Ngr. Jr. Med. Sc. vol-2, issue-4 (Apr-2026) pp-114-116

ISSN: 3139-5309 (Online)

Nexus Global Research Journal of Medical Sciences

Journal Homepage: https://nexusglobalresearch.com/journals/ngrjms/

Review Article:

A Critical Review of Modern Approaches to Enamel Remineralization: Efficacy and Clinical Integration

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ABSTRACT:

Enamel demineralization is a global health challenge, requiring advanced remineralization strategies beyond traditional fluoride, whose efficacy and clinical integration require critical evaluation. The aim of this study is to critically review and synthesize modern enamel remineralization approaches. This PRISMA-guided review synthesized 12 English studies (2020-2023) from PubMed, Scopus, and Web of Science. Modern strategies integrate biomimetic regeneration and material science. Chitosan-amelogenin composites reduce caries depth, and specific chitosan systems restored enamel hardness to 3.8 ± 0.3 GPa. Nano-hydroxyapatite excels for white spot lesions, and 38% Silver Diamine Fluoride is prioritized for arresting coronal lesions. These approaches offer promising advancements, but require more evidence for full fluoride substitution.

Keyword: Enamel Remineralization, Biomimetic Strategies, Nano-Hydroxyapatite, Advanced Materials, Clinical Efficacy, Dental Caries, Fluoride, Silver Diamine Fluoride

Citation: Fayziyeva, A. S. (2026). A Critical Review of Modern Approaches to Enamel Remineralization: Efficacy and Clinical Integration . Nexus Global Research Journal of Medical Sciences, 2(4), 114–116.

INTRODUCTION

Dental enamel demineralization, a precursor to dental caries, represents a pervasive global health challenge, impacting individuals across all age groups [1, 4, 6]. The constant challenge from acidic oral environments leads to mineral loss and lesion formation, often overwhelming natural remineralization mechanisms [5, 8]. While conventional fluoride-based treatments have long been successful in caries prevention [2, 11], the limitations of these traditional approaches necessitate the exploration of advanced strategies. However, despite significant advancements in materials science and biotechnology, a cohesive and critically synthesized evaluation of the diverse modern approaches to enamel remineralization, particularly their comparative efficacy and clinical integration, remains an open question [1, 9]. The aim of this study is to critically review and synthesize the current landscape of modern approaches to enamel remineralization.

MAIN BODY

Literature Review: Modern approaches to enamel remineralization integrate biomimetic strategies with advanced material science. Biomimetic regenerative technologies leverage self-assembling peptides and protein-based systems to guide crystal growth; for instance, chitosan-amelogenin composites significantly reduce caries depth, while specific chitosan-based systems like CMC/LYZ-ACP restore enamel hardness [3, 5]. Gelatin and silk fibroin scaffolds also promote heterogeneous nucleation [3]. Nano-hydroxyapatite (nHA) mimics natural enamel crystals, adhering to demineralized surfaces and acting as a calcium and phosphate reservoir for subsurface repair [2, 5]. While nHA shows excellent results for white spot lesions, current evidence is insufficient for its full substitution of fluoride in non-cavitated lesions, per ADA guidelines [1, 2]. Fluoride-doped amorphous calcium phosphate (ACP) nanoparticles offer rapid conversion to crystalline apatite, effectively restoring demineralized enamel to native tissue structures [5]. Bioactive glass formulations release calcium, phosphate, and silicon ions, elevating local pH to favor mineral precipitation [5]. Advanced nanosystems, including liposomes and polymeric micelles, improve penetration into subsurface lesions, prolong surface retention, and enable triggered ion release under acidic conditions [5]. Xylitol varnishes further facilitate remineralization and inhibit S. mutans, offering an alternative for non-cavitated lesions during orthodontic treatment [1, 2].

Research Methodology: This critical review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was conducted across electronic databases including PubMed, Scopus, and

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Received: 15 Mar 2026 | **Accepted:** 02 April 2026 | **Published:** 07 April 2026

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Web of Science for articles published in English between January 2020 and December 2023 [8]. The search strategy employed a combination of keywords such as "enamel remineralization," "modern approaches," "biomimetic strategies," "nano-hydroxyapatite," "advanced materials," and "clinical efficacy" [1, 6, 9].

Inclusion criteria: Peer-reviewed original research, systematic reviews, and meta-analyses focusing on novel enamel remineralization techniques.

Exclusion criteria: Editorials, opinion pieces, conference abstracts, and studies not directly addressing enamel remineralization or published before 2020.

Initial database searches yielded 257 articles. After duplicate removal, 189 unique articles were screened by title and abstract. Full-text review of 45 potentially relevant articles led to the final inclusion of 11 studies for critical synthesis, addressing the research questions [3, 7, 10].

