

Remineralisation of Enamel Subsurface Lesions with Casein Phosphopeptide - Amorphous Calcium Phosphate in Patients with Fixed Orthodontic Appliances

SUMMARY

One of the most common problems in everyday dental practice is the occurrence of dental caries. The easiest way to deal with this problem is its prevention. A lot of research has been done to find a material that would help to prevent the occurrence of dental caries, which means to stop tooth demineralization (loss of minerals from the tooth structure) and replace it with the process of remineralisation (reincorporating minerals in dental tissue).

In this review article we will present the remineralisation potential of casein phosphopeptide - amorphous calcium phosphate (CPP-ACP) in clinical studies. We considered all articles that were available through the browser of Pubmed Central. After analyzing the results obtained from these studies, we concluded that casein phosphopeptide - amorphous calcium phosphate has significant remineralisation effect when used in patients with fixed orthodontic appliances.

Keywords: Dental Remineralisation; Casein Phosphopeptide; Amorphous Calcium Phosphate

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Introduction

Dental caries is defined as localized destruction of tooth hard tissue with acids, produced during fermentation of carbohydrates, by bacteria in dental plaque^{1,2}. Scientific advances in restorative dentistry, new materials and techniques used, as well as understanding of its pathogenesis, have led us to more efficient preservation of oral health³⁻⁵. Main efforts are focused on reducing the risk of caries in patients by preventing its occurrence^{6,7}. Particular role in this has the correct approach of the dentist with the patient, patient's motivation to maintain oral hygiene and regular dental checkups.

The emergence of the subsurface tooth enamel lesions in patients with fixed orthodontic appliances is a common problem in dental practice⁸. The use of orthophosphoric acid as a dental etching material, in order to get better connection between the tooth surface and orthodontic rings and brackets, makes the structure

of the enamel porous and sensitive to internal and external factors⁹. Apart of this, maintaining oral hygiene is difficult in patients with fixed orthodontic appliances; this is the reason for accumulating food debris on the tooth surface¹⁰. Moreover, with this condition, a lot of bacteria are accumulated also. Acids produced by bacteria demineralise the tooth hard tissue¹¹. These initial demineralised parts of the tooth are called white spots. They have white chalky colour and indicate an area of demineralization of the enamel. This is the earliest sign of new carious lesion. According to Gorelick et al¹², their incidence in such patients reaches 49.6%. White spots have the potential to develop for a period of 4 weeks after the placement of these appliances¹³. Without acting, these spots furthermore will possibly turn into a cavitation^{14,15}. Before the cavity forms the process is reversible, but once a cavity forms the lost tooth structure cannot be regenerated. Therefore, efforts are made to prevent this process and replace it with

the process of remineralisation¹⁶. Remineralisation of teeth is a process in which minerals, such as fluoride, calcium and phosphate ions, already lost in the process of demineralization of the tooth itself, are returned in place. This process strengthens the structure of the enamel¹⁷.

Nowadays people are searching for new products, which would prevent or to some point reduce the process of demineralisation¹⁸. Pharmaceutical companies are constantly in rush to provide new materials that will be easily accepted by the masses, simple to use and their results will represent a major step towards improvement of oral health.

Listing the literature we can find a lot of information about the anti-cariogenic effect of the dairy products¹⁹. This effect is due to multiple-phosphoseryl, which contains sequences of casein. By enzymatic reaction these sequences can turn into casein phosphopeptide. Casein phosphopeptide has great ability to stabilize casein phosphate, as a solution of amorphous calcium phosphate complex. Anti-cariogenic mechanism of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) is due to localising of amorphous calcium phosphate on the tooth surface, wherefrom free active ions of calcium and phosphate are released and incorporated into the tooth enamel²⁷. Following this, it prevents demineralisation and increases the process of remineralisation of the tooth structure^{20,21}.

Casein phosphopeptide - amorphous calcium phosphate (CPP-ACP) is a natural protein derived from milk. Lately, it has great use in the prevention of the occurrence of dental caries²⁷. Therefore, its application and role in remineralisation process of dental structures is subject of many scientific studies. Clinical studies are taken to provide what are the benefits of its use, what are possible ways of application, when is the best time to start using it and over what period, as well as which patients could benefit from it.

In this article, we will briefly try to summarize the results and conclusions obtained from multiple clinical trials performed on this issue.

Method of Search

Searching the literature through Pubmed Central browser, we found approximately 15 papers where clinical trials related to this issue were performed. The purpose of these studies was to prove the remineralisation effect of CPP-ACP ions on the initials subsurface enamel lesions. These studies were done *in vitro*. Electron microscope was used as a method of inspection of the treated teeth.

The conclusions of all the papers we found highlight the positive effect of CPP-ACP in the process of remineralisation.

