Review Article

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Dentistry Section

Remineralisation Potential of Self-assembling Peptide (P11-4) Compared to Other Remineralising Agents: A Narrative Review

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ABSTRACT

Dental caries is a chronic infectious disease that affects the hard tissues of the teeth, primarily the enamel. Remineralisation involves depositing minerals back into demineralised enamel, repairing the damage, and preventing the formation of caries. Self-Assembling Peptide (SAP) P11-4 is a promising new remineralisation agent that mimics the natural process of remineralising dental enamel. It is a biomimetic peptide that binds to the surface of demineralised enamel, forming a three-dimensional network that supports mineral deposition and induces the production of reparative proteins. P11-4 is still in the early stages of development, but it has the potential to revolutionise the treatment of dental caries. SAP P11-4 has been shown to be safe and effective in remineralising early carious lesions. However, there is insufficient evidence to conclude that SAP P11-4 is more effective than other remineralising agents, such as fluoride, Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP), and Silver Diamine Fluoride (SDF). The present review focuses on recent studies discussing the remineralisation potential of SAP P11-4 and compares it to other available remineralising agents. Overall, the review suggests that SAP P11-4 is a promising new remineralisation agent that is effective in treating early carious lesions. However, further research is needed to compare its effectiveness to other remineralisation agents and assess its long-term efficacy.

Keywords: Dental caries, Fluorides, Peptides, Tooth remineralisation

INTRODUCTION

Dental caries is a chronic infectious disease that affects the hard tissues of the teeth, primarily the enamel [1]. It is caused by the action of acids produced by bacteria that reside in the mouth. These acids demineralise the enamel, leading to the formation of caries [1]. In recent decades, the dental profession has shown interest in remineralisation. The term "remineralisation" refers to the process by which minerals are redeposited into the demineralised enamel, repairing the damage and preventing caries formation [1]. The management of caries is shifting towards a minimally invasive approach, which emphasises prevention, reduction, and reversal of incipient caries lesions. Fluoride can interact with saliva at the surface and subsurface of the enamel to promote remineralisation through the formation of fluorhydroxyapatite [2]. However, current fluoride therapies have demonstrated limitations, particularly in the treatment of caries that have already manifested as white spots [2].

White Spot Lesions (WSLs) are the earliest clinical manifestations of enamel demineralisation [3]. Remineralisation therapy, which aims to restore lost minerals to the tooth enamel, is a growing trend in treating WSLs [3]. Several remineralising agents are available, including fluoride, calcium phosphate, Casein Phosphopeptide-Amorphous Calcium Phosphate with Fluoride (CPP-ACPF), and SDF [2]. Although all these mentioned materials are referred to as remineralising agents, the mechanism of action for each is different. Fluoride, for instance, incorporates ions into the tooth enamel, making it more resistant to acid attack and inhibiting the growth of bacteria that can cause caries [4]. On the other hand, CPP-ACP binds to the surface of demineralised enamel and forms a protective layer that helps prevent further demineralisation and promotes remineralisation [5]. SDF works by forming a silver precipitate on the tooth surface. This silver precipitate kills bacteria and inhibits demineralisation [6].

The SAP P11-4 is a protein that can mimic the natural process of remineralising dental enamel [1]. It is a biomimetic peptide, meaning it is designed to imitate the structure and function of natural enamel proteins. SAP P11-4 functions by binding to the surface of demineralised enamel, which has lost minerals and weakened [1]. When SAP P11-4 binds to demineralised enamel, it forms a three-dimensional network.

This network provides a support structure for depositing minerals, aiding in the remineralisation of the enamel. SAP P11-4 has also been shown to induce the production of reparative proteins, which can help repair damaged enamel. It is a non invasive treatment that can be applied to the teeth by a dentist. SAP P11-4 is still in the early stages of development, but it has the potential to revolutionise the treatment of dental caries [1]. SAP P11-4 is commercially available as Curodont™ Repair, administered as a water solution using an applicator [1]. It is a non invasive treatment that can be applied to the teeth by a dentist [1].

The SAP P11-4 has shown promising results in preclinical and clinical studies [7-11]. Multiple clinical studies were conducted to compare the effects of SAP P11-4 to other remineralising agents in treating early carious enamel or WSLs [12-26]. The present review focuses on the most recent studies discussing the remineralising potential of SAP P11-4 and compares it to other available remineralising agents.

