

Biomimetic Regeneration Of Enamel Using Self-Assembling Peptides: A Systematized Review

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Abstract.

Background: Noninvasive methods of treating initial caries lesions have been a widely researched topic in this scientific era. Various biomimetic materials are available on the market. Self-assembling peptides focus on the biomimetic regeneration of enamel and stand out from the others due to their ability to restore the enamel matrix

Data: This systematized review was conducted on articles with the remineralization effects of SAP on initial enamel lesions published between 2019 January to 2024 September.

Sources: The search of this review was carried out in the electronic databases PUBMED, COCHRANE, EMBASE, and Google Scholar. Only primary researches were included

Results: Out of 122 articles obtained, 28 articles were included in this review after screening. The studies demonstrate the effect of SAP on reversing WSLs and its efficacy in comparing and combining with other remineralizing agents such as fluorides, and CPP-ACP.

Conclusion: With the limited evidence, SAP can be used as a promising solution for WSLs in permanent as well as primary teeth

Keyword: Biomimetic, peptide p11-4, initial enamel lesion, remineralization, regeneration, systematic review

Date of Submission: 24-09-2024

Date of Acceptance: 04-10-2024

I. Introduction

Dental caries is a complex disease initiated by microbiological changes within the complex biofilm.¹ It was stated that the global incidence of dental caries in children's permanent teeth was 53.8% and in their primary teeth 46.2%²

The highest mineralized tissue in the body is found in healthy enamel, which is composed of 96% hydroxyapatite (by weight) and 4% organic fluids. On the other hand, this mineral phase is significantly reduced and replaced by organic fluids when a white spot (WS) is present. For this reason, the term "enamel hypo mineralization" is used. Changes in the substrate's chemical composition are the cause of this enamel defect.³

The process of regaining minerals in the form of mineral ions to the hydroxyapatite latticework structure is known as remineralization. Remineralization is a natural healing process for non-cavitated lesions that uses phosphate and calcium ions to build a new surface on the crystal remnants that are still present in subsurface lesions after demineralisation.⁴ However, the idea of remineralization was modified from repair to regeneration, which allowed for the total regeneration of enamel. Self-assembling peptides are one type of such agent in this class.

This review article's objectives are to provide an overview of the available scientific evidence for SAP11-4 its advantages over the other remineralization agents and discuss its mechanism of action.

II. Material And Methods

Inclusion criteria:

All the primary studies such as Randomized controlled clinical trials (RCTs), prospective controlled clinical trials (CCTs), prospective and retrospective cohort studies, studies with split-mouth and parallel-arm designs, and invitro studies that were peer-reviewed were included.

Exclusion criteria:

literature and systematic reviews, meta-analysis, letters to the editor, and articles irrelevant to the scope of this review were excluded.

Databases & search strategy:

The search of this review was carried out in the electronic databases PUBMED, COCHRANE and EMBASE. The search terms and operators (AND and OR) used in the bases were: (remineralization) AND (self-assembling peptide). Studies published between the years 2019 and 2024 were selected. A companion search used Google Scholar to find new studies and relevant articles.

Selection process:

The searches for the articles were carried out from JULY/2024 to SEPTEMBER/2024. Articles in the English language were only selected. For all the identified studies' titles, abstracts, and complete articles were analyzed by two reviewers to determine whether they meet the inclusion criteria. The duplicates were removed. The articles were read in detail by the third reviewer to check for any bias. Conclusions were made after discussing with all three reviewers.

Data collection and synthesis:

The data extraction included specific details, such as search strategy, PICOS items, objectives, and several included studies. Studies of SAP done in permanent and primary teeth were separated because of the variations in their composition and enamel rod arrangement. Then they were tabulated as author, type of study, year, samples included, purpose, parameters used for assessment, and conclusion. A narrative summary was made based on the cumulative results of the articles reviewed.

