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Review of Uses Casein Phosphopeptide-Amorphous Calcium Phosphate in Dentistry

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Certification of the Supervisor

I certify that this project entitled "…Review of Uses Casein Phosphopeptide-Amorphous Calcium Phosphate in Dentistry …" was prepared by the fifth-year student .. Abu-Bakr Hasan … under my supervision at the College of Dentistry/University of Mosul in partial fulfillment of the graduation requirements for the Bachelor Degree in Dentistry.

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Date : 15 \ 2 \ 2025

Dedication

Special appreciation to those whom I love my family for sharing me this lovely, difficult days and supporting me to have Bachelor's Degree.

Abu-Bakr

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Abu-Bakr

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List of abbreviations

Abbreviations	***WORD***
etc.	and other similar things
CPP-ACP	Casein Phosphopeptide-Amorphous Calcium Phosphate
et al.,	and others
pH	Potential of Hydrogen
FDA	US Food and Drug Administration
%	Percentage
Ca^{2+}	Calcium
PO_4^{3-}	Phosphate
HA	Hydroxyapatite
GICs	A glass ionomer cements
CPP-ACPF	Casein phosphopeptide amorphous calcium phosphate fluoride
MIH	Molar incisor hypomineralization

INTRODUCTION

The teeth are one of the most important oral organs in the body because they enable proper enunciation, good look, and the ability to cut, bite and chew food to generate energy. Teeth are subject to different problems and risks over time as dental caries (Jing *et al*., 2022).

Dental caries is a major public health problem globally as the disease affects all age groups, with an onset in early childhood and continued increase over the life course. Dental caries, commonly known as tooth decay, arises when the balance between demineralization and remineralization processes in the tooth is disrupted, favoring demineralization (Richa *et al.*, 2025).

Preventive methods have become a key concept in dentistry because, as the old adage goes, "Prevention is better than cure." (Nagaveni *et al.*, 2022). As a result, the focus of dental research has changed to the creation of methodologies for the early identification and application of noninvasive approaches by utilizing remineralizing agents for the efficient management of demineralization (Manchery *et al.*, 2019).

Several remineralizing substances aid in remineralization to stop the spread of illness and enhance the structure and function of the teeth. When calcium and phosphate ions are added to crystal gaps in demineralized enamel, the process is known as remineralization and results in a net mineral gain (Rather *et al.*, 2020).

For many years, the main method used by humans to prevent dental cavities was fluoride. It benefits through a variety of methods, including reducing pathology, promoting remineralization and preventing microbe maturation (Nayak, 2020). When various fluoride sources (such as fluoride toothpaste, fluoride lozenges, fluoride mouthwash, fluoride gel, fluoridated

salt, etc.) are combined, the chance of developing dental fluorosis or other negative effects increases especially in children (Aulestia *et al.*, 2020).

As a result, another remineralizing agent known as Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) a milk protein derivative, was commercially marketed, its helps in remineralization of the carious lesion by replenishing lost minerals like calcium, phosphate ions into the tooth structure, useful in the treatment of white spot lesions, early childhood caries, dental erosion, root caries, and dentin hypersensitivity. CPP–ACP is delivered in the form of oral hygiene products such as chewing gum, tooth cream, and even incorporated in dental restorative materials (Rahmath Meeral *et al*., 2024; Bandekar *et al.*, 2025).

AIMS OF THE STUDY

The aim of present review is to reviewing the Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) and explain it uses in dentistry.

CHAPTER ONE

REVIEW OF LITERATURE

1.1 Casein Phosphopeptide–Amorphous Calcium Phosphate (CPP–ACP) and Dental Caries

When the pH in the oral environment falls below 5.5, demineralization occurs, permitting calcium and phosphate ions to diffuse from the enamel surface, figure (1.1). The frequency and duration of the acid challenge can affect the level of damage to the tooth substance, which can range from small white lesions to frank cavitations. It should be emphasized that there is a possibility of arresting or even reversing the lesion when the surface remains partially intact. This challenge can be arrested or reversed by the combined action of salivary minerals and fluoride therapy (Muhammad and Ahmed, 2022).