Structure

SAP P11-4 is a peptide that self-assembles. It is an 11-amino acid short-chain peptide with the unique ability to self-assemble into three-dimensional fibrillar scaffolds [10,27]. Its chemical makeup, Ace-Gln-Gln-Arg-Phe-Glu-Trp-Glu-Phe-Glu-Gln-Gln-Gln-NH2, consists of 11 amino acids, enabling it to self-assemble into higher-order structures such as tapes, ribbons, fibrils, and fibers. These higher-order structures can mimic the enamel matrix structure of dental enamel [28]. The 20 naturally occurring α-amino acids that make up proteins and peptides can construct the hierarchy of supramolecular structures similarly due to their intrinsic chirality. They can self-assemble to create "double tapes," "helical tapes (single molecule thick)," "fibrils (twisted stacks of ribbons)," and fibers with increasing concentration [29]. Most self-assembling molecules include both hydrophilic and hydrophobic components, making them amphiphilic. The amphiphilicity of peptides, which allows functional

groups to be present on the surface of the structure, is the primary factor promoting self-assembly [29]. Due to structural folding, various folded surfaces are exposed to different environmental conditions, resulting in distinct "faces." Peptides with greater complexity and amphiphilicity are more suitable for self-assembly [29].

Synthesis: Aggeli A et al., designed a de novo 11-residue peptide, CH3CO-Gln-Gln-Arg-Phe-Gln-Trp-Gln-Phe-Glu-Gln-Gln-NH2, using criteria for designing gel-producing peptides gathered from their observations and existing literature, with the aim of creating β-sheet polymer tapes in water [30].

Glu (-CH2 CH2 COOH) or Orn (-CH2 CH2 CH2 NH2) were added to the primary structure of the 11-amino acid peptides by Aggeli A et al., demonstrating that pH adjustment can rapidly (within a matter of seconds) control self-assembly [31]. The synthetic peptide P11-4 (CH3 CO-Gln-Gln-Arg-Phe-Glu-Trp-Glu-Phe-Glu-Glu-Phe-Glu Gln-Gln-NH2) forms scaffolds through hierarchical self-assembly in response to specific environmental cues and increasing peptide concentrations [18]. The scaffold-like structures of self-assembled P11-4, with negatively charged domains, resemble biological macromolecules found in the extracellular matrix of mineralised tissues [32].

It has been demonstrated that the SAP P11-4 promotes the nucleation of hydroxyapatite on its surface through the resulting fibers [33]. After surface treatment with SAP P11-4, two in-vitro investigations effectively demonstrated the secondary conformation of the fibrils formed on the lesion surface, specifically the pleated sheets, using a Transmission Electron Microscope (TEM) and congo red stain [18,33].

Mechanism of action of Self-Assembling Peptide (P11-4)

Remineralising potential: The demineralised tooth surface serves as the initial stage. SAPs extend their charged amino acid side chains, forming electrostatic bonds with the oppositely charged mineral surface through a series of ionic interactions [32]. For minerals from saliva and remineralising agents to be effective, nucleation sites, which are places for minerals to begin building up on the tooth surface, are required [27]. SAPs fold their peptide chains to present a template for hydroxyapatite crystals. Specific amino acid sequences within the scaffold act as potent mineral binding sites, attracting and coordinating calcium and phosphate ions. These ions assemble into ordered lattices that mimic the complex architecture of natural enamel. The ordered structure and interactions with the mineral surface influence crystal growth, determining size and morphology with remarkable precision [32]. This precise control results in the formation of smaller, densely packed crystals that faithfully replicate the natural enamel architecture and ensure seamless integration with the existing structure. Furthermore, SAPs possess the ability to inhibit enzymes such as matrix metalloproteinases, which would otherwise dissolve the enamel. This dual action, promoting remineralisation while protecting the existing structure, strengthens the tooth's defensive barrier and promotes long-term oral health [27,32].

Clinical Applications and Studies

Non clinical studies: Early laboratory studies from the last few decades have demonstrated that monomeric low-viscosity peptide solutions can be injected into enamel defects to stably produce scaffolds capable of nucleating hydroxyapatite, thereby promoting remineralisation [27,32]. Non clinical studies comparing the effect of SAP P11-4 to other remineralising agents are summarised in [Table/Fig-1] [12-17,34].