PICOS schema: Population (P), Intervention (I), Comparison (C), Outcomes (O), and Study Design (S)

P – Participants: Patients of any age with initial caries lesions

I – Intervention: Self-assembling peptide

C – Control: Any other (placebo) treatment or untreated control or standard control (e.g. fluoride varnish)

O – Outcome: Primary: Development (initiation and progression/regression) of demineralization e.g. Visual Analogue Scale, laser fluorescence or morphometric measurements

S – Studies: Randomized controlled clinical trials (RCTs), prospective controlled clinical trials (CCTs), prospective and retrospective cohort studies, studies with split-mouth and parallel-arm designs, invitro studies

Search results:

The search performed in the database using the descriptors (remineralization) AND (self-assembling peptides) presented a total of 43 articles in PUBMED, 28 articles in COCHRANE & EMBASE, and 51 articles from Google Scholar that were published from 2019 to 2024. Out of these 122 articles in total, 72 articles that did not meet the inclusion criteria such as literature and systematic reviews, meta-analysis, letters to the editor, and articles irrelevant to the scope of this review were excluded. Of the 50 articles, 20 were duplicates. On full-text reading 2 articles were excluded because they did not assess SAP. so finally, 28 articles were taken for this review. (Figure 1)

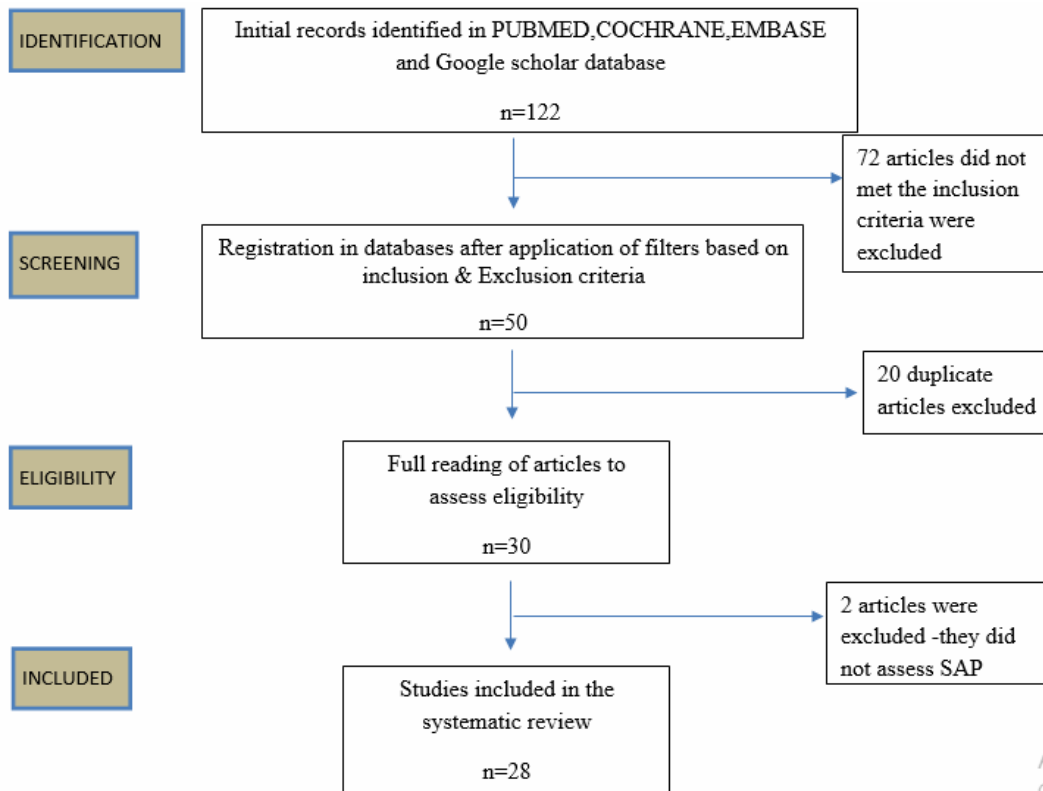


Figure 1: Search strategy

III. Results Of This Review

28 articles were reviewed in this article. Out of these 28, 10 studies were done on primary teeth (Table 2) and 18 were on permanent teeth (Table 1). 22 were in vitro studies, 5 were randomized controlled trials and 1 being the retrospective cohort study.

Remineralization of enamel:

20 studies were done on evaluating the remineralization of enamel using SAP. In that, 19 studies reported SAP whether used alone or in combination with other remineralization agents were promoted remineralization of enamel.

