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A review of novel dental caries preventive material: Casein phosphopeptide–amorphous calcium phosphate (CPP–ACP) complex

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Abstract A paradigm shift is emerging in dentistry and dental treatments are now aimed at maximum conservation of tooth structure. It is nowadays considered an ethical duty of a dentist to provide their patients with minimally invasive treatment. Remineralization therapy is preferred in cases, where there is a chance of gaining success by preventive methods. Many novel caries preventive materials are now available in the market which contain components that have the ability to initiate remineralization. One such component which is caries preventive and is present in many dental materials is Casein phosphopeptide–amorphous calcium phosphate (CPP–ACP).

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1. Introduction

Dental caries belongs to a group of complex diseases and it ensues because of multiple contributing factors. Many strategies are nowadays being applied for the prevention of dental caries but no single strategy can guarantee 100% success.[1]

Conventionally, it was believed that dental caries is an irreversible disease. The traditional approach of treating dental caries was to remove the caries affected enamel or dentine and to replace it with a restorative material.[2]

This approach resulted in a considerable loss of tooth structure. As a result of the recent studies, old concepts have changed and now there is a paradigm shift in the aetiology, diagnosis, preventive strategies and treatment of dental caries and many novel materials have been formulated for its prevention.

2. Novel dental caries preventive materials

The process of demineralization and remineralization occurs continuously in the oral cavity. Some methods or materials provide aided remineralization like the application of topical fluoride. A restorative material that contains preventive elements for dental caries has been desired for a long time.[3]

Many novel dental materials can aid remineralization like materials containing CPP–ACP and calcium sodium phosphosilicate or bioactive glasses.[4]

Dental research has shown the importance of calcium and phosphate ions in the remineralization process. Longbottom C. et al., proposed in 2009 that an ideal caries preventive material should release calcium and phosphate in the oral environment.[5] Therefore, manufacturers of novel caries preventive dental materials are now incorporating CPP–ACP in the composition of their products for the prevention of caries.

3. Casein phosphopeptide–amorphous calcium phosphate complexes (CPP–ACP)

CPP–ACP is a milk product which helps in remineralization and prevents dental caries. Casein phosphopeptide can deliver amorphous calcium phosphate and can also help the ACP to bind with the dental enamel. Casein phosphopeptide can also decrease the count of Strept. Mutans as it has got the ability to integrate in the pellicle[6] (Fig. 1).

CPP is a peptide which contains elements that can bind calcium. Casein phosphopeptide can stabilize calcium phosphate present in the solution as amorphous calcium phosphate. Several *in vitro* studies have shown the role of CPP–ACP in the reversal of the early white spot lesion.[9,10]

4. Mechanism of action

Casein phosphopeptide forms nanoclusters with amorphous calcium phosphate thus providing a pool of calcium and phosphate which can maintain the super saturation of saliva. Since CPP–ACP can stabilize calcium and phosphate in the solution, it can also help in the buffering of plaque pH and so calcium and phosphate level in plaque is increased. Therefore calcium

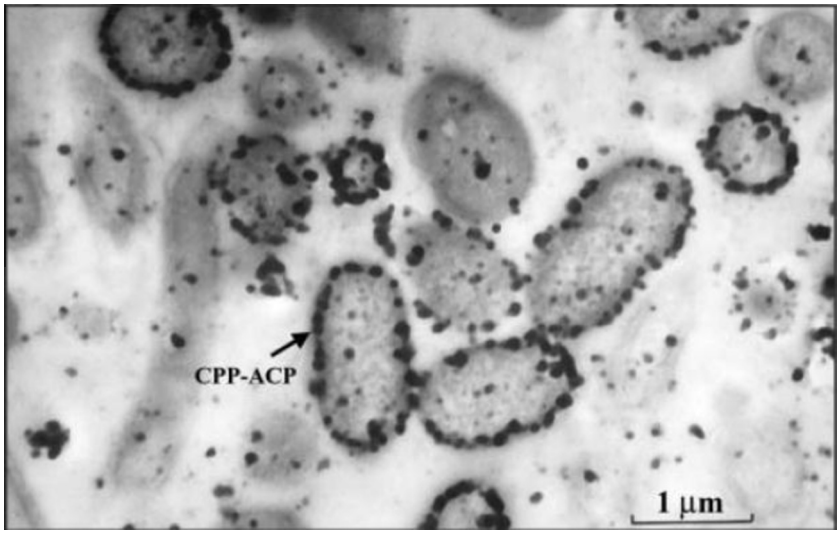

Figure 1 Electron histochemistry of a supragingival plaque sample demonstrating CPP–ACP nano complexes confined in the plaque matrix and on the surface of bacterial cells.7,8