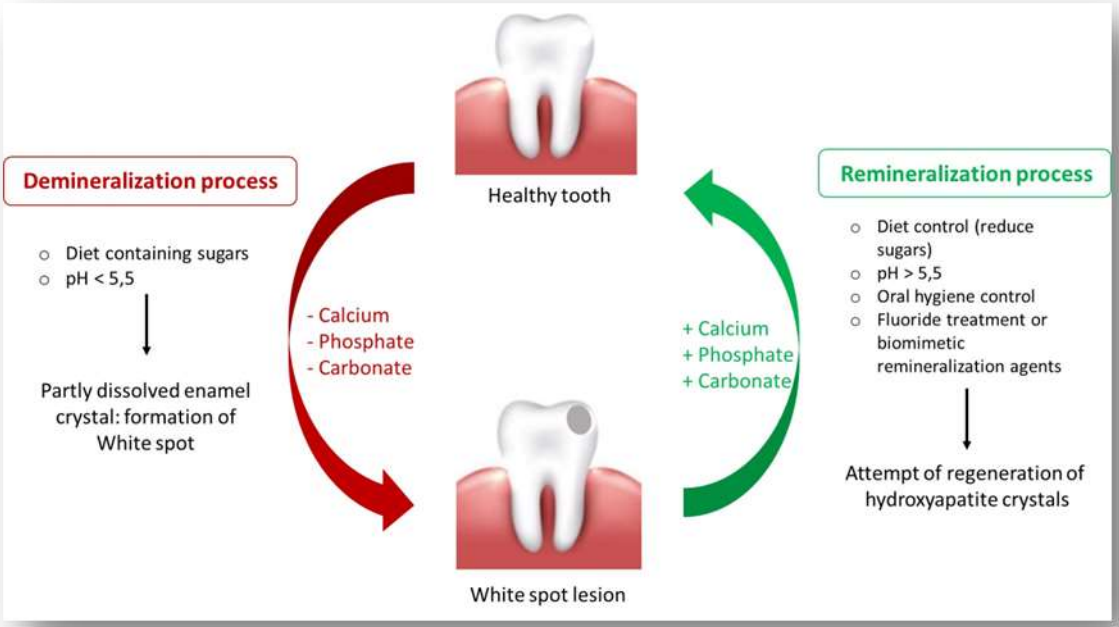

Figure (1.1): Diagram of tooth demineralization and remineralization (Malcangi *et al.*, 2023).

To maximize the clinical significance of remineralization, a series of preventive agents containing non-fluoridated products has been developed to stimulate remineralization of the enamel (Ma *et al.*, 2019; Rahmath Meeral *et al*., 2024). A new type of bioactive material derived from the milk protein casein which is called casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) can act as a reservoir of bio-available calcium and phosphate, assisting their precipitation on the enamel surface and thus effectively improving remineralization (Zhou *et al.*, 2014; Sionov *et al.*, 2021).

Currently, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) derived from milk protein casein has been reported to decrease demineralization of the tooth structure and stimulate remineralization (Rahmath Meeral *et al*., 2024).

1.2 Amorphous Calcium Phosphate:

Amorphous calcium phosphate (ACP) was first described by Aaron S Posner in the mid-1960s. It is the early solid phase that precipitates from a highly supersaturated calcium phosphate solution and can be converted readily to stable crystalline phases, such as octa-calcium phosphate or apatitic products. ACP has been established to have better biodegradability than tricalcium phosphate, better in vivo osteo- conductivity than HA, and good bioactivity but no cytotoxicity. ACP has been broadly applied in the biomedical field because of its excellent bioactivity, adjustable biodegradation rate, high cell adhesion and good osteoconduct on. However, unstabilized ACP rapidly converts to crystalline phases in the mouth and in doing thus may act to enhance dental calculus. The unstabilized ACP may produce fluorapatite in the presence of fluoride ions. The formation of fluorapatite intra-orally would sequester available fluoride ions and in that way decrease the ability to remineralize subsurface enamel during acid

challenge. Therefore, the stability of ACP is an issue (Walsh, 2009; Sionov *et al.*, 2021).

1.3 Development of Casein Phosphopeptide:

The anticariogenic effect of milk products was not attributed to a change in the level of infection of Streptococci but to a direct chemical effect by milk components such as calcium, phosphate and casein. The casein forms a layer on the tooth surface and it attracts more calcium and phosphate ions from the saliva. Yet, the usage of casein has not been implemented due to its adverse organoleptic properties and the large amount required for its efficacy (Gupta and Prakash, 2011).