1 study reported no evidence of remineralization. Parameters used to assess the remineralization potential were DIAGNOdent, μ CT, QLF, QLF-D Biluminator, SMH, SEM-EDX, microcomputed tomography, nanomechanical testing for MD, H, EM, micro-CT, Transversal micro radiography, polarized light microscopy, Surface microhardness test, X-ray diffraction (XRD), atomic force microscope, Vita Easy Shade For In vitro studies and Morphometric analysis ICDAS Scores, Nyvad scores for Clinical trials.

i) SAP when used alone :

SAP found to be superior in remineralizing the enamel of Permanent teeth in 7 studies on comparison with CPP-ACPF (15), Fluoride varnish (15,16,19,25,31), TCPF(17), enamel matrix protein derivative (19), leucine-rich amelogenin peptides (26)

Where as in primary teeth SAP found to be superior in 3 studies than CPP-ACPF(35), Fluoride varnish(37), EMH (39)

ii) SAP when combined with other remineralization agents :

5 articles reported that Combining SAP with other remineralization agents were found to be superior in its effect than SAP used alone. SAP +FV (16,30,42), SAP+CPP-ACPF(18,39), SAP with n-HA(20), Fluoride varnish with TCP (33) were superior than SAP alone

Some studies reported no significant difference between SAP with NaF (22,35,41), fluoride varnish with xylitol-coated calcium phosphate (40) and CPP-ACPF(41). Some studies reported that SAP did not show any significant caries-preventive or progression inhibition effects(28,38.)

2. Antimicrobial efficacy

One study tested the antimicrobial efficacy of SAP and reported an inhibitory influence on *S. mutans* (23)

3. Cytocompatibility and migration of odontoblast-like cells

A study done to evaluate the cytotoxicity of SAP found that P₁₁-4 did not affect cell viability, induces mineral deposition and MDPC-23 migration like DMP1 (21).

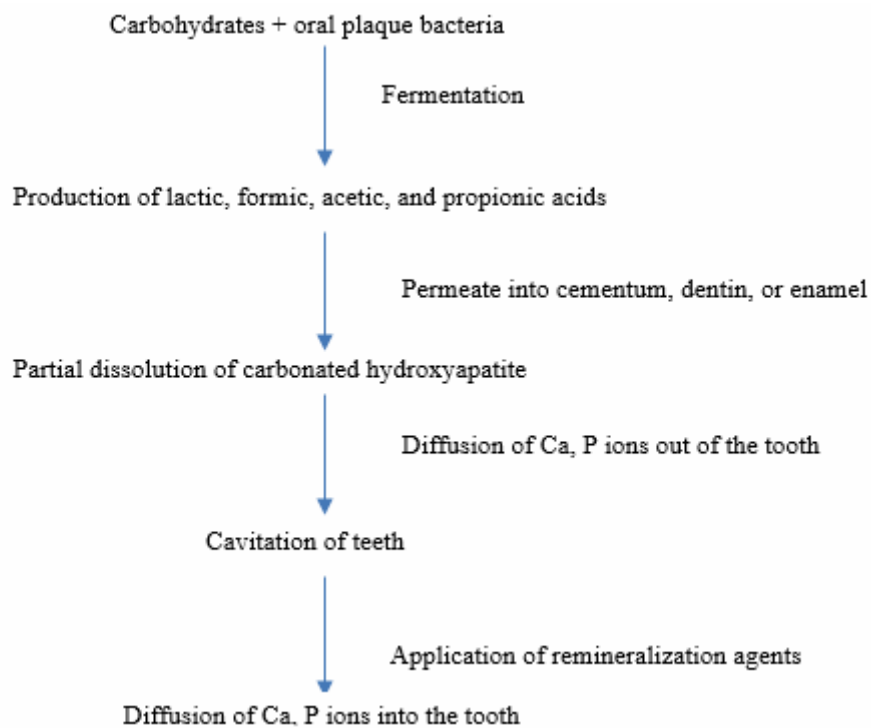
4. Prevention against acidic erosion

SAP prevents the enamel against acidic erosion as that of Fluoride varnish, CPP-ACPF was reported in one study (41).

IV. Discussion

Process of dental caries & initial caries lesion:

In theory, dental caries is a straightforward process, but in practice, it is intricate. According to Featherstone (2000), the caries mechanism can be summed up as follows:⁵



In the initial carious process, the body of the carious lesion extends in a half-moon shape (also known as the "cone shape") to the "demineralisation front" beneath alternating phases of demineralisation and remineralisation that cause preferential dissolution and reprecipitation.⁶ This preserves the relatively intact "surface layer." Kaqueler has reviewed this histological organisation, and Silverstone has provided an excellent description of it. When the mineral deficit of the lesion's body relative to healthy enamel reaches 10%, the lesion is considered clinically noticeable. In a more advanced stage, it may increase to over 40%⁷

The crystalline structures in the enamel dissolve along the weak spots due to caries; that is laterally along Retzius's striae and longitudinally along the prisms, forming wide channels of communication that are directly accessible from the outside world. Enlargement of the enamel's initial pores results from hypomineralization of the WS subsurface.⁸