Discussion

Calcium and phosphate are essential components of enamel and dentin. They form insoluble complexes but, in the presence of CPP, they become soluble and biologically available. These CPP-ACP complexes applied on tooth surface by chewing gums, mouth rinses, tooth pastes or applied by using a spray, are able to adhere to dental biofilm and enamel hydroxyapatite crystals. Thus, bioactive calcium and phosphate ions are formed in the biofilm. Also, CPP-ACP complex serves as a reservoir of bioactive calcium and phosphate ions. The oral environment becomes supersaturated, which enables an uninterrupted supply of these ions in places that are previously demineralised²². This is proved by the fact that significantly higher levels of calcium and phosphate are found in biofilms, as well as lower levels of demineralisation of dental tubules and enamel surfaces, in patients previously treated with CPP-ACP based products.

Numerous clinical studies prove the anti-cariogenic effect of CPP-ACP, as well as in laboratory conditions, animal and human *in situ* experiments²⁰. This examination usually is made by using scanning electron microscope (SEM) with energy dispersive X-ray analysis (Fig. 1). SEM provides detailed high resolution images of the sample by rastering a focussed electron beam across the surface. An Energy Dispersive X-Ray Analyser (EDX or EDA) is also used to provide elemental identification and quantitative compositional information. This allows us to estimate quantitatively the amount of minerals present at the tooth sample. Based on the results taken from the analysis we can calculate the amount of minerals loss during the process of demineralisation, or amount of minerals incorporated by the process of remineralisation. From the microscopic images, noted below, we can easily see zones of remineralisation, as thickened hyper-calcified lines around the porous spots of the enamel structure (Fig. 2)²³.

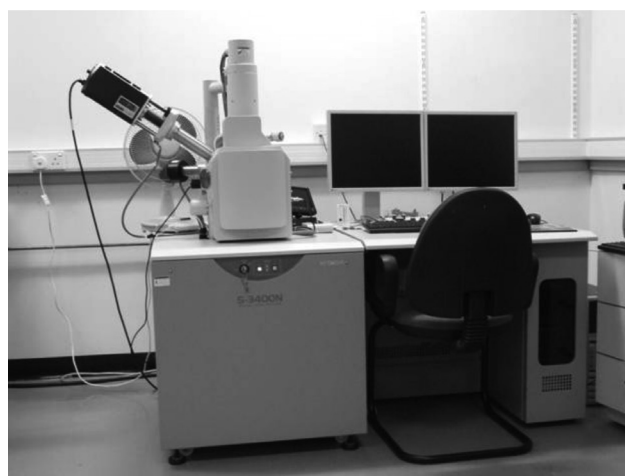


Figure 1. Scanning electron microscope that uses energy dispersed X-rays

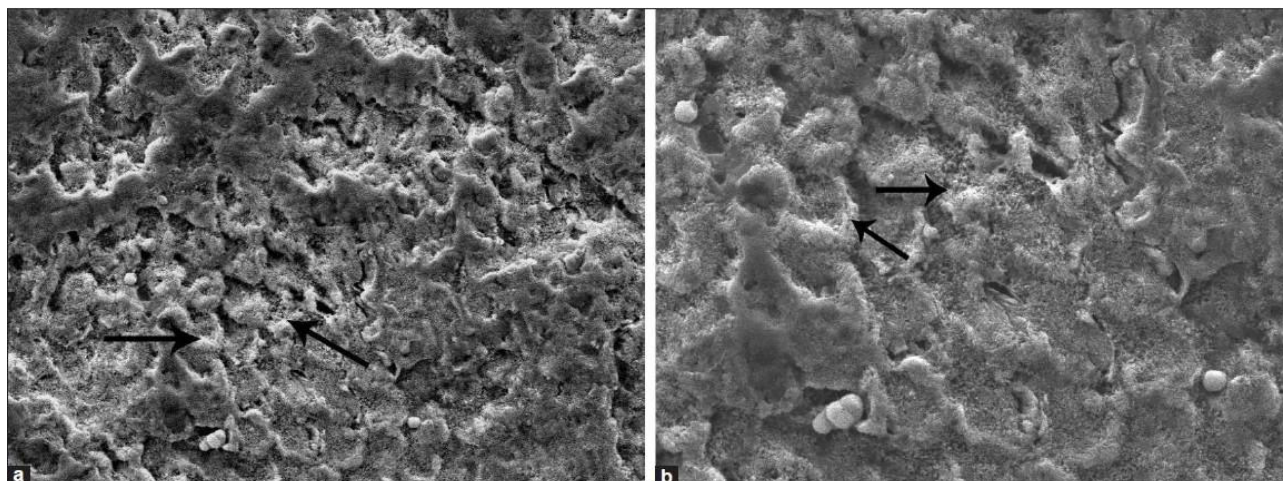


Figure 2. CPP-ACP treated inter-prismatic enamel surface. (a) Porous spots and zones of remineralisation around them, 1000x (b) Thickened hyper-calcified areas around enamel prisms, 2000x

Couple of clinical studies confirm the increased remineralisation effect of CPP-ACP by using chewing gum²⁰Error: Reference source not found, tooth paste²⁴ or gel based products²⁵. Last one is especially important in patients with fixed orthodontic appliances, as they are high risk subjects for occurrence of enamel defects²⁶.

Tooth paste rich with CPP-ACP complexes, applied on the tooth surface with an initial carious lesion, can prevent tooth demineralisation process and increase remineralisation. They also speed up the fluoride activation process²⁷.