CPP contains the cluster sequence of Serm (P) - Ser (P) - Glu - Glu from casein. These multiple phosphor-seryl residues obviously raise the apparent solubility of calcium phosphate by stabilizing ACP under neutral and alkaline conditions. The multiple phosphor-seryl residues of CPP bind to nanoclusters of ACP in supersaturated solutions, thus preventing the growth to the critical size required for phase transformation and precipitation. CPP–ACP works efficiently as a remineralizing agent at acidic pH levels, in addition to in neutral and alkaline phosphate range (Divyapriya *et al.*, 2016; Sionov *et al.*, 2021).

1.4 Manufacturer of Casein Phosphopeptide–Amorphous Calcium Phosphate (CPP–ACP):

The CPP–ACP complex was patented by the University of Melbourne, Victorian Dairy Industry Authority, Abbotsford and Bonlac Foods Limited, Australia. It is in general marketed in the USA as MI Paste and MI Paste Plus and outside the USA, the products are marketed as GC Tooth Mousse™ (India) and GC Tooth Mousse plus™ (India) (Deepa *et al*., 2015).

This nanocomplex is an agent that saturates saliva and biofilm, enhancing the dental remineralization process by providing Ca^{2+} and PO_4^{3-} ions, which then become available, decreasing the risk of demineralization of hard dental tissues. Alterations to the original nanocomplex have lately been made, incorporating NaF concentrations to enhance its preventive effect (Güçlü *et al.*, 2016).

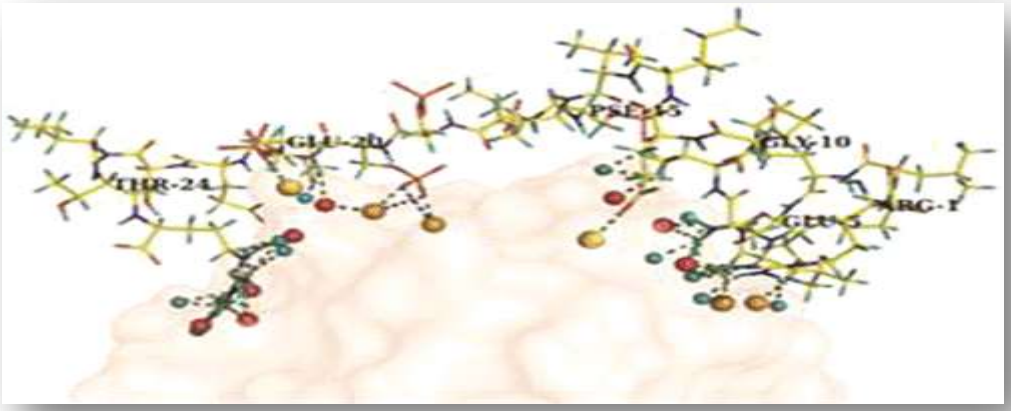

Figure (1.2): Structure of Casein Phosphopeptide–Amorphous Calcium Phosphate (Cross *et al*., 2016).

It is formed of the phosphopeptide casein protein (CPP), which is derived from milk and it is structured by residues of phosphorylated serine and glutamic amino acid (Meyer-Lueckel *et al.*, 2015). Additionally, it contains a precursor of dental hydroxyapatite: amorphous calcium phosphate (ACP), whose ions are phosphorylated by the serine residues in CPP (Nongonierma and Fitzgerald, 2012). Figure (1.2).

1.5 Mechanism of Action of Casein Phosphopeptide–Amorphous Calcium Phosphate:

1. Inhibition of Demineralization and Promoting Remineralization of Enamel.

Casein phosphopeptide–amorphous calcium phosphate acts as calcium phosphate reservoir. CPP–ACP has the ability to localize ACP at the tooth

structure, increasing the level of calcium and phosphate ions in plaque and therefore may act as a calcium and phosphate reservoir, buffering the free calcium and phosphate ions activities, thus helping to sustain a state of super saturation with respect to tooth enamel, so it reduces enamel demineralization and enhances remineralization of enamel (Divyapriya *et al.*, 2016).

The remineralizing effect results from the stabilization of Ca^{2+} and PO_4^{3-} ions that are in solution, by binding ACP to multiple amine residues of phosphorylated serine present in CPP. As a result, it permits the formation of nano-sized clusters, also called CPP-ACP nanoclusters, which increase the total surface area, in addition to its interaction with biofilm and dental structure. The clusters inhibit nucleation and spontaneous precipitation of Ca^{2+} ions, and act like salivary proteins, for example, estaterin and other proline-rich proteins (Cochrane and Reynolds, 2012). The continuous use of dental products containing CPP-ACP yields ion saturation in saliva and biofilm so making it available for subsequent precipitation in the form of ACP, favoring the dental tissue remineralization process, figure (3) (Madrid Troconis and Perez-Puello, 2019).