Ideal Requirement Of An Remineralizing Agent:

- ❖ The following are the ideal specifications:⁹
- ❖ It should function at an acidic pH to stop demineralisation during a carious attack;
- ❖ It should also work in xerostomic patients, as saliva cannot effectively stop the carious process;
- ❖ It should be able to boost the remineralising properties of saliva;
- ❖ It should deliver calcium and phosphate into the subsurface;
- ❖ It shouldn't deliver any excess calcium; it shouldn't favour calculus formation

Remineralizing agents available so far includes:¹⁰

- Fluoride
- Non-fluorinated remineralizing agents
 - Alpha tricalcium phosphate (TCP) and beta TCP (β -TCP)
 - Amorphous calcium phosphate
 - CPP-ACP
 - Sodium calcium phosphosilicate (bioactive glass)
 - Xylitol
 - Dicalcium phosphate dehydrate (DCPD)
 - Nanoparticles for remineralization
 - Calcium fluoride nanoparticles
 - Calcium phosphate-based nanomaterials.
 - Nano-HAP particles
 - ACP nanoparticles
 - Nano-bioactive glass materials
- Polydopamine
- PA
- Oligopeptides
- Theobromine
- Arginine
- Self-assembling peptides
- Electric field-induced remineralization

The void in the concept of remineralization:

Proteins had significant effects in enamel because they are a type of biopolymer with viscoelastic properties that result from configurational rearrangements, macromolecule interactions, and their disposition in both short- and long-range interrelationship. This small protein component was thought to be the cause of enamel's "metal-like ductility" as opposed to its "brittleness."

The minerals were more abundant after remineralisation, but the crystals were not as compact as they were in the original enamel. The protein's effect lessened after remineralisation simply because more crystal accumulated on the surface. Elevated mineral content caused the enamel to become brittle, protein content dropped, and the characteristic "metal-like ductility" was less noticeable. Because of the stress, the brittle cracks were likely to enlarge and could cause delamination.¹¹

Sadly, the majority of the remineralizing agents available so far focuses on restoring the last enamel but ignores to replace the matrix which is absolutely necessary for the enamel's ductility and resistance to brittleness and these properties were not been used as a parameter to evaluate the efficiency of remineralization agents in so far in researches.

Enamel formation

Thin ribbon-like crystals that first deposit in the enamel matrix eventually grow into flat hexagonal prisms during the enamel crystal formation process. The main structural component of the extracellular protein framework of the growing enamel matrix is made up of amelogenin proteins. According to recent research, amelogenin, the predominant protein in enamel, forms nanospheres (18–20 nm in diameter) through self-assembly mediated by protein–protein interactions. After further assembly, hydrophobic nanospheres reach larger diameters of 20–200 nm, stabilising the matrix that holds the original enamel crystallites. By interacting with particular surfaces of hydroxyapatite crystallites in growth, nanospheres can restrict crystal growth to specific orientations that are preferred kinetically. After secretion, the amelogenins are broken down by proteases, causing the crystallites to thicken and possibly fuse together to form mature enamel.¹²

Thus materials which perform the functions as that of ameloblasts is needed nowadays and restoring lost enamel matrix have become the added criteria for choosing the ideal remineralization agent to reverse the incipient caries lesions

History of self assembling peptides

Shuguang Zhang made the initial discovery of self-assembling peptides in 1990. The hydrophilic sides of these self-assembling peptides include positively charged lysine, arginine, histidine, and negatively charged aspartic and glutamic acids, while the hydrophobic sides are made up of alanine, valine, leucine, isoleucine, and phenylalanine. These clearly defined sequences enable them to go through ordered self-assembly, forming nanofibres with a diameter of about 10 nm. These nanofibres then interweave to form scaffolds that maintain a

remarkably high hydration level—more than 99% in water. This is the the fundamental concept behind the self-assembling peptide building blocks. One crucial feature is their ability to self-assemble and reassemble, which means that even after being physically destroyed, they can do so again. The easier scaffold formation and the better the mechanical properties are, the higher the hydrophobicity content.

Additionally, there are various categories of peptide materials:

- ❖ Peptides that resemble Lego can self-assemble to form nanofibres;
- ❖ Peptides that resemble lipids or surfactants can self-assemble to form nanotubes and nanovesicles;
- ❖ Peptides that resemble biological paint can self-assemble to alter surfaces at the nanoscale.

