

Original Research Article

## The benefits of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) in pediatric dentistry

Hariri El Mehdi<sup>1</sup>, Ramdi Hind<sup>2</sup>, Chhoul Hakima<sup>3</sup><sup>1</sup>Resident in Pediatric dentistry, faculty of dentistry, center of consultation and dental treatment, Mohammed V University in Rabat, Morocco.<sup>2</sup>Professor in Pediatric Dentistry, Faculty of Dentistry, center of dental treatment and consultation, Mohammed V University in Rabat, Morocco.<sup>3</sup>Professor in Pediatric Dentistry, Faculty of Dentistry, center of dental treatment and consultation, Mohammed V University in Rabat, Morocco.

### \*Corresponding author

Hariri El Mehdi

Email: [haririelmehdi@gmail.com](mailto:haririelmehdi@gmail.com)

**Abstract:** The pathogenesis of enamel caries involves an imbalance in the physiological process of remineralization/demineralization of the dental structure. White-spot lesions are the earliest macroscopic evidence of enamel caries. The subsurface loss will continue if early treatment was not made, and eventually the surface layer will collapse and lead to a cavity formation. Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) is a unique, naturally derived protein-based remineralizing mechanism. By its incorporation at this stage, the lesion can be reversed. It will have a strong impact on the public health aspects of caries control. The aim of this review is to describe the chemical nature, mechanism of action, and effectiveness of CPP-ACP as a remineralizing agent and its various uses in clinical conditions as well as the different methods of application of CPP-ACP products in modern practice.

**Keywords:** casein phosphopeptide-amorphous calcium phosphate(CPP-ACP), enamel caries, remineralization

### Introduction :

Dental caries is a bacterial biofilm induced acid demineralization of enamel or dentin, mediated by saliva. The disease of early childhood caries (ECC) is the presence of 1 or more decayed (noncavitated or cavitated lesions), missing (due to caries), or filled tooth surfaces in any primary tooth in a child 71 months of age or younger[1]. In children younger than 3 years of age, any sign of smooth-surface caries is indicative of severe early childhood caries (S-ECC).

It is a serious problem that progresses rapidly and often goes untreated. Current traumatic treatments may be replaced by safe and effective remineralization at very early stages especially a recent advancement in the phenomenon of remineralization known as the casein phosphopeptide-amorphous calcium phosphate (CPP-ACP)[9].

### What is CPP-ACP ?

CPP-ACP is an acronym for a complex of casein phosphopeptides (CPP) and amorphous calcium phosphate (ACP). Caseins are the predominant phosphoproteins in bovine milk, they are an

heterogenous family of proteins predominated by alpha 1 and 2 and beta caesins. CPPs are phosphorylated casein-derived peptides produced by tryptic digestion of caesin. This protein nanotechnology combines specific phosphoproteins from bovine milk with forming nanoparticles of ACP. The precise ratio is 144 calcium ions; 96 phosphate ions and six peptides of CPP[2].

### Mechanism of Action of CPP-ACP :

The possible cariostatic potential of dairy products is the subject of many reports in the literature. In 1991, the complex CPP-ACP, derived from a major protein found in milk called casein, was patented in the United States[3].The complex is presented as an alternative remineralizing agent that is remarkably capable of stabilizing calcium phosphate, maintaining a state of supersaturation of these ions in the oral environment. In the past, the clinical use of calcium and phosphate ions for remineralization was relatively unsuccessful due to the low solubility of calcium phosphates, particularly in the presence of fluoride ions. To overcome these difficulties, a new calcium phosphate remineralization technology was developed based on casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), where CPP stabilizes high

concentrations of calcium and phosphate ions, together with fluoride ions, at the tooth surface by binding to biofilm[10]. The ACP technology was introduced in the early 1990 and has demonstrated anticariogenic activity in laboratory, animal and human in situ experiments. Reynolds and colleagues reported that CPP-ACP binds readily to the surface of the tooth, as well as to the bacteria in the plaque surrounding the tooth. In this way, CPP-ACP deposits a high concentration of ACP in close proximity to the tooth surface[16]. Therefore under acidic conditions, this localized CPP-ACP buffers the free calcium and phosphate ions, substantially increasing the level of calcium phosphate in plaque and maintaining a state of supersaturation that inhibits enamel demineralization and enhances remineralization.

#### **Application of CPP-ACP in paediatric dentistry**

- Remineralization of White-Spot Lesions :

White-spot lesions are considered as a non-cavitated carious lesions extending up to the dentin-enamel junction. They can be arrested by using remineralizing agents. The casein phosphopeptides and amorphous calcium phosphate CPP-ACP is biologically active and able to release calcium and phosphate ions to maintain the supersaturated state, thus improving the remineralization process[11,25].