Also, there is a similarity between salivary statherin and casein phosphopeptide–amorphous calcium phosphate. Actually, statherins in saliva, phosphoproteins and calcium phosphopeptide share a remarkable similarity. All of these regulate the behavior of calcium and phosphate and stabilize calcium phosphate compounds (Walsh, 2009).

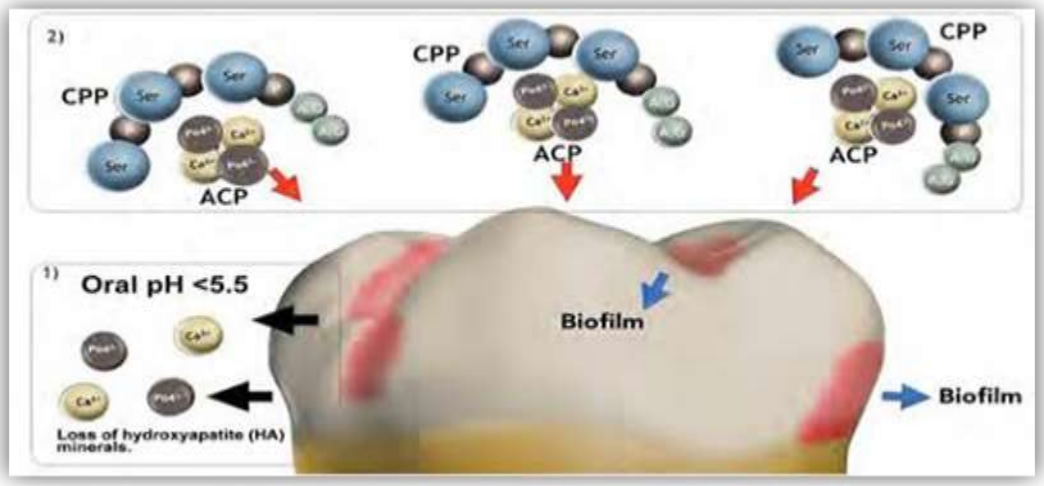

Figure (3): Graphic Representing the Process of Dental Demineralization/Remineralization. 1) Oral pH < 5.5 Induces Loss of Hydroxyapatite (HA) Minerals. 2) Saturation of the Oral Environment and Biofilm with Ca^{2+} and PO_4^{3-} Ions, Promoting the Dental Remineralization Process (Madrid-Troconis and Perez-Puello, 2019).

2. Antibacterial Activity:

CPP–ACP has the ability to prevent cariogenic effect of Streptococci to the tooth surface enhancing the formation of non-cariogenic plaque. CPP–ACP can be integrated into the pellicle in exchange for albumin to prevent the adherence of *Streptococcus mutans* and *Streptococcus sobrinus* so producing both neutralization and stimulation of remineralization. The high extracellular free calcium concentrations may have bacteriostatic or bactericidal properties which decrease the adhesion between bacterial cells and in addition casein buffers plaque acid directly or indirectly through bacterial catabolism. This agent as well releases basic amino acids which accept proton ions and act as an inert barrier inhibiting diffusion of protons (Pukallus *et al.*, 2013).

The bacteriostatic mechanism is explained for the reason that the nanocomplex is capable to bind to the biofilm matrix, saturating it with Ca^{2+} and PO_4^{3-} ions from ACP, figure (1.4). It has been noticed that CPP-ACP slows down growth and reduces the number of colony forming units of bacteria that have a high cariogenic potential, for example *Streptococcus mutans* (Dashper *et al.*, 2016).