Certain environmental factors can cause certain peptide secondary structures to become more dynamic.

These factors include:

- (i) The arrangement of amino acid sequences (even if the composition remains the same);
- (ii) The peptide's molecular size;
- (iii) Peptide concentration;
- (iv) The pH of the solution;
- (v) Temperature;
- (vi) The medium composition, which may include solvent or substrate;
- (vii) Ionic strength; and
- (viii) The presence of de-naturation agents like sodium dodecylsulfate, urea, and guanidium, HCl.

These elements have the potential to greatly impact both the process and the dynamic behaviours of peptide secondary structures.

Creating an authentic three-dimensional microenvironment is crucial in order to replicate the actual tissue and bodily conditions. The size of their micropores and microfibrils renders the widely used biomaterials insufficient. Collagen gel derived from animals and Matrigel contain residual materials that may not be sufficient for studies under strict control. Designer scaffolds are therefore becoming more and more in demand. Because the designer self-assembling peptide scaffolds are made entirely of synthetic amino acid materials, they are safe for human use and contain no harmful substances, organic solvents, biological or chemical contaminants, or impurities derived from animals.

The following characteristics are present in this class of materials:

- ❖ The peptides have several characteristics in common with natural extracellular matrices, including being truly three-dimensional nanofiber matrices that support cell maintenance, proliferation, and differentiation.
- ❖ They are also easily synthesised and made by rational design, resulting in chemically defined biomaterials.
- ❖ As far as is known, they do not appear to produce any immune responses.
- ❖ They are biodegradable, breaking down into amino acids.
- ❖ They are injectable, gelling after interaction with body fluids and adopting the geometry of the tissue defect.¹³

SAP in remineralization of teeth

Thus, Matrix mineralization is a different type of matrix function that modulates the creation of a suitable cell microenvironment rather than requiring direct cell interaction and instruction. The extracellular matrix's collagenous and non-collagenous proteins with bioactive motifs, which have been utilised to create self-assembling peptides with increased activity in fostering HAP crystal growth, are the components in charge of the biomineralisation process.¹³

Self-Assembling Peptide P11-4 is a recent material used to prevent caries, made up of arginine, tryptophan, phenylalanine, glutamine, and glutamic acid. These amino acids undergo hierarchical self-assembly into fibrillar scaffolds in response to high ionic strength and acidic pH found in the caries lesion body thus guiding the regeneration of enamel tissue and promoting remineralization.¹⁴

The three-dimensional structures formed by these agents imitate the extracellular matrix of teeth, thereby initiating remineralization. For calcium along with phosphorus ions found in saliva, this matrix has a strong affinity. As a result, it aids in Denovo's production of enamel-like hydroxyapatite compounds. SAP is its ability to attract calcium and Phosphorus ions from Saliva. So it's called Denovo synthesis of Enamel. This process is denoted as Guided Enamel Regeneration¹³

Table 1: Invitro & Invivo Studies Of Sap In Remineralization (2019-2024)

