PEPTIDES IN REMINERALISATION - A REVIEW

Arungani NS¹, Kalaivani Venkadessan²

¹ Department of Oral Pathology and Microbiology, Indira Gandhi Institute of Dental Sciences, Pondicherry

² Department of Public Health Dentistry, Saveetha Dental College and Hospitals, Vellapanchavadi, Poonamallee, Chennai- 600 077

ABSTRACT

Caries develops when the remineralization and demineralization equilibriums are out of balance. When the demineralization level exceeds 30%, the enamel suffers irreversible damage. As a result, non-invasive techniques for early detection and management of these reversible incipient lesions are recommended. Fluorides are the most important and effective, and their local efficacy has been widely researched. Many new innovations have been introduced for remineralisation of early lesion, such as ACP-CPP, Self-assembling peptides, etc., CPP–ACP is a milk product that aids in remineralization and dental caries prevention. Amorphous calcium phosphate is delivered by casein phosphopeptide, which also aids ACP binding to dental enamel. The natural amino acids Glutamine, Glutamic acid, Phenylalanine, Tryptophan, Serine, and Arginine make up the self-assembling peptide P11-4, which is intended to form brils at low pH and to be monomeric at higher pH. Furthermore, studies to be conducted to learn about the mechanism of Self assembling peptides.

KEYWORDS- Dental Caries, Peptides, Remineralization.

INTRODUCTION

The tooth enamel is the tooth's most mineralized and has uniquely arranged outermost layer. Enamel matrix proteins, which are known to create selfassembling supramolecular structures, are thought to control the shape of hydroxyapatite crystals throughout development, eventually defining the mature tissue's physico-mechanical properties ^[1,2].

Within the oral environment, this enamel is constantly exposed to a variety of problems. Due to the absence of functional capacity of ameloblasts, adult enamel, unlike other skeletal structures, cannot be regenerated ^[3]. Any reduction in pH below the threshold value triggers the demineralization process due to this intrinsic

Address for correspondence

Dr. Kalaivani V, Department of Public Health Dentistry, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-600077

E-mail address-kalai11venki@gmail.com

constraint. Caries develops when the remineralisation and demineralization equilibriums are out of balance. When the demineralization level exceeds 30%, the enamel suffers irreversible damage. As a result, non-invasive techniques for early detection and management of these reversible incipient lesions are recommended ^[4].

For non-invasive therapy of these incipient lesions, a variety of remineralizing medicines are available. Fluorides are the most important and effective, and

How to cite this article:

Arungani NS and Kalaivani V, Peptides in Remineralisation - A Review. Int J Comm Dent 2022; 10 (1):18-22.

Received: 28-04-22; Accepted: 10-06-22; Web Published: 14-06-22.

their local efficacy has been widely researched. Several agents that enter an initial lesion as liquid (ICON caries inltrant) or encourage resin remineralisation by releasing calcium and phosphate have been launched in recent years (e.g., casein phosphopeptideamorphous calcium phosphate, CPP-ACP complex). Furthermore, nanohydroxyl apatite-based products (such as BioRepair) have been proposed for "repairing" enamel^[5]. These agents, on the other hand, were unable to produce matrix-mediated mineralization in the same way as the natural process does. To combat this, the self-assembling peptide (SAP) P11-4 was developed to rebuild enamel by matrixmediated mineralization ^[6,7]. This article gives detailed information about the various peptides responsible in the remineralisation process of early enamel lesions.

FLUORIDES:

1) Fluoride varnish

It's an adhesive compound that's applied by a professional and isn't meant to last as long as pit and fissure sealer. The usage of F varnish is based on the assumption that longer contact times and closer interaction between F ions and enamel result in greater Fluoride uptake by the enamel. When large F concentrations, around 22,000 mg F/L, are applied to a little amount of material, Fluoride is slowly released into the environment. This emission has been seen to last for 5 to 6 months ^[8].

Fluoride varnish has been regularly used for over three decades in both community-based and individual programmes. It works to prevent new caries lesions from forming and to slow the advancement of existing ones. It is the therapy of choice for children who are at high risk of developing cavities. Fluoride varnishes typically include 5% sodium fluoride (NaF), which is comparable to 2.26 percent fluoride (Duraphat), while organic Fluoride varnishes have 0.1 percent fluoride (Fluor Protector). The paint-on method is used to apply it on the teeth ^[8].

2) Fluoride mouth rinse

Due to the risk of F consumption, it is not recommended in fluoridated communities or for children under the age of six. NaF is available in two concentrations: 0.05 percent (225 ppm F) and 0.2 percent (900 ppm F). To be used on a daily and weekly basis, accordingly ^[9].