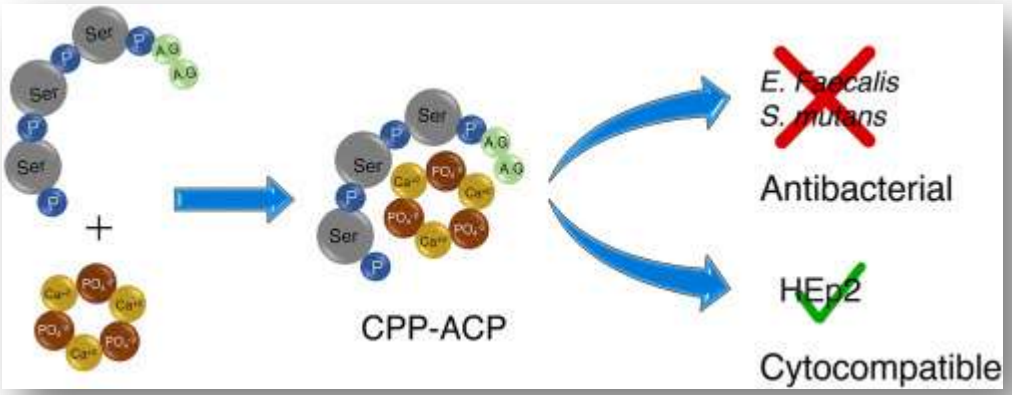

Figure (1.4): Antibacterial Activity of CPP–ACP (Beigoli *et al*., 2023).

3. Dental Desensitizing Mechanism of CPP-ACP:

The precipitated Ca^{2+} and PO_4^{3-} ions from ACP are spread through the phosphorylated fibrils of the exposed intertubular dentin collagen, stimulating the formation of apatite .Though both ions are mainly incorporated into hyper-mineralized peritubular dentin, producing deposits at the intratubular level. This strategy seeks to partially block the external stimuli that affect the hydrodynamic behavior of dentin pulpar fluid; as a result it reduces dentin hypersensitivity. Yet, the blocking action in the dentin tubules is partial; resembling that produced by other desensitizing strategies, for example the arginine-calcium carbonate complex or strontium acetate (Li *et al.*, 2012).

4. Anti-Calculus Action:

The binding of ACP to CPP is pH responsive so binding decreases as the pH falls and vice versa. It stabilizes free calcium and phosphate therefore spontaneous precipitation of calcium and phosphate does not happen which is an inherently anti-calculus action (Reema *et al.*, 2014).

5. Similarity between salivary statherin and casein phosphopeptide–amorphous calcium phosphate

In fact, statherins in saliva, calcium phosphopeptides, and phosphoproteins share a remarkable similarity. All of these regulate the behavior of calcium and phosphate and stabilize calcium phosphate compounds (Walsh, 2009).

6. Delays biofilm formation Immunolocalization

Studies indicated that incorporation of CPP–ACP into plaque by binding to the surface of bacterial cells, to components of intercellular plaque matrix, and to adsorbed proteins on tooth surfaces, thereby possibly influence the process of biofilm formation. These interactions lead to the formation of less cariogenic plaque. It is also observed that CPP–ACP reduces the fall in plaque pH following a sucrose challenge (Rose, 2000).

1.6 Interaction of Casein Phosphopeptide–Amorphous Calcium Phosphate with Fluoride:

The combination of CPP–ACP with fluoride caused localization of calcium and phosphate ions with fluoride ions at the enamel surface. The benefit of CPP–ACPF is the availability of calcium, phosphate and fluoride in one product. Each molecule of CPP can bind up to 5 fluoride ions, 25 calcium ions and 15 phosphate ions. The calcium and phosphate in these complexes are biologically available for remineralization of subsurface lesions in dental enamel (Srinivasan *et al*., 2010).

1.7 Indications of CPP-ACP:

1. Remineralization of White Spot Lesions:

Enamel lesions, which have been remineralized with topical exposure to CPP–ACP, have shown to be more resistant to consequent acid challenge in comparison with normal remineralized enamel because CPP–ACP is able to

stimulate the remineralization of enamel subsurface lesions with HA, figure (1.5). Furthermore, the relatively low carbonate environment of the CPP–ACP treated subsurface lesions may as well show improved crystallinity and lower micro strain than normal tooth enamel (Talaat *et al.*, 2018).