Author	Type Of Study	Year	Samples Included	Materials Compared	Purpose	Parameter Used For Assessment	Conclusion
Üstüün ¹⁵	Invitro Study	2019	32 Extracted Impacted Third Molar	P11-4, CPP-ACPF,NaF	Re-Mineralization	Diagnodent And MHT	The Highest Remineralization Efficacy Findings In All Periods Were Determined In P11-4 Followed By Groups CPP-ACPF,NaF
Jablonski-Momeni A ¹⁶	Invitro Study	2020	108 Human Enamel Samples	SAP,SAP+FV	Enamel Remineralization	QLF	Application Of P11-4 With Fluoride Varnish Was Superior To The Use Of Fluorides Alone For Remineralisation Of Enamel Adjacent To Brackets.
Kobeissi R ¹⁷	Clinical Randomized Trial	2020	40 Young Permanent Teeth	TCPF, SAP ₁₁₋₄	Enamel Remineralization	Diagnodent, ICDAS II Scores	Both TCPF And SAP ₁₁₋₄ Were Effective In Treating WSLs However, The Success Of Guided Enamel Regeneration By The SAP ₁₁₋₄ Through The Biomaterialization Has Proven Superiority Of This Material Compared To TCPF.
Kamal D ¹⁸	In Vitro Study	2020	60 Specimens	FV, CPP-ACPF, Varnish ,SAP, SAP+FV, SAP+CPP-ACPF Varnish	Remineralizing Potential	SMH,SEM	Complementary Effect Was Obtained After Combining Self-Assembling Peptide With CPP-ACPF Or Fluoride Showing The Highest Remineralizing Potential Early After 1 Week And Even After 4 Weeks Compared To When Each Agent Used Alone. Added Benefits Can Be Obtained Through Combining Self-Assembling Peptide With Other Remineralizing Agents Allowing Faster And Enhanced Regeneration Of Non-Cavitated Caries Lesions
Lena Sezici Y ¹⁹	In Vitro Study	2021	60 Bovine Enamel Samples	Fluoride Varnishes, Self-Assembling Peptide, And Enamel Matrix Protein Derivative	Re-Mineralization	QLF-D Biluminator	The Fluorescence Loss Was Significantly Reduced With Enamel Matrix Protein, Self-Assembling Peptide, And Light-Curable Fluoride Varnishes In The Analysis For 21 Days. Curodont And Clinpro XT Were Effective In Diminishing The Fluorescence Loss And Lesion Area Compared To The Duraphat, Enamel Pro Fluoride Varnishes, And Emdogain In Different Time Points.
Rangappa Kg Et Al ²⁰	Invitro	2022	66 First Premolar Teeth	Chitosan With N-Ha & SAP With N-Ha	Remineralizing Potential	SEM-EDX	Combination Of Chitosan With N-Ha And Self-Assembling Peptides With N-Ha Can Be Considered Effective Demineralizing Agents.
Araújo	Invitro	2022	Cell	SAP	Cytocom And Effective	Light MTT, Alizarin Red	P ₁₁₋₄ Did Not Affect Cell Viability, Induces Mineral Deposition And MDPC-23 Migration Like DMP1.

					ness Of P ₁₁₋₄ On Inducing Mineralization And Migration Of Odontoblast-Like Cells		
Atteya Sm ²²	Randomized Control Trial	2023	147 Teeth In 66 Patients	Self Assembling Peptides (SAP11-4), Nanosilver Fluoride (NSF) And Sodium Fluoride (NaF)	Remineralizing Effect	Icdas Scores, Nyvad Scores, Diagnodent	P11-4 And NSF Varnish Reduced The Icdas Scores, Caries Activity And Diagnodent Readings Of WSLs In Permanent Teeth. However, The Change In Icdas Scores Was Not Significantly Different From NaF.
Gayas Z Et Al ²³	Invitro Study	2023	Unstimulated Human Saliva Was Obtained From A Single Healthy Volunteer	SAP11-4, Fluoride Enhanced Hydroxy-Apatite Gel, Acidulated Phosphate Fluoride Gel, Chlorhexidine Gluconate Gel	Antimicrobial Efficacy	<i>S.Mutans</i> Colony-Forming Units (CFUs)	The Self-Assembling Peptide P ₁₁₋₄ -Based Tooth Remineralization Agent Exhibited An Inhibitory Influence On <i>S. Mutans</i> And Hence Formation Of Cariogenic Bacteria Dominant Biofilm Can Thus Be Affected By Its Application.
Godenzi D ²⁴	A Retrospective Cohort Study	2023	405 Proximal Lesions In Posterior Teeth	SAP	Remineralizing Potential	Radiographic Evaluation	Real-World Clinical Data Indicate That SAP ₁₁₋₄ Can Lead To Recovery And A Healthier Tooth Stage.
Shetty Ss ²⁵	In Vitro Study	2023	20 Premolars	SAP11-4, Fluoride Varnish	Re Mineralization	Diagnodent, ICDAS II Scoring, SEM-EDX Analysis	Curodont™ (SAP)Repair Showed Better Remineralizing Potential Compared With Bifluorid 10® (FV) Varnish. In Terms Of The Mineral Gain, Curodont™ Repair Showed Better Results For Calcium And Phosphorus Post-Remineralization. Whereas Bifluorid 10® Showed A Higher Gain In Terms Of Fluoride. Self-Assembling Peptide P ₁₁₋₄ Can Be Used As An Alternative To Fluoride Varnish For Remineralizing Wsl.
Nath Et Al ²⁶	Invitro Study	2023	25 Premolars	P11-4, Leucine-Rich Amelogenin Peptides And 5% Naf Varnish.	Enamel Remineralization	Microcomputed Tomography, Nanomechanical Testing For MD,H,EM	Mineral Density (MD), Hardness (H), And Elastic Modulus (EM) Were Highest For P11-4 Followed By Leucine-Rich Amelogenin Peptides And 5% Naf Varnish.
Ghaly Y ²⁷	In Vitro Study	2023	80 Extracted Human Maxillary Premolars	SAP (P ₁₁₋₄), CPP-ACPF, Fluoride Varnish	Enamel Remineralization	Ca/P, Surface Microhardness	SAP (P ₁₁₋₄) Had The Greatest Remineralizing Efficacy Compared To FV And CPP-ACPF. Moreover, Extended Period Of Time Improved The Preventive Efficacy Of SAP (P ₁₁₋₄) Compared To The Other Regimens.