3) Fluoride gel

The introduction of Fluoride gels alleviated many of the concerns associated with Fluoride solutions. Gels are made by increasing the viscosity of the Fluoride preparation by adding a gelling ingredient such methyl or hydroxyethyl cellulose. Fluoride gel was discovered to be beneficial in reducing dental cavities by 28 percent.

Fluoride Acidulated Phosphate Fluoride (12,300 ppm) is the most widely used gel (APF). The APF thixotropic gel is available; thixotropic refers to a solution that sets in a gel-like form but isn't a real gel when pressure is applied. The thixotropic gel has the same properties as a solution. Due to the risk of Fluoride Ingestion, it is not recommended for children under the age of 6. Using the tray technique, it is administered to teeth ^[9].

4) Silver diamine fluoride (SDF)

SDF is used to prevent and treat caries all around the world, but especially in developing countries. Staining of carious tooth structure is one of its potential side effects, however in certain situations, this is acceptable to patients and their parents. In both primary and permanent dentations, SDF has the potential to play a key role in the management of dental disease ^[10].

CASEIN PHOSPHOPEPTIDE- AMORPHOUS CALCIUM PHOSPHATE:

CPP–ACP is a milk product that aids in remineralisation and dental caries prevention. Amorphous calcium phosphate is delivered by casein phosphopeptide, which also aids ACP binding to dental enamel. Due to its ability to incorporate in the pellicle, casein phosphopeptide can also reduce the number of Streptococcus mutans ^[11-13].

Mechanism of action: Casein phosphopeptide creates nanoclusters with amorphous calcium phosphate, resulting in a calcium and phosphate pool that can keep saliva hyper saturated. Because CPP–ACP helps to stabilise calcium and phosphate in the solution, it can also aid in the buffering of plaque pH, resulting in an increase in calcium and phosphate levels in plaque. As a result, the concentration of calcium and phosphate within the subsurface lesions is kept high, resulting in remineralisation ^[14].

The anti-cariogenic action of CPP-ACP (Tooth mousse, GC Co., Japan) has been linked to casein sequences that contain several phosphoseryls. As a calcium reservoir, CPP can help to keep the level of ACP in saliva stable. Chewing gum, mouthrinses, lozenges, topical cream, dentifrices, sprays, and energy beverages are all available. CPP-ACP is a cost-effective approach for preventing caries in high-risk populations by remineralizing early carious lesions. CPP-ACP tooth-mousse has an advantage over F toothpaste in neutralising acids in the oral cavity, according to studies ^[15, 16].

SELF ASSEMBLING PEPTIDES - P11-4:

All living cells are made up of proteins, which are the basic components and building blocks. They are made up of one or more amino acid chains. A peptide molecule is made up of two or more amino acids connected by a peptide bond. Proteins are made up of large numbers of peptide molecules arranged in various ways to form various types of proteins. The peptide sequence, concentration, pH, presence of salts, and time or kinetics all play a role in the self-assembly process. Self-assembling peptides (SAP) have been successfully used to create innovative biomimetic nanomaterials with a wide range of applications, including dentistry ^[17].

Mechanism of action: Long assumed to influence initial mineral deposition ('nucleation') and subsequent crystal formation are proteins of the growing enamel ECM, which are known to create self-assembling supramolecular structures ^[18]. The natural amino acids Glutamine, Glutamic acid, Phenylalanine, Tryptophan, Serine, and Arginine make up the self-assembling peptide P11-4, which is intended to form brils at low pH and to be monomeric at higher pH ^[19]. The negative charged surfaces and phosphorylated erine residues in the peptide attract the dissolved 2+ Ca.

The bioactive peptide generated from amino acids diffused into the porosities and assembled within the spaces in the subsurface lesion into a threedimensional brillar scaffold mimicking extracellular matrix, according to one possible for SAP P11-4-mediated explanation mineralization. P11-4 when assembled generates scaffold-like structures with negative charge domains, similar to biological macromolecules seen in extracellular matrix of mineralised tissues (ECM). This a nucleus serves as for hydroxyapatite, which triggers tissue regeneration by drawing calcium and phosphate ions from saliva, resulting in a higher Ca:P ratio. Furthermore, when peptides form bres, they contain negative charge clusters made up of 2+ four Glu residues, which could serve as a Calcium binding site.

These binding sites are 9.4A apart, which is the distance between the 20 natural hydroxyapatite crystals. The peptides' structural similarity to biological macromolecules in the mammalian skeleton explains their ability to enable matrix-mediated mineralization ^[20].

CONCLUSION

Remineralization potential of CPP ACP and SAP P11-4 seem to be quite evident and further more studies to be conducted with Self Assembling Peptides to know about its mechanism in detail. Recent advances in Self assembling offer a potentially exciting route to smart dental biomaterials.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTERESTS: All the authors declare that there was no conflict of interest in the present study.