- Remineralization of Early Enamel Lesions of Primary Teeth :

Early childhood caries (ECC) is a major public health problem world wide. It corresponds at any form of caries in infants and preschool children. It begins with white-spot lesions, and caries can progress rapidly, leading to complete destruction of the crown. Calcium and phosphate ions are more readily lost for children because they eat mainly soft and sweet foods, and due to lower mineralization of deciduous enamel. The disease usually develops very quickly and causes many childhood health problems, such as caries-related toothache and infection. Demineralization and remineralization are dynamic processes in caries initiation, progression, and reversal. Therefore, regulation of the demineralization-remineralization balance is a key to caries prevention and treatment[3,6]. Reynolds et al have shown CPP-ACP to be effective in the remineralization of carious lesions. In their study, the use of CPP-ACP resulted in an increase in the remineralization of the dental enamel and dentin as observed under scanning electron microscopy (SEM)[16]. Another study suggests CPP-ACP can be expected to be effective in high-risk children who have not developed good oral hygiene habits. When used in combination with fluorides, CPP-ACP shows better results and lower caries scores than when used individually[4]. Synergistic effects of CPP-ACP and fluoride have been reported in several studies. An in-situ study conducted by Srinivasan et al compared the remineralizing potential of CPP-ACP and CPP-ACP with 900 ppm fluoride on enamel softened by cola drink. The study showed better results in CPP-ACP

with 900 ppm fluoride and confirmed the synergistic effects of CPP-ACP with fluoride on remineralization of eroded enamel[5,7].

- Prevention of white-spot lesions during orthodontic treatment :

The casein phosphopeptides and amorphous calcium phosphate (CPP-ACP) has been used to prevent demineralization during orthodontic treatment which can cause white-spot lesions at the tooth surface that can further develop into caries, as explained by Ogaard et al. The application of CPP-ACP resulted in a reduction in the demineralized areas, and this effect was more pronounced when CPP-ACP was combined with fluoride toothpaste[8,11,25].

- Prevention of enamel erosion caused by sports drink, soda or swimming pool water :

Ramalingam et al conducted an in-vitro study to determine if the incorporation of CPP-ACP to a powerade sports drink would eliminate enamel erosion. The authors concluded that there was significant reduction in the beverage's erosivity without affecting the product's taste[12,22].

- Prevention of caries in patients with xerostomia :

In vivo studies in patients with xerostomia treated with CPP-ACP as mouth rinses show a lower rate of new caries lesions than for patients treated with 0.05% fluoride mouth rinses, although there were no significant differences between the groups after a control period for 12 months[4].

#### **Delivery method :**

Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) is available in different presentations:

**CPP-ACP in toothpaste :** toothpastes containing CPP-ACP with a concentration of 10% are effective in the remineralization of early enamel lesions[14].

**CPP-ACP in mouthrinse :** mouthrinse containing CPP-ACP, with a concentration from 2% to 10% increase significantly the concentration of ions of calcium and phosphate in the biofilm[15].

**CPP-ACP in varnish :** varnish containing 2.26% CPP-ACP has the highest release of calcium and phosphate ions in oral environment[13].

**CPP-ACP in sealants :** Sealants based on ACP-filled methacrylate composites have the potential to remineralize carious enamel lesions[27].

**CPP-ACP in chewing-gum :** by adding 3% CPP-ACP in chewing gum enhances significantly the remineralization of early enamel lesions and prevents

the appearance of new lesions[20].

#### Conclusion :

CPP-ACP is a unique, naturally derived protein-based remineralizing technology that is now used globally in chewing-gums and topical past. The aim of this review is to present the benefits of CPP-ACP in pediatric dentistry as an effective agent for enamel remineralization and for prevention of early dental caries and dental erosion.