Clinical studies: The first in-vivo clinical trial of SAP P11-4, conducted by Brunton PA et al., demonstrated that a single treatment of SAP P11-4 resulted in a significant decrease in the size of early carious lesions in

Study	Study design	Sample	Comparison	Agents used	Results and conclusion
Soares R, (2017) [13]	In-vitro study	60 premolars	Effect of SAP P11-4 versus other remineralising on artificial enamel lesion	SAP P11-4, CPP-ACPF, Bioactive Glass (BAG), fluoride-enhanced HA gel.	Based on the results of Surface Microhardness (SMH) testing, P11-4 was the most effective remineralising agent, followed by CPP-ACPF, BAG, and fluoride-enhanced HA gel. SAP P11-4 also had the highest percentage of SMH recovery, followed by CPP-ACPF, BAG, and fluoride-enhanced HA gel.
Tripathi P et al., (2021) [14]	In-vitro study	60 premolars	Effect of SAP P11-4 versus other remineralising agents on carious lesions	SAP, SDF, CPP-ACP, and NovaMin.	SAP P11-4 was the most effective remineralising agent of the four tested agents, followed by CPP-ACP, SDF, and NovaMin. The percentage difference from SAP P11-4 shows that CPP-ACP, SDF, and NovaMin were less effective by 8.4%, 8.9%, and 10.5%, respectively.
Mohamed RN et al., (2021) [12]	Systematic review of in-vitro studies	12 studies	Effect of SAP P11-4 versus other remineralising agents in remineralising initial carious lesion	SAP P11-4, Fluoride Varnish, (FV) CPP-ACPF, Casein Phosphopeptides (CPPs).	Total 10 studies showed that SAP P11-4 is effective in remineralising tooth enamel compared to other treatments. One study showed that combining SAP P11-4 with FV or CPP-ACPF is even more effective, and SAP P11-4 is an effective treatment for tooth enamel remineralisation.
Lena Sezici Y et al., (2021) [17]	In-vitro study	60 Bovine incisors	Evaluation of FV, SAP -based remineralisation agent, and enamel matrix protein derivative on artificial enamel remineralisation	Emdogain ,Curodont Repair) Duraphat, Enamel Clinpro XT, Pro Varnish.	Enamel matrix protein, SAP, and light-curable FV were significantly more effective in reducing fluorescence loss and lesion area compared to other treatments. Curodont and Clinpro XT were particularly effective, with Curodont showing the greatest reduction in lesion area between the first and second week and Clinpro XT showing the greatest reduction in fluorescence loss between the second and third week.
Wahba N et al., (2022) [15]	In-vetro study	180 primary teeth	The ability of SAP P11-4 to prevent caries and slow the course of lesions in primary teeth compared to other recognised agents	In the prevention group: SAP for prevention (SAPP), FV/mouthwash (FV/FMW), CPP-ACP, or nano-hydroxyapatite (nHA). In the arrest group, SAP for Repair (SAPR), FV, CPP-ACP plus fluoride, or resin infiltration.	The established methods, such as FV and Fluoride Mouthwash (FMW), were the most effective at preventing and arresting caries lesions. Novel strategies such as (SAPP), (CPP-ACP), CPP-ACPF, and nano-hydroxyapatite (nHA) did not have any significant preventive or arresting effects on caries lesions. RI was the most effective agent at arresting caries lesions, followed by FV. SAPR and CPP-ACPF did not have any significant inhibiting effect on lesion progression. FV and FMW are the most effective agents for preventing and arresting caries lesions in primary teeth. RI is also an effective agent for arresting caries lesions. SAPP and CPP-ACPF are not effective in preventing or arresting caries lesions in primary teeth.
Ghaly YS et al., (2023) [16]	In-vitro study	80 freshly extracted human maxillary premolars	The effect of SAP and other remineralising agents on preventing initial enamel lesions around orthodontic brackets	SAP P11-4, CPP-ACPF, FV.	SAP P11-4 was the most effective, followed by CPP-ACPF and FV. SAP P11-4 was significantly more effective than the control group in improving both Ca/P ratio and SMH (by 28.3% and 63.1%, respectively). CPP-ACPF was also significantly more effective than the control group in improving both Ca/P ratio and SMH (16.0% and 33.1%, respectively). FV was less effective than SAP (P11-4) and CPP-ACPF, but it was still significantly more effective than the control group in improving SMH (by 23.4%).
Shetty N et al., (2023) [34]	In-vitro study	48 freshly extracted human premolars	the remineralisation of artificial WSLs using SAPs, nanohydroxyapatit, and FV	Artificial saliva; SAP curodent gel, nanohydroxyapatite, duraphat FV.	SAPs (Curodont gel) achieved the highest level of remineralisation after 90 days, followed by FV and nanohydroxyapatite toothpaste.