According to the results of several studies conducted in order to determine the remineralisation effect of CPP-ACP right after etching of the tooth surface with orthophosphoric acid, it has been proven that there is a significant difference in structure of the enamel in patients treated with CPP-ACP and those who are not²⁸. So, we can conclude that the use of CPP-ACP significantly reduces the risk of caries after the micro-abrasion has been made.

As clinical practitioners, we are witnesses on great presence of white spots (initial subsurface enamel lesions) in patients while wearing fixed orthodontic appliances. These sub-structural changes are visible with a naked eye, due to the change of the colour of tooth enamel and they are confirmed by electron microscopy. White spots are created because of the reduced ability to maintain oral hygiene. Therefore, lot of bacteria deposits are present on tooth surface, with their acids damaging the hard dental tissue. So, preventing the development of white spots into the carious lesion is the main goal in patients with fixed orthodontic appliances. Daily application of CPP-ACP, regress the process of demineralisation and supports the dental tissue with new calcium and phosphate ions on the place of already lost ones²⁹.

The positive effect of CPP-ACP makes it applicable to various ranges of patients:

- Patients with mineral disbalance in oral cavity;
- Patients with high risk of caries;
- Patients with xerostomia;
- High dental sensitivity;
- After professional teeth cleaning and curettage;
- Before, during and after teeth whitening;
- During the entire orthodontic treatment;
- In patients with dental erosion or recession of the gingiva;
- At sufficiently formed early lesions;
- Lesions of the white spots;
- Stimulating the process of remineralisation;
- For patients with diabetes or HIV;
- Patients who are treated by radiotherapy or chemotherapy.

There are many methods of application and they are quite simple. For example, special individual template can be made for this purpose in which we put paste that contains CPP-ACP. Then, we can apply it by using dental micro-brush, interproximal brush, dental sponge stick, or simply put the required amount of paste on a finger and abundantly coat the tooth surface.

One of the studies that we process in this review article indicates the dependence of dose and duration of use of CPP-ACP products in remineralisation process. So, it is noted that the process of remineralisation reaches its maximum effect after 35 days of its use, if it is applied twice a day for a period of 3 minutes (Figs. 3 and 4)³⁰.

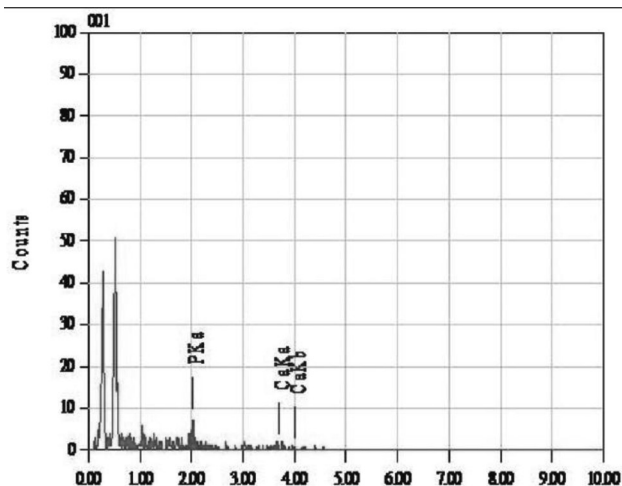


Figure 3. Analysis of demineralised enamel sample by Energy Dispersive X-ray

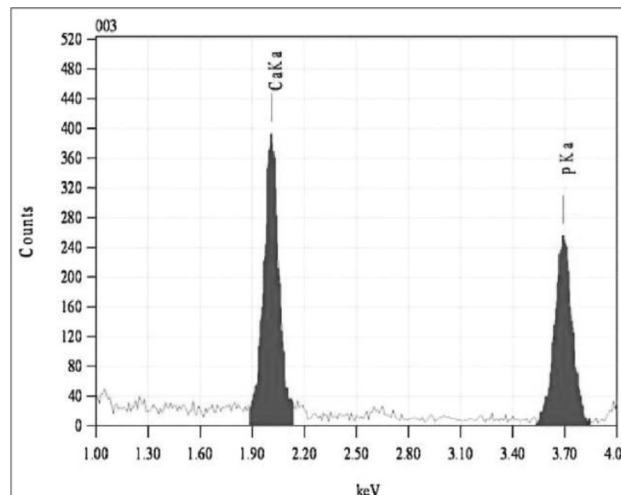


Figure 4. Analysis of enamel sample by Energy Dispersive X-ray after 35 days of use of 10% CPP-ACP paste - GC Tooth Mousse

Beside the use of CPP-ACP as a material for remineralisation of the tooth surface in dental practice, also other fluoride based materials are used for this occasion, such as fluoride rinses and fluoride pastes. However, it is proven that the use of fluoride rinsing solutions has significantly lesser effect than the use of CPP-ACP ions - GC Tooth Mousse³¹.

Based on the results obtained, we can conclude that CPP-ACP complexes have a positive effect in dental practice. Therefore they should be included in treatment of patients with fixed orthodontic appliances, such as risk group that has a predisposition for the occurrence of enamel defects.

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