Kharbot B ²⁸	Invitro Study	2024	90 Bovine Enamel Specimens	Calcium–Coacervate Solution, Polyacrylic Acid Solution, SAP 11-4,	Enamel Remineralization	Transversal Micro Radiography	Infiltration With The CC And PAA Resulted In A Consistent Mineral Gain Throughout The Lesion Body. No Significant Mineral Gain With Sap
A.S. Al-Qahtani Et Al ²⁹	Invitro Study	2024	75 Human Molars	NHA, CPP-ACPF	Pretreatment For Composite Restoration	Vickers Microhardness, μ bs And Stereo-Microscope	Remineralizing Pretreatment With NHA Gel Activation Via Invisible Infrared Light And Casein Phosphopeptide-Amorphous Calcium Phosphate Fluoride Seem To Improve The Dentin MH And μ bs Of The Composite Restoration Whereas Sap Showed Minimum Scores Of MH And μ bs
Shaanan O ³⁰	Randomized Controlled Clinical Trial	2024	28 Participants With 58 Incipient Carious Lesions	SAPF, NAF	Remineralizing Potential	Diagnodent	The Self-Assembling Peptide Combined With Fluoride Varnish Showed Higher Remineralization Potential Than Fluoride Varnish Alone For Incipient Carious Lesions Over A Six-Months Follow Up.
Nath Sjc ³¹	Invitro Study	2024	50 Premolar Teeth	SAP P11-4, P-26, Porcine Leucine-Rich Amelogenin Peptide, 5% NaF Varnish	Remineralizing Potential	Micro-Ct, Mineral Density (Md), Hardness (H), And Elastic Modulus (Em)	P26 And P11-4 SAP Are More Effective Than 5% NaF Varnish In Remineralising The Depth Of Eccls
Patil Sv Et Al ³²	Invitro Study	2024	60 Extracted Premolars	MI Varnish (Control), MI Varnish + Zwitterionic Material, MI Varnish + Self-Assembling Peptide, And MI Varnish + BGA	Enamel Remineralization	Polarized Light Microscopy, Surface Microhardness Test	MI Varnish Alone Had Remineralizing Properties Of WSLs, But When Novel Materials Like Zwitterionic Ion, Self-Assembling Peptide, And BGA Are Incorporated, Its Efficacy Increases. Among All Zwitterionic Ions Showed Superior Results For Fluoride And Calcium Ion Release And Remineralization And BGA For Phosphorus Ion Release And SMH.
Güven E ³³	In Vivo Study	2024	Thirty-Two Subjects With 107 Post-Orthodontic WSLs	Tricalcium Phosphate (TCP) Containing Fluoride Varnish, Self-Assembling P11-4 Peptides And Combined Application Of The Two Products.	Re-Mineralization	QLF Inspektor™ Pro, Diagnodent And Vita Easy Shade.	Fluoride Varnish With TCP Showed Highest Remineralization At 6 Months, And The Remineralization Was Positively Affected In The Short Term (Three Months) After The Use Of Self-Assembling P11-4 Peptides And Their Combined Application.
Chen K ³⁴	In Vitro Study	2024	Bovine Enamel	SAP26,SAP26 With Fluoride,	Remineralizing Potential	Micro-Computed Tomography, Scanning Electron Microscopy With Energy Dispersive X-Ray And X-	The Present Study Provided A First Indication Of Better Remineralisation Effects Of The Combined Use Of The Bioinspired Self-Assembling Peptide P26 And Fluoride Varnish Compared To The Effects Of The Respective

					Ray Diffraction (XRD)	Individual Uses Of P26 Or Fluoride Varnish
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Table 2 : Studies On The Remineralization Effect Of Sap In Primary Teeth