[Table/Fig-1]: Summary of the non clinical studies on the comparison of the effect of the SAP P11-4 to other remineralising agents [12-17,34].

15 healthy adults. After six months of observation, most lesions were found to be inactive [18]. The present study led to a series of clinical trials, which are summarised in [Table/Fig-2] [3,8,10,18-26].

Disadvantages: In a study by Brunton PA et al., two drawbacks were identified. Firstly, there was transient dental hypersensitivity, and secondly, participants showed sensitivity to the Corsodyl mouthwash provided for the study. Among the 11 adverse events recorded by Brunton PA et al., two were considered to be probably related to the study protocol [18].

In 2017, Wierichs RJ et al., discussed the limitations of the SAP method. They concluded that flocculation occurs in the nematic form of SAP in oral environmental conditions, where cycles of demineralisation and remineralisation cause pH fluctuations. The flocculated state of SAP is relatively inactive and may hinder the remineralisation process. They observed that the presence of these flocculates on the enamel surface affects the migration of calcium, phosphate, and fluoride ions during the remineralisation process. Consequently, there is reduced availability of fluoride ions in the later stages of demineralisation [19].

Study	Study design	Sample	Comparison	Agents used	Results and conclusion
Brunton PA et al., (2013) [18]	Randomised controlled trial	15 healthy adults with Class V "white spot" lesions	Single treatment of SAP P11-4 versus no treatment	SAP P11-4	Treatment with SAP P11-4 significant decrease in the size of early carious lesions after treatment with SAP P11-4.
Alkilzy M et al., (2018) [10]	Randomised controlled trial	70 children and adolescents	Effect of SAP P11-4 versus FV in treatment of early occlusal caries	SAP P11-4, FV	SAP P11-4 was more effective than FV in reducing the size of early carious lesions.
Gözetici B et al., (2019) [21]	Randomised controlled trial	113 individuals who had at least four evident WSLs on the buccal surface	Compared SAP P11-4 to resin infiltration technique and other remineralising therapies	SAP P11-4, resin infiltration technique, FV	All three intervention groups showed a statistically significant decrease in LF pen measurements after six months compared to baseline. The most remarkable lesion regression was observed with Icon, followed by the Duraphat and Curodont repair group with a difference of 19.1±16.9, 13.9±9.7, and 15.0±12.7, respectively.
Bröseler F et al., (2020) [20]	Randomised controlled trial	37 participants who had 90 teeth with early buccal carious lesions	SAP P11-4 versus FV in the treatment of early caries	SAP P11-4, FV	Over a year, the lesion's size in the FV control group stabilised, whereas it reduced in the SAP P11-4, with the average size of the cavities decreasing by 14% at 30 days, 26% at 90 days, 36% at 180 days, and 38% at 360 days.
Sedlakova Kondelova P et al., (2020) [8]	Randomised controlled trial	44 subjects presenting two teeth with White-Spot-Lesions (WSLs)	The safety and efficacy of SAP P11-4 (SAP P11-4) compared to placebo or FV	SAP P11-4, placebo, FV	SAP P11-4 is more effective than the placebo in reducing the severity of WSLs, with an average Visual Analogue Scale (VAS) score change of -8.5 compared to -4.8 for the placebo. The results of the Global Impression Of Change Questionnaire (GIOCQ) 4 suggest that SAP P11-4 is more effective than placebo in improving the appearance of enamel carious lesions, as evidenced by the higher percentage of patients in the SAP P11-4 groups who reported improvement in their lesion appearance.
Welk A et al., (2020) [3]	Randomised controlled trial	23 patients with atleast two teeth with WSL	The effect of SAP P11-4 compared to conventional treatment on early carious lesions after debonding of orthodontic brackets	SAP P11-4, FV	SAP P11-4 was more effective than conventional treatment in reducing the severity of early carious lesions. The mean baseline impedance in the SAP P11-4 WSL was 46.7, and after 45, 90, and 180 days, it decreased to 21.1, 18.4, and 19.7, respectively. The mean baseline value for the conventual treatment WSL was 42.0, and it afterwards decreased to 35.0, 29.5, and 33.7, respectively.