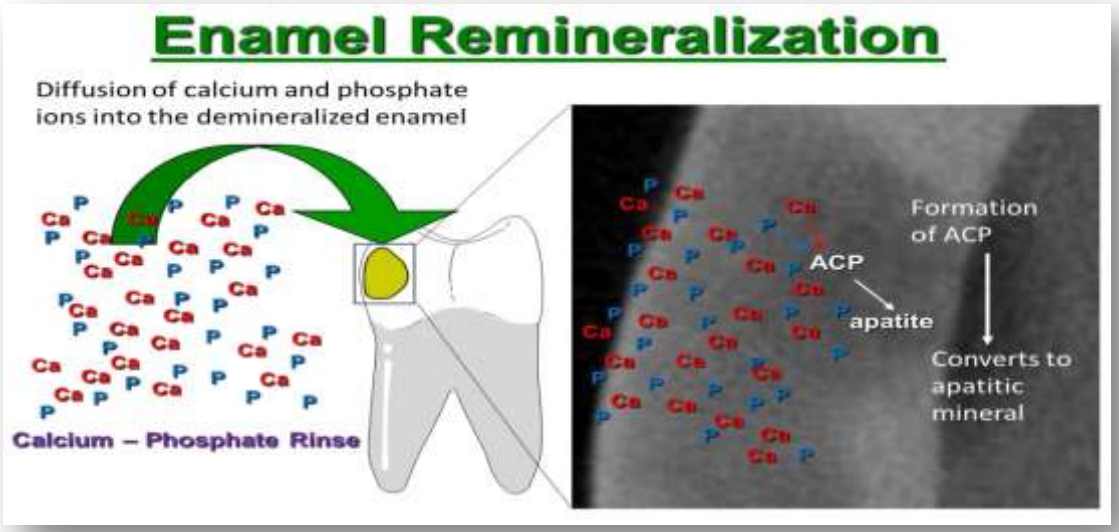

Figure (1.5): Enamel reminelization (Carey, 2023).

2. Dentin Hypersensitivity:

In recent times, introduction of newer materials such as CPP-ACP is the acronym for a complex of CPPs and ACP, which is used as a desensitizing agent. Dentin surface treated with CPP-ACP exhibited substantial crystal-like deposits within the tubule lumen. However, in few zones, the layer of amorphous calcium phosphate presents on the dentin covers the orifices of dentinal tubules (Mathew *et al*., 2020; Ratanachina *et al.*, 2024). CPP-ACP is useful in decreasing dentinal hypersensitivity by blocking dentinal tubules. On the other hand, while the peptide complex binds to plaque or the tooth surface, it is thought to deliver bioavailable calcium and phosphate for remineralization, leading to obstruction of dentin tubules (Mathew *et al*., 2020).

3. Dental Erosion:

In both CPP – ACP and CPP–ACPF, the fluoride has anti-erosive property. When the eroded enamel specimens were treated with remineralizing agents, like CPP–ACP and CPP–ACPF, there was a significant increase in microhardness and remineralization effect of CPP–ACPF which was found to be greater than that of CPP–ACP alone. This probably was caused by the interaction of CPP–ACP with hydrogen ions resulting in the formation of calcium hydrogen phosphate, therefore help in remineralization (Kasraei *et al*., 2021).

4. Casein Phosphopeptide–Amorphous Calcium Phosphate in Early Childhood Caries

The use of CPP–ACP provides a significant benefit in remineralization effects of decalcified tooth enamel, it can form HA crystals to repair the enamel prisms and enamel inter-prisms along c-axis, and allows a rapid return to resting calcium concentrations and permits more intermediate remineralization of enamel substrate (Rose, 2000).

5. Casein Phosphopeptide–Amorphous Calcium Phosphate in Root Dentinal Caries:

The application of CPP–ACP on dentine surfaces was able to inhibit demineralization of dentine, so suggesting its use in the prevention of dental root caries which could be as a result of buffer capacity of this agent (Ratanachina *et al.*, 2024).

6. Casein Phosphopeptide–Amorphous Calcium Phosphate with Laser Application:

Laser irradiation followed by CPP–ACP application permitted for incorporation of nanocomplexes of calcium onto the tooth surfaces. These

numerous calcium deposits behave like a reservoir to refill the soluble calcium and phosphate ions that diffuse into the subsurface enamel (Baniasad *et al.*, 2024).

7. Casein Phosphopeptide–Amorphous Calcium Phosphate on Bleached Enamel Surface

Regarding both intrinsic and extrinsic aspects of tooth structure, mineral loss and erosive damage brought on by bleaching agents continue to be serious concerns. Bleaching agents produce degradation, demineralization and alterations in the surface enamel roughness (Alsabeel and Qasim, 2024). Roughness is considered as a predisposing factor for adhesion of bacteria and stain adsorption (Heshmat *et al.*, 2016). CPP–ACP can increase the flexural strength of tooth surface and reverse the structural damage resulted from bleaching agents. It appears to raise the calcium and phosphate content of dental tissue after bleaching and furthermore it improves the tooth resistance to demineralization effect of bleaching agents (Kula and Mocny-Pachońska, 2022).