REFERENCES

- Tecilla P, Dixon RP, Slobodkin G, Alavi DS, Waldeck DH, Hamilton AD. Hydrogenbonding self-assembly of multichromophore structures. Journal of the American Chemical Society. 1990 Dec;112(25):9408-10.
- Subramani K, Ahmed W. Self-Assembly of Proteins and Peptides and Their Applications in Bionanotechnology and Dentistry. InEmerging Nanotechnologies in Dentistry 2012 (pp. 209-224).
- Moradian-Oldak J. Protein-mediated enamel mineralization. Front Biosci (Landmark Ed) 2012; 17:1996-2023
- Sindhura V, Uloopi KS, Vinay C, Chandrasekhar R. Evaluation of enamel remineralizing potential of self-assembling peptide P11-4 on articially induced enamel lesions in vitro. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2018 Oct 1;36(4):352
- Wierichs RJ, Kogel J, Lausch J, Esteves-Oliveira M, Meyer-Lueckel H. Effects of selfassembling peptide P11-4, uorides, and caries inltration on articial enamel caries lesions in vitro. Caries research. 2017;51(5):451-9.
- Kyle S, Aggeli A, Ingham E, McPherson MJ Production of self-assembling biomaterials for tissue engineering. Trends Biotechnol 2009; 27:423-33
- 7. Jablonski-Momeni A. Heinzel-Gutenbrunner M. 2014. Efcacy of the selfassembling peptide p11-4 in constructing a remineralization scaffold on articially-induced enamel lesions on smoothsurfaces. J Orofac Orthop. 75(3):175-190

 Weyant RJ, Tracy SL, Anselmo TT, Beltrán-Aguilar ED, Donly KJ, Frese WA, et al. Topical fluoride for caries prevention: executive summary of the updated clinical recommendations and supporting systematic review. J Am Dent Assoc. 2013; 144: 1279-91

SOURCE OF FUNDING: Nil

- 9. National Collaborating Centre for Acute Care (UK). Dental recall: recall interval between routine dental examinations. London: National Collaborating Centre for Acute Care (UK). 2004.
- 10. Timms L, Sumner O, Deery C, Rogers HJ. Everyone else is using it, so why isn't the UK? Silver diamine fluoride for children and young people. Community Dent Health. 2020; 37: 143-9.
- 11. P. Schupbach, J.R. Neeser, M. Golliard, M. Rouvet, B. Guggenheim Incorporation of caseinoglycomacropeptide and caseinphosphopeptide into the salivary pellicle inhibits adherence of mutans streptococci J Dent Res, 75 (1996), pp. 1779-1788
- 12. E.C. Reynolds Remineralization of enamel subsurface lesions by casein Phosphopeptide–stabilize calcium phosphate solutions J Dent Res, 76 (9) (1997), pp. 1587-1595
- 13. P. Shen, F. Cai, A. Nowicki, J. Vincent, E.C. Reynolds Remineralization of enamel subsurface lesions by sugar free chewing gum containing casein phophopeptide– amorphous calcium phosphate J Dent Res, 80 (12) (2001), pp. 2066-2070
- 14. Nairn Wilson. Minimally invasive dentistry-The management of dental caries. 1st ed. London; 2007. p. 69–70.

- 15. Shyam R, Manjunath BC, Kumar A, Narang R, Ghanghas M, Rani G. Role of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) in prevention of dental caries: a review. Int J Adv Res. 2017; 5: 999-1004.
- 16. Al-Batayneh OB. The clinical applications of tooth mousseTM and other CPP-ACP products in caries prevention: evidencebased recommendations. Smile Dent J. 2009; 4: 8-12.
- 17. Subramani K, Ahmed W. Self-Assembly of Proteins and Peptides and Their Applications in Bionanotechnology and Dentistry. InEmerging Nanotechnologies in Dentistry 2012 (pp. 209-224).
- Brunton PA, Davies RP, Burke JL, Smith A, Aggeli A, Brookes SJ, Kirkham J. Treatment of early caries lesions using biomimetic self-assembling peptides–a clinical safety trial. British dental journal. 2013 Aug;215(4): E6.

- Kind L, Stevanovic S, Wuttig S, Wimberger S, Hofer J, Müller B, et al. Biomimetic remineralization of carious lesions by self-assembling peptide. J Dent Res 2017; 96:790-7
- 20. Thomson BM, Hardaker L, Davies RP, Dennis C, Bronowska A, Aggeli A. P11-14 (NNRFEWEFENN): A Biocompatible, Self-assembling Peptide with Potential to Promote Enamel Remineralisation. Paper Presented at: 61 ORCA Congress. Greifswald, Germany: Abstracts. Caries Research 2014; 48:384-450