Riad M et al., (2020) [26]	Randomised controlled trial	Not mentioned	To compare the colour change as an effect of applying two remineralising agents, either Curodont repair or Duraphat FV, on anterior teeth	Curodont Repair, Duraphat FV	Curodont repair was more effective than Duraphat FV in improving the colour of white spots.
Wierichs RJ et al., (2021) [19]	A systematic review and meta-analysis	7 studies	Treatment with SAP (plus FV) versus no treatment (plus FV)	SAP P11-4, FV	SAP P11-4 was significantly more effective than no treatment in improving the appearance of enamel caries lesions. There was no significant difference between SAP P11-4 and no treatment in terms of lesion activity or size. This means that SAP P11-4 could not significantly reduce the activity or size of enamel caries lesions.
Ali D et al., (2022) [23]	Randomised controlled trial	40 patients	SAP P11-4 versus ACPV versus combination of SAP P11-4 and ACPV versus control	SAP P11-4™ Repair/ Regenamel®, ACPV, Enamel Pro® Varnish 5% Sodium Fluoride Premier Dental combination of SAP P11-4 and ACPV	The results showed that the combination treatment was the most effective at reducing white spots, followed by the SAP P11-4 group. The control group had the lowest remineralisation levels. The authors concluded that combining organic and inorganic remineralising analogues, such as SAP P11-4 and ACPV, may have a synergistic effect on the remineralisation of post-orthodontic enamel WSLs.
Amin O et al., (2023) [22]	Randomised controlled trial	48 WSLs	To compare the remineralisation capacity of Curodont Repair Fluoride Plus and CPP-ACP in the treatment of WSLs	Curodont Repair Fluoride Plus, MI Paste	There is no significant difference between the two treatments in terms of the ICDAS II criteria. However, within the curodont repair fluoride plus group, there was a statistically significant difference in the percentage of WSLs between the different follow-up periods, with a decrease in the percentage of lesions over time. The study also found that Curodont Repair Fluoride Plus was associated with a 25% lower risk of developing ICDAS 1 and 2 lesions after six months than MI Paste.
Keeper JH et al., (2023) [24]	Systematic review and meta-analysis	Six studies	The Effect of SAP P11-4 on Initial Caries Lesions	P11-4 products Curodont™ Repair (CR) and Curodont™ Repair Fluoride Plus (CRFP), FV	CR showed significant improvements in Caries arrest: 45% increase compared to controls (RR: 1.82), Lesion size: 32% decrease (Hedge's g: -0.59). Positive trends were observed for the following: Cavitation: 68% reduction (RR: 0.32). Merged ICDAS score: 3.68 times lower (RR: 3.68). No studies used CRFP or reported adverse esthetic changes.
Gohar RAAEG et al., (2023) [25]	Randomised controlled trial	58 WSL	Clinical performance of SAPs versus fluoride-based delivery systems in postorthodontic WSLs.	SAP P11-4, FV	SAPs showed much lower fluorescence values (6.45) in DIAGNOpen Readings than fluoride material (10.51). This suggests greater subsurface remineralisation with SAPs. However, in terms of CDAS Scores, there was not a significant difference between the two groups at any point throughout the follow-up. Both treatments showed similar effects in masking WSLs.

[Table/Fig-2]: Summary of the clinical studies on comparison of the effect of the SAP P11-4 to other remineralising agents [3,8,10,18-26].

CONCLUSION(S)

Self Assembling Peptide P11-4 has recently emerged in dentistry as a highly promising biomaterial for biomimetic regeneration, primarily due to its ability to mimic the extracellular matrix of enamel. Overall, it represents a groundbreaking remineralising agent that has the potential to revolutionise the treatment of dental caries. There is sufficient evidence to conclude that SAP P11-4 is more effective than other remineralising agents such as fluoride, CPP-ACP, and SDF. However, its efficacy when used alone is still considered inferior. There is a potential synergistic effect when combining SAP P11-4 with fluoride, but further investigation is recommended. More clinical trials with longer follow-up periods are necessary to establish a fair comparison, particularly in terms of short- and long-term effectiveness, efficacy in different populations, and safety.