8. Xerostomia:

In vivo study in patients with xerostomia treated with CPP–ACP based mouth rinses revealed a lower rate of new dental caries lesions in comparison with patients treated with fluoride mouth rinses (Alkarad *et al.*, 2023). The use of CPP-ACPF caused a slight rise in saliva pH and a significant rise in biofilm pH. As well, increased the concentrations of Ca^{2+} and PO_4^{3-} in the dental surface, and reduced the micro morphological defects of the enamel surface, which might be of clinical significance to patients who have this condition (Peric *et al.*, 2015).

1.8 Mode of Delivery of Casein Phosphopeptide–Amorphous Calcium Phosphate:

- **Chewing gum:** Sugar-free chewing gum containing CPP–ACP paste has revealed to enhance remineralization of caries and moreover it increases concentration of calcium in saliva (Morgan *et al*., 2008).
- **Lozenges:** When CPP–ACP was delivered in the form of lozenges, it exhibited an increase in remineralization of subsurface caries lesions, which is dose dependent and as well increase flow rate of saliva (Cai *et al*., 2003).
- **Added to foodstuffs:** CPP-ACP has been described as effective in decreasing demineralization and promoting remineralization, particularly when added to foodstuffs such as milk and sweets (candy), apparently without serious adverse effects (Giacaman *et al.,* 2023).
- **Topical cream:** The twice daily application of CPP–ACP paste caused prevention of demineralization. Prolonged use of CPP–ACP based paste together with enamel is beneficial for treating white spot enamel lesions. It can be applied directly with clean finger onto the teeth, smeared over all surfaces, and left in position to dissolve gradually overnight (World Wellness Centre - MI Paste. 2016).
- **Dentifrices:** The addition of 2% CPP–ACP to the 1100 ppm fluoride dentifrice increases enamel subsurface remineralization comparative to that produced by fluoride alone dentifrice and furthermore the integration of CPP- ACP into 250–500 ppm / 900 ppm of fluoride was revealed to be effective in increasing enamel remineralization**.** CPP-ACP can serve as a suitable alternative to fluoride in daily-use toothpaste for enamel remineralization. The concurrent use of fluoride and CPP-ACP in toothpaste can generate a synergistic remineralizing effect at the enamel surface layer (Rafiei *et al*., 2024).

- **Varnish:** Calcium, phosphate ions and fluoride (5% sodium fluoride) bioavailable for an enhanced varnish treatment GC MI Varnish with recaldent™ (CPP-ACP) stimulates high release of fluoride and promotes enamel acid resistance (Abufarwa, *et al.*, 2019).
- **Sprays:** The CPP-calcium phosphate complex mouth rinse, when used as an atomized spray in the mouth, it has a moistening and lubrication action (Hay and Thomson, 2002).
- **Energy drinks**: Addition of CPP-ACP to energy drinks decreases their erosive capacity without any change in flavor (Shadman *et al*., 2015).
- **Incorporation of casein phosphopeptide–amorphous calcium phosphate into glass ionomer cement:** Bochun *et al.* (2020) determined the effect of incorporation of CPP–ACP into glass ionomer cement and this modified GICs exhibiting anti-demineralization effects potentially lead to a reduction in the cariogenicity of plaque and can serve as a putative promising remineralization system with both enhanced antimicrobial and remineralization properties..
- **Incorporation of casein phosphopeptide–amorphous calcium phosphate into noneugenol cement:** Setting time was delayed with incorporation of ≤8.0% (w/w) CPP–ACP in both noneugenol cements like Freegenol™ and Temp-Bond® NE but a progressive weakening in mean compressive and tensile strength values was found (Wong *et al*., 2011).
- **Casein phosphopeptide–amorphous calcium phosphate complex and resin bonding:** The application of CPP–ACP may influence the subsequent resin adhesion to dentine. The presence of CPP–ACP on the dentine surface may compromise the bonding effectiveness of the etch-and-rinse adhesive system. The enamel etching may not be inhibited by the use of CPP–ACP paste with or without prior bleaching (Elmalawany *et al.*, 2023).

- **Casein phosphopeptide–amorphous calcium phosphate sealants:** The solubility of ACP enables it to release supersaturating levels of calcium and phosphate ions in proportion that is favorable for HA formation. These fortified sealants have a higher remineralizing capacity with the potential to remineralize enamel subsurface lesions. It is marketed as Aegis® pit and fissure sealant (USA) (Aref and Alrasheed, 2022).

