trial evidence (in quality and quantity or both) to make a recommendation regarding the long-term effectiveness of CPP-ACP in preventing caries, treating dentin hypersensitivity, and treating dry mouth.

Participants applied the topical crème CPP-ACP (GC Tooth Mousse, Asia Pty. Ltd, Japan) to the tooth surfaces by using a clean finger twice a day, after brushing their teeth. A minimum of a pea-sized amount of crème was considered necessary for each dental arch. For areas that are difficult to reach (between the teeth), patients were advised to use an interproximal tooth-cleaning brush. The CPP-ACP crème was left undisturbed on the teeth by asking the participants to ensure that they kept their mouths open at least for 3 minutes after applying the crème. Eating and drinking were prohibited for 30 minutes after application.

In the 1980s, Reynolds drew attention to the fact that casein phosphopeptide amorphous calcium phosphate, which is a product derived from milk casein, was capable of absorbing through the enamel surface and could affect the carious process. CPP-ACP is a delivering system that allows freely available calcium and phosphate ions to attach to enamel and reform into calcium phosphate crystals. The free calcium and phosphate ions move out of the CPP-ACP and into the enamel rods and free-form as apatite crystals. Studies of the effects of CACP-ACP have shown promising dose-related increases in enamel remineralization within already demineralized lesions. The exact extent of substantivity of Recaldent has been reported to be from 30 minutes to several hours. Thus, several daily applications might be beneficial in high-risk patients, and, for this reason, MI Paste or MI Paste Plus can be recommended for daily use in patients undergoing fixed appliance orthodontic treatment.34 MI Paste Plus contains 900 ppm of fluoride and so may be helpful with 1000-ppm, but not 5000-ppm fluoride toothpaste to optimize thorough remineralization and minimize superficial remineralization.8 If recommended, MI Paste Plus should be used after meals and snacks (if possible) and after brushing with 1000-ppm fluoride toothpaste before, during, and after orthodontic treatment, or MI Paste can be used, if the selected toothpaste contains 5000 ppm of fluoride. A pea-size amount can be gently brushed on and around the teeth and orthodontic appliances. The combination of Recaldent and 900 ppm of fluoride toothpaste is adequate to ensure maximum remineralization of enamel.
fluoride in the MI Paste Plus used with 1000 ppm of fluoride would need to be used for several weeks or months to maximize gradual and thorough remineralization. MI Paste contains milk products and therefore cannot be used in patients with milk-protein allergies, but lactose-intolerant patients can use it.

**Conclusion**

White spot lesions affect many orthodontic patients who show poor compliance with intratreatment oral hygiene and preventive advice.1,2 The presence of fixed orthodontic appliances further affects oral hygiene and makes the cleaning of teeth more difficult; hence, accumulation of plaque around brackets and bands increases, which causes enamel demineralization.3 In addition, factors such as appliance design, improper use of cement lute, salivary flow and composition, enamel susceptibility, and, of course, dietary practices greatly influence the development of white spot lesions.4 Estimates of the overall prevalence of white spot lesions arising during fixed appliance therapy range was widely from 2% to 96%.5 Restorative treatment is the conventional approach for treating white spot lesions; however, this technique has the disadvantage of being invasive.6 If salivary or plaque calcium, phosphate ions, and fluoride ions are present in adequate amounts, they can also promote the remineralization of previously demineralized enamel. Therefore, fluoride application can be used to promote remineralization after debonding.7 The use of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) has been reported to induce remineralization because of its ability to stabilize calcium and phosphate in an amorphous state, preventing the accumulation of calcium phosphate to a critical amount that leads to precipitation.8,9 The potential of CPP-ACP in promoting remineralization was demonstrated in animal caries models in 1995, but it was used for the first time in treating white spot lesions in 2009.

**References**