REFERENCES

[1] Alkilzy M, Santamaria RM, Schmoeckel J, Splieth CH. Treatment of carious lesions using self-assembling peptides. Adv Dent Res. 2018;29(1):42-47.
[2] Kobeissi R, Badr SB, Osman E. Effectiveness of self-assembling peptide P11-4 compared to tricalcium phosphate fluoride varnish in remineralisation of white spot lesions: A clinical randomized trial. Int J Clin Pediatr Dent [Internet]. 2020 Sep 1 [cited 2023 Oct 4];13(5):451-56. Available from: /pmc/articles/PMC7887159/.
[3] Welk A, Ratzmann A, Reich M, Krey KF, Schwahn C. Effect of self-assembling peptide P11-4 on orthodontic treatment-induced carious lesions. Sci Rep. 2020;10(1):6819.
[4] Nayak P. Topical fluoride for prevention of dental caries: A review. Indian Journal of Forensic Medicine and Toxicology. 2020;14(4):9120-23.
[5] Guanipa Ortiz MI, Alencar CM, Freitas De Paula BL, Alves EB, Nogueira Araújo JL, Silva CM. Effect of the casein phosphopeptide-amorphous calcium phosphate fluoride (CPP-ACPF) and photobiomodulation (PBM) on dental hypersensitivity: A randomized controlled clinical trial. PLoS One. 2019;14(12):e0225501.
[6] Zhao IS, Gao SS, Hiraishi N, Burrow MF, Duangthip D, Mei ML, et al. Mechanisms of silver diamine fluoride on arresting caries: A literature review. Int Dent J. 2018;68(2):67-76.
[7] El-Sayed B, Davies RPW, El-Zehery RR, Ibrahim FM, Grawish ME, Kirkham J, et al. An in-vivo intraoral defect model for assessing the use of P11-4 self-assembling peptide in periodontal regeneration. Front Bioeng Biotechnol. 2020;8:559494.
[8] Sedlakova Kondelova P, Mannaa A, Bommer C, Abdelaziz M, Daeniker L, di Bella E, et al. Efficacy of P11-4 for the treatment of initial buccal caries: A randomized clinical trial. Sci Rep. 2020;10(1):20211.
[9] Alkilzy M, Qadri G, Splieth CH, Santamaría RM. Biomimetic enamel regeneration using self-assembling peptide P11-4. Biomimetics (Basel). 2023;8(3):290. [Internet]. Available from: https://www.mdpi.com/2313-7673/8/3/290/htm.
[10] Alkilzy M, Tarabaih A, Santamaria RM, Splieth CH. Self-assembling Peptide P11-4 and fluoride for regenerating enamel. J Dent Res. 2018;97(2):148-54.
[11] Jablonski-Momeni A, Heinzel-Gutenbrunner M. Efficacy of the self-assembling peptide P11-4 in constructing a remineralisation scaffold on artificially-induced enamel lesions on smooth surfaces. J Orofac Orthop. 2014;75(3):175-90.
[12] Mohamed RN, Basha S, Al-Thomali Y, Saleh Alshamrani A, Salem Alzahrani F, Tawfik Enan E. Self-assembling peptide P11-4 in remineralization of enamel caries–a systematic review of in-vitro studies. Acta Odontologica Scandinavica. 2021;79(2):139-46.
[13] Soares R, De Ataide IN, Fernandes M, Lambor R. Assessment of enamel remineralisation after treatment with four different remineralising agents: A Scanning Electron Microscopy (SEM) Study. J Clin Diag Res. 2017;11(4):ZC136-41.
[14] Tripathi P, Mengi R, Gajare SM, Nanda SS, Wani SA, Kochhar AS. Evaluation of remineralising capacity of P11-4, CPP-ACP, Silver Diamine Fluoride, and NovaMin: An in-vitro study. J Contemp Dent Pract. 2021;22(4):357-60.
[15] Wahba N, Schwendicke F, Kamel MA, Allam G, Kabil N, Elhennawy K. Preventing and arresting primary tooth enamel lesions using self-assembling peptide P11-4 in-vitro. J Int Soc Prev Community Dent. 2022;12(1):58-70.
[16] Ghaly YS, El-Wassefy NA, Shamaa MS, Tawfik MA. Effect of self-assembling peptide and other remineralising agents on preventing initial enamel lesions around orthodontic brackets: An in-vitro comparative study. Int Orthod. 2023;21(2):100751.
[17] Lena Sezici Y, Yetkiner E, Aykut Yetkiner A, Eden E, Attin R. Comparative evaluation of fluoride varnishes, self-assembling peptide-based remineralization agent, and enamel matrix protein derivative on artificial enamel remineralization in-vitro. Prog Orthod. 2021;22(1):4.