Author	Year	Type Of The Study	Samples Included	Materials Compared	Application & Parameters Used For Assessment	Conclusion
Üstün N ³⁵	2022	Invitro	40 Primary Molars	SAP11-4, CPP-ACPF,NaF	Enamel Remineralization -Microhardness Tester And Atomic Force Microscope	All Agents Had A Significant Remineralization Effect On Eroded Primary Tooth Enamel. After Further Erosive Challenge, Enamel Loss In The Cpp-Acftp Group Was Found To Be Significantly Lower Than In All Other Groups, And No Significant Difference Was Found Between The P ₁₁₋₄ And Naf Groups.
Elmitwalli ³⁶	2022	Invitro Study	40 Primary Second Molars	P ₁₁₋₄ , NHA, CPP-ACPF	Enamel Remineralization- SEM-EDX	Restoration Of Enamel Surface With Appearance Of Mineralized Deposits Was Highly Observed With P ₁₁₋₄ & NHA Then In CPP-ACPF
Özdemir Ş ³⁷	2022	Invitro Study	Primary Molars	Sap ₁₁₋₄ ,Fluoride Varnish	Remineralization Of Secondary Caries Primary Enamel- Micro-Ct Analysis	Remineralization Depths Of The Peptide Group Were Higher Than Those Of The Fluoride Group And Its Statistically Significant
Wahba N Et Al ³⁸	2022	Invitro	180 Primary Incisors And Canines	SAP-Protect,SAP-Repair,Fluoride Varnish, CPP-ACPF, CPP-ACPF Fluoride Mouth Wash, NHA, Resin Infiltrate.	Preventing And Arresting Primary Tooth Enamel Lesions -Transversal Microradiography	FV,FMW Showed Consistent And Significant Caries-Preventive Effects & Effective To Inhibit Caries Lesion Progression On Human Primary Teeth Enamel <i>In Vitro</i> . SAP, CPP-ACP, CPP-ACPF, And NHA Did Not Show Any Significant Caries-Preventive Or Progression Inhibition Effects.
Memarpour M ³⁹	2022	Invitro	154 Primary Teeth	P ₁₁₋₄ , Fluoridate Toothpaste, P ₁₁₋₄ + Ft, CPP-ACP, P ₁₁₋₄ + CPP-ACPF, Fluoridate Bioactive Glass Toothpaste, P ₁₁₋₄ + BT	Remineralization Of Enamel- FESEM, AFM	P ₁₁₋₄ + CPP-ACPF, BT Groups Shows Higher Values Of EMH No Significant Difference Between P ₁₁₋₄ + Ft & Ft. Control Group & P ₁₁₋₄ Groups Had Lowest EMH
Nambi Natchiyar ⁴⁰	2023	Randomized Clinical Trial	60 Primary Anteriors	SAP ₁₁₋₄ , Fluoride Varnish With Xylitol-Coated Calcium Phosphate	Enamel Permeability-Icdas, Morphometric Analysis, SEM	A Statistically Significant Reduction In The Icdas Scores And Percentage Area Of WSLs Seen In The Cr Group After Six Months But Not In The EV Group. The SEM Evaluation Did Not Show A Significant Reduction In The Percentage Area Of Droplets In Both The Cr And Ev Groups. No Significant Difference Was Seen Between Ev And Cr In The Three Parameters Assessed.
Baltaci E ⁴¹	2023	Invitro Study	40 Primary Anterior Teeth	SAP ₁₁₋₄ ,Fluoride Varnish, CPP-ACPF	Prevention Against Acidic Erosion- Extra Oral Scanner	All Experimental Groups Showed Superior Results Than The Control Group Regarding Microhardness, Surface Roughness, And Substance Loss And There Was No Significant Difference Between Them.
Claudine Mamdouh Badie ⁴²	2022	Randomized Controlled Clinical	24 Primary Teeth	Sap ₁₁₋₄ With NaF, NaF	Remineralization	Self- Assembling Peptide P11-4 In Conjunction With 5% NaF Varnish Is Superior To

	3	Trial			5% NaF Varnish Only In The Remineralization Of White Spot Lesion.
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V. Conclusion

On reviewing the available data on the remineralization capacity of Self-assembling peptides, it can be said that the SAP has been a proven remineralization agent and unique on comparing with other agents because of its Denovo synthesis of enamel.

It should be noted that the majority of evidence were invitro studies with fewer randomized controlled studies. And its evident that there is very few studies on SAP in remineralizing white spot lesions present in deciduous teeth with only one in vivo study so far. ECC being a rapidly progressing condition, the need for its prevention in its early stages in very much needed. Thus in future more clinical studies on SAP especially involving the primary teeth is required.

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