1.9 Safety of casein phosphopeptide–amorphous calcium phosphate:

Divyapriya *et al.* (2016) assessed the cytotoxicity of CPP–ACP in rat fibroblast culture and it showed that allowable cell viability >70% and low cytotoxicity. Hence, it is considered to be safe to use topically in dentistry. Thus, the US Food and Drug Administration accepted CPP–ACP products as generally recognized as safe for its intended use in dentistry.

1.10 Potential area of improvement:

1. As 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.
2. Need to conduct cost-effectiveness studies of CPP–ACP in current situation.
3. Further clinical trials should be conducted to explore more detailed clinical benefits of CPP–ACP. Need to investigate on the public perception of these agents (Divyapriya *et al.*, 2016).

CHAPTER TWO

DISCUSSION

CPP–ACP is a milk product which helps in remineralization and prevents dental caries. Casein phosphoPeptide can deliver amorphous calcium phosphate (ACP) and can also help the ACP to bind with the dental enamel. Casein phosphopeptide can also decrease the count of Streptococcus. Mutans as it has got the ability to integrate in the pellicle. The CPP-ACP nanocomplex incorporates into dental plaque, bonds to bacteria, acting as a reservoir for calcium and phosphate. That way, Ca and P in plaque help maintain a state of supersaturation with respect to enamel, thereby depressing enamel demineralization and enhancing remineralization. Under acidic conditions, CPP-ACP buffers plaque pH by increasing the concentration of Ca and P ions, balancing any fall in pH, and preventing enamel demineralization (Thimmaiah *et al*., 2019).

The reviewed literature by Giacaman *et al.* (2023) provides support to a remineralizing activity of CPP-ACP, based on its capacity to act as a reservoir of calcium and phosphate that can adhere to dental biofilm and the tooth surface. In addition, it has been shown that, when exposed to an acidic environment, CPP-ACP releases calcium and phosphate ions, generating mineral saturation, which would promote remineralization.

Caries preventive properties of the CPP-ACP also addressed by Markovic *et al.* (2024) they clinically evaluated the remineralization potential of casein phosphopeptide amorphous calcium phosphate nanocomplexes for enamel decalcification in orthodontics. After using CPP-ACP they found that CPP-ACP can effectively improve the demineralized enamel lesions during orthodontic treatment, so it has some remineralization potential for enamel decalcification in orthodontics.

CHAPTER THREE

CONCLUSIONS AND SUGGESTIONS

3.1 Conclusions

This review article presents the use of CPP–ACP and concluded that CPP–ACP has provided a new arena to preventive dentistry. It has shown anticariogenic, anti-erosive efficiency and reduces dentine hypersensitivity. It is delivered in the form of chewing gum, mouthwashes, dentifrices, and also added in various restorative materials. Hence, it is proven as adjunctive treatment to fluorides in the noninvasive management of early caries lesion, root dentinal caries, dental erosion, and dentine hypersensitivity. It has the ability to counteract the action of acids in cases of erosion. 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. CPP–ACP can also block the dentinal tubules and in turn can reduce the sensitivity. CPP–ACP alone or its combination with fluoride can be utilized as a prophylactic agent before the bonding of orthodontic brackets. Used in cases of molar incisor hypomineralization (MIH). This is done for remineralizing hypoplastic molars and remineralization of white spot lesions (enamel opacities and some cases of mild fluorosis). Used in the prevention of dental caries as a cost effective method in high risk population. Used in patients with orthodontic appliances for the purpose of caries prevention and prevention /remineralization of white spot lesions.

Based on the previous literature and the proven efficacy of CPP-ACP products through clinical and laboratory studies, it seems that we should shift our ways of caries prevention to include products such as CPP-ACP in our prevention schemes for patients through remineralization of enamel and application of minimal invasive approaches in dentistry.

3.2 Suggestions

1. CPP-ACP could be incorporated as a therapeutic measure for the management of dental caries through food technologies or other means.

2. Further studies and future development of more effective products than CPP-ACP are needed in addition to fluoride to achieve healthy oral hygiene.

3. Further studies are required to evaluate the properties of different types of bonding agents and cements containing ACP in the long term. Clinical studies are also recommended to assess the remineralizing efficacy of ACP-containing bonding and cements agents in vivo.

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