[18] Brunton PA, Davies RPW, Burke JL, Smith A, Aggeli A, Brookes SJ, et al. Treatment of early caries lesions using biomimetic self-assembling peptides-A clinical safety trial. Br Dent J. 2013;215(4):E6.
[19] Wierichs RJ, Carvalho TS, Wolf TG. Efficacy of a self-assembling peptide to remineralize initial caries lesions-A systematic review and meta-analysis. J Dent. 2021;109:103652.
[20] Bröseler F, Tietmann C, Bommer C, Drechsel T, Heinzel-Gutenbrunner M, Jepsen S. Randomised clinical trial investigating self-assembling peptide P11-4 in the treatment of early caries. Clin Oral Investig. 2020;24(1):123-32.
[21] Gözetici B, Öztürk-Bozkurt F, Toz-Akalın T. Comparative evaluation of resin infiltration and remineralisation of noncavitated smooth surface caries lesions: 6-month results. Oral Health Prev Dent. 2019;17(2):99-106.
[22] Amin OA, Shaalan OO, Riad M. Remineralization potential of curodont repair flouride plus versus CPP-ACP in white spot lesions. Advanced Dental Journal. 2023;5(1):110-18.
[23] Ali DM, Abo-Elezz A, Nadim M, Fahmy O. Effect of two remineralizing analogues on treatment of post orthodontic enamel white spot lesions using laser fluorescence-based caries detector (an in-vivo study). Dental Science Updates. 2022;3(2):231-35.
[24] Keeper JH, Kibbe LJ, Thakkar-Samtani M, Heaton LJ, Desrosiers C, Vela K, et al. Systematic review and meta-analysis on the effect of self-assembling peptide P11-4 on arrest, cavitation, and progression of initial caries lesions. Journal of the American Dental Association. 2023;154(7):580-91.e11.
[25] Gohar RAAEG, Ibrahim SH, Safwat OM. Evaluation of the remineralizing effect of biomimetic self-assembling peptides in post-orthodontic white spot lesions compared to fluoride-based delivery systems: Randomized controlled trial. Clin Oral Investig. 2023;27(2):613-24.
[26] Riad MF, Raafat R, Nabil Amin AM. Comparative study using biomimetic remineralization versus fluoride varnish in management of white spot lesion in post orthodontic treated patient: Split mouth randomized clinical trial. Indian Journal of Public Health Research & Development. 2020;11(4):646-52.
[27] González-Cabezas C, Fernández CE. Recent advances in remineralization therapies for caries lesions. Adv Dent Res. 2018;29(1):55-59.
[28] Kyle S, Aggeli A, Ingham E, McPherson MJ. Recombinant self-assembling peptides as biomaterials for tissue engineering. Biomaterials. 2010;31(36):9395-405.
[29] Aparna BK, Yashoda R, Puranik MP. Self-assembling Peptide P11-4 as a new approach in biomimetic enamel remineralization: A review. RGUHS Journal of Dental Sciences. 2022;14(3):17-24.
[30] Aggeli A, Bell M, Carrick LM, Fishwick CW, Harding R, Mawer PJ, et al. pH as a trigger of peptide β-sheet self-assembly and reversible switching between nematic and isotropic phases. J Am Chem Soc. 2003;125(32):9619-28.
[31] Kind L, Stevanovic S, Wuttig S, Wimberger S, Hofer J, Müller B, et al. Biomimetic remineralisation of carious lesions by self-assembling peptide. J Dent Res. 2017;96(7):790-97.
[32] Kirkham J, Firth A, Vernals D, Boden N, Robinson C, Shore RC, et al. Self-assembling peptide scaffolds promote enamel remineralization. J Dent Res. 2007;86(5):426-30.
[33] Liu L, Liu X, Deng H, Wu Z, Zhang J, Cen B, et al. Something between the amazing functions and various morphologies of self-Assembling peptides materials in the medical field. J Biomater Sci Polym Ed. 2014;25(13):1331-45.
[34] Shetty N, Kini S, Nair P, D'costa VF, Jayasheelan N. A comparative evaluation of the enamel remineralizing potential of self assembling peptide, nanohydroxyapatite toothpaste and duraphat fluoride varnish- An in-vitro study. Res J Pharm Technol. 2023;16(6):2900-04.

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