Table 1 Percentage of increase or decrease in the lesion depth after getting treated by fluoride toothpaste, non-fluoride tooth paste and CPP–ACP.

Treated with	Decrease in the lesion depth (%)	Increase in the lesion depth
Fluoride tooth paste	7	–
Non fluoride tooth paste	–	23%
CPP–ACP tooth paste	10.1	–
CPP–ACP as a coating	10.1	–
CPP–ACP as a coating after the use of fluoride tooth paste	13.1	–

and phosphate concentration within the subsurface lesions is kept high which results in remineralization.[4]

5. Delivery of CPP–ACP

Mazzaoui et al., in 2003 used CPP–ACP with fluoride and demonstrated a synergistic remineralization potential.[11] It can be delivered via tooth mousse, chewing gum (chewing gum increases the salivary stimulation and the benefits of CPP–ACP are also present), mouth rinses and toothpastes[4] and CPP–ACP helps in the reduction of tooth sensitivity when it is present in tooth pastes.[12]

6. Evidence of preventive role of CPP–ACP in dental caries present in the literature

Reynolds EC et al., performed a study in 2003 and showed that when CPP–ACP was present in a mouthwash, it resulted in the increase of calcium and phosphate levels in supragingival plaque.[13]

Kanako Yamaguchi et al., carried out an *in vitro* study in 2005 on bovine enamel and concluded that CPP–ACP paste prevented demineralization. The paste also increased remineralization of enamel as compared to the other paste that was CPP–ACP free.[14]

Maki Oshiro et al., used CPP–ACP paste on bovine teeth in 2007 to demonstrate its remineralizing potential. Bovine teeth were cut into blocks. Few of the specimens were placed in lactic acid (demineralizing solution) and were then placed in artificial saliva. Remaining specimens were stored in CPP–ACP paste solution and they were then placed in demineralizing solution and artificial saliva. Scanning electron microscopy (SEM) was utilized to observe morphological features and it revealed that the specimens which were treated with CPP–ACP first, showed little morphological changes as compared to the remaining specimens and so it was concluded that CPP–ACP has the ability to prevent demineralization.[15]

Christos and George in 2007[16] carried out an *in vitro* study on human teeth to demonstrate the effect of CPP–ACP commercial paste on demineralization and remineralization. They used multiple internal reflection–Fourier transform infrared