#### References :

1. Li Y, Zhang Y, Yang R, Zhang Q, Zou J, Kang D. Associations of social and behavioural factors with early childhood caries in Xiamen city in China. *International Journal of Paediatric Dentistry*. 2011;21(2):103-11.
2. Gurunathan D, Somasundaram S, Kumar SA. Casein phosphopeptide-amorphous calcium phosphate: a remineralizing agent of enamel. *Australian dental journal*. 2012;57(4):404-8.
3. Chunhua Zhou, Dongliang Zhang, Yuxing Bai, Song Li. Casein phosphopeptide-amorphous calcium phosphate remineralization of primary teeth early enamel lesions. *Journal of dentistry* 42 (2014) 21–29.
4. Gupta N, Mohan MC, Nagpal R, Singh OS, Dhingra C. A Review of Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) and Enamel Remineralization. *Compendium of continuing education in dentistry (Jamesburg, NJ: 1995)*. 2016;37(1):36-9.
5. Cochrane NJ, Saranathan S, Cai F et al. Enamel subsurface lesion remineralization with casein phosphopeptide stabilized solutions of calcium, phosphate and fluoride. *Caries Res*. 2008; 42: 88-97.
6. Fejerskov O. Changing paradigms in concepts on dental caries: consequences for oral health care. *Caries Res*. 2004, 38: 39-42.
7. Gurunathan D, Somasundaram S, Kumar SA. Casein phosphopeptide-amorphous calcium phosphate: a remineralizing agent of enamel. *Austr Dent J*. 2012; 57: 404-408.
8. He WD, Liu YZ, Xu YY et al. Study of application of CPP-ACP on tooth mineralization during orthodontic treatment with fixed appliance. *Shanghai Kou Qiang Yi Xue*. 2010; 19: 140-143.
9. Hennequin M. La dynamique du processus carieux initial. *Réalités Clin*. 1999 ; 10(4) : 483-501.
10. Li J, Xie X, Wang Y et al. Long term remineralizing effect of casein phosphopeptide – amorphous calcium phosphate (CPP-ACP) on early caries lesions in vivo: a systematic review. *J Dent*. 2014; 42: 769-777.
11. Mickenauts S. MI PastePlus effect to prevent white spot lesions associated with orthodontic treatment. *J Minim Interv Dent*. 2016; 9: 1-3.
12. Moezizadeh M, Alimi A. The effect of casein phosphopeptide-amorphous calcium phosphate paste and sodium fluoride mouthwash on the prevention of dentin erosion: An in vitro study. *J Cons Dent*. 2014; 3(17): 244-249.
13. Nongonierma AB, Fitz Gerald RJ. Biofunctional properties of casein phosphopeptides in the oral cavity. *Caries Res*. 2014; 46: 234-267.
14. Rao SK, Bhat GS, Aradhya S et al. Study of the efficacy of toothpaste containing casein phosphopeptide in the prevention of dental caries: a randomized controlled trial in 12 to 15-year-old high caries risk children in Bangalore, India. *Caries Res* 2009. (43): 430-435.
15. Raphael S, Blinkhorn A. Is there a place for tooth Mousse in the prevention and treatment of early dental caries: A systematic review. *BMC Oral Health*. 2015;15: 113.
16. Reynolds EC. Casein phosphopeptide-amorphous calcium phosphate. The scientific evidence. *Adv Dent Res*. 2009; 21(1): 25-29.
17. Selwitz RH, Ismail AL, Pitts NB. Dental Caries. *Lancet* 2007; 369(9555): 51-59.
18. Sitthisetapong T, Phantumvanit P, Huebner C, Derouen T. Effect of CPP-ACP paste on dental caries in primary teeth: a randomized trial. *J Dent Res*. 2012; 91: 847-852.
19. Somasundaram P, Vimala N, Mandke LG. Protective potential of casein phosphopeptide amorphous calcium phosphate containing paste on enamel surfaces. *J Cons Dent*. 2013; 2(16): 152-156.
20. Tang B, Millar BJ. Effect of chewing gum on tooth sensitivity following whitening. *Br Dent J*. 2010; 208(12): 571-577.
21. Skrtic D, Hailer AW, Takagi S, Antonucci JM, Eanes ED. Quantitative assessment of the efficacy of amorphous calcium phosphate methacrylate composites in remineralizing caries-like lesions artificially produced in bovine enamel. *J Dent Res* 1996; 75:1679-1686.
22. Agrwal N, Shashikiran ND, Singla S. Effect of remineralizing agents on surface microhardness of primary and permanent teeth after erosion. *J Dent Child*. 2014; 81(3): 117-121.
23. Aimutis WR. Bioactive properties of milk proteins with particular focus on anticariogenesis. *J Nut*. 2004; 134: 989S – 995S.
24. Andersson A, Sköld-Larsson K, Haligren A, Petersson LG, Twetman S. Effect of a Dental Cream Containing Amorphous Calcium Phosphate Complexes on White Spot Lesion Regression Assessed by Laser Fluorescence. *Oral health & preventive dentistry*. 2007;5(3):229 – 233.
25. Ardu S, Castioni NV, Benbachir N, Krejci I. Minimally invasive treatment of white spot enamel lesions. *Quintessence Int*. 2007; 38: 633 – 636.
26. Bailey DL, Adams GG, Tsao CE, Hyslop A, Escobar K, Manton DJ, Reynolds EC, Morgan MV. Regression of post-orthodontic lesions by a remineralizing cream. *Journal of dental research*. 2009;88(12):1148-53.

27. Beauchamp J, Caufield PW, Crall JJ, Donly K, Feigal R, Gooch B, Ismail A, Kohn W, Siegal M, Simonsen R. Evidence-based clinical recommendations for the use of pit-and-fissure sealants: a report of the American Dental Association Council on Scientific Affairs. The Journal of the American Dental Association. 2008;139(3):257-68.