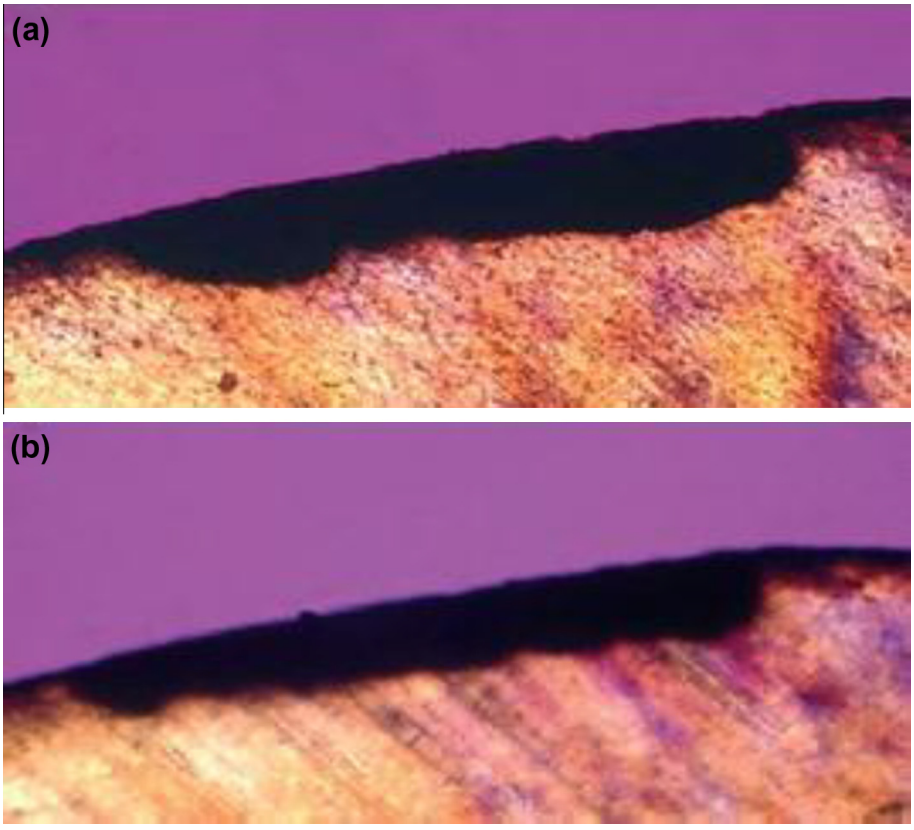

Figure 2 Polarized light micrograph of the lesion treated with the coating of CPP–ACP after the use of fluoride toothpaste showing a decrease in the lesion depth. (a) Before treatment. (b) After treatment.[17]

spectroscopy (MIR–FTIR) for analysis and concluded that the presence of CPP–ACP agent on dentine caused decreased demineralization and increased remineralization when compared with the surfaces of dentine where CPP–ACP agent was not applied.

An *in vitro* study was performed by Kumar et al.,[17] to compare the remineralization potential of fluoridated toothpaste and CPP–ACP (in various forms). Artificial caries like lesions was developed in the permanent extracted teeth by keeping them in the demineralizing solution for 96 h. The tooth samples were then treated with fluoride toothpaste, non-fluoride toothpaste and CPP–ACP. Following values were obtained after the study (Table 1) (Fig. 2).

It can be clearly seen from the results of the above mentioned study that the application of CPP–ACP after the use of fluoride toothpaste is the most effective method for remineralization.

7. Indications of CPP–ACP

CPP–ACP can be used to remineralize early carious lesions.[18] It has the ability to counteract the action of acids in cases of erosion.[19] It has been proposed that CPP–ACP (Tooth-Mousse) has an edge over fluoride tooth paste when it comes to neutralizing acids in the oral cavity.[20] CPP–ACP can also block the dentinal tubules and in turn can reduce the sensitivity.[21] CPP–ACP alone or its combination with fluoride can be utilized as a prophylactic agent before the bonding of orthodontic brackets.[22]

8. Potential areas for improvement

Calcium, phosphate and fluoride are all very important for remineralization of tooth. CPP–ACP ensures increased availability of calcium and phosphate but not of fluoride. The solution to this problem is to deliver it through a product like fluoride varnishes so that there is an increased level of fluoride available which will ensure increased remineralization.

Also since CPP–ACP is a milk product, it cannot be given to patients having intolerance to milk. Therefore a suitable alternative for these patients is required. The total time taken by CPP–ACP for remineralization is still not clearly established and needs further investigation.

Apart from the combination of CPP with ACP, if a combination of CPP with amorphous calcium fluoride phosphate (ACFP) is used, CPP would stabilize ACFP just like it stabilizes ACP. In this scenario, there would be an increase in the degree of saturation because phosphate, calcium and fluoride ions localize at the surface of tooth and this enhances remineralization which is also described in an *in vitro* study.[23]

Addition of CPP–ACP complex into restorative dental materials is also a potential area of further research. Some researchers have already added CPP–ACP into Glass ionomer cements (GIC) and have concluded after their *in vitro* study that GIC containing CPP–ACP provided increased protection to dentine during acid attack.[24]

9. Conclusion

CPP–ACP products have provided a new direction to preventive dentistry. From this literature review, the role of CPP–ACP in the prevention of dental caries is quite evident and therefore its incorporation in various dental materials should be encouraged.

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