Results and Analysis: The principal mechanisms underlying contemporary enamel remineralization strategies integrate biomimetic regeneration with advanced material science. Biomimetic approaches leverage self-assembling peptides and protein-based systems, such as chitosan-amelogenin composites, to guide crystal growth and promote heterogeneous nucleation [3, 5]. For instance, chitosan-amelogenin systems have demonstrated significant reduction in caries depth, while specific chitosan-based systems like CMC/LYZ-ACP restored enamel hardness to 3.8 ± 0.3 GPa, approaching the natural enamel value of 4.3 ± 0.5 GPa [3]. Material-based strategies include nano-hydroxyapatite (nHA), which mimics natural enamel crystals, adhering to demineralized surfaces and acting as a calcium and phosphate reservoir for subsurface repair [2, 5]. Fluoride-doped amorphous calcium phosphate (ACP) nanoparticles offer rapid conversion to crystalline apatite upon contact with water, effectively restoring demineralized enamel surfaces to structures closely resembling native tissue [5]. Bioactive glass formulations release calcium, phosphate, and silicon ions over several weeks, elevating local pH to favor mineral precipitation [5]. Concurrently, traditional fluoride mechanisms involve replacing hydroxyl ions in hydroxyapatite, forming Ca–F and OH–F bonds, which reduces unit cell volume, increases acid resistance, and inhibits bacterial enolase [1, 2]. Xylitol, a 5-carbon sugar polyol, facilitates remineralization into mid- and deep demineralized enamel layers, with optimal S. mutans inhibition occurring at 5–8 g daily [2].

Novel biomimetic and material-based approaches demonstrate varied efficacy and clinical applicability. Nano-hydroxyapatite shows excellent results for white spot lesions (WSLs); however, current evidence is insufficient for its full substitution of fluoride in non-cavitated lesions, as per ADA guidelines [1, 2]. Self-assembling peptide p11-4 also yields excellent results for WSLs [1]. Caries depth reduction from ~100 to ~30 μm has been observed with chitosan-amelogenin [3]. CPP-ACFP varnish is strongly advised for WSLs and provides protection comparable to resin-based sealants during orthodontic treatments [1]. The ADA prioritizes biannual application of 38% Silver Diamine Fluoride (SDF) solution over 5% NaF varnish for arresting coronal lesions in both primary and permanent dentition [2]. Advanced nanosystems, including liposomes and polymeric micelles, improve penetration into subsurface enamel lesions, prolong surface retention, target cariogenic biofilms, and provide triggered ion/drug release under acidic conditions [5]. Table 1 summarizes the key modern remineralization approaches and their characteristics.

Table 1. Modern Remineralization Approaches and Mechanisms

Approach	Principal Mechanism	Efficacy/Application
Nano-hydroxyapatite (nHA)	Mimics enamel crystals, acts as Ca/P reservoir	Excellent for WSLs; ADA notes insufficient evidence for full fluoride substitution [1, 2]
Self-assembling peptides	Guides crystal growth, promotes nucleation	Reduced caries depth (e.g., CS-AMEL), restored hardness (e.g., CMC/LYZ-ACP) [3, 5]
Fluoride-doped ACP	Rapid conversion to crystalline apatite	Restores demineralized enamel to native tissue structures [5]
Bioactive glass	Releases Ca, P, Si ions; elevates local pH	Favors mineral precipitation over weeks [5]
CPP-ACP/ACFP	Stabilizes amorphous calcium phosphate	"Gold standard" for WSLs, comparable to sealants [1]

Discussion: The current review underscores a significant paradigm shift in enamel remineralization, moving beyond conventional fluoride-centric approaches towards sophisticated biomimetic and advanced material-based strategies [3, 5]. These modern methods, leveraging self-assembling peptides, nano-hydroxyapatite (nHA), and ion-releasing bioactive glasses, aim to mimic natural biomineralization processes and provide targeted repair [3, 5]. The principal mechanisms involve guided crystal growth and sustained ion delivery, offering more comprehensive and durable remineralization than traditional methods [5]. While nHA and self-assembling peptide p11-4 demonstrate excellent efficacy for white spot lesions, their full substitution for fluoride in non-cavitated lesions remains unsupported by current ADA guidelines, highlighting a critical gap in evidence [1, 2]. This aligns with broader calls for more robust clinical data to validate novel approaches and address challenges in clinical integration [1, 9]. The varied clinical applicability, from CPP-ACFP varnishes for orthodontic patients to silver diamine fluoride for lesion arrest, reflects a diverse but not yet fully integrated therapeutic landscape [1, 2]. A limitation of this review is its focus on literature published between 2020 and 2023, which may not capture all foundational or very recent advancements. Future research should prioritize long-term clinical trials comparing the synergistic effects and cost-effectiveness of these diverse modern approaches, alongside clearer regulatory pathways for novel biomaterials [1, 9].

CONCLUSION AND RECOMMENDATIONS

Modern enamel remineralization, integrating biomimetic and advanced material science, offers diverse mechanisms for targeted repair. Agents like nano-hydroxyapatite, self-assembling peptides, and fluoride-doped amorphous calcium phosphate demonstrate significant potential for enhanced acid resistance and lesion reversal. Clinicians should integrate these novel approaches, alongside conventional fluoride and CPP-ACFP, for comprehensive caries management, particularly for white spot and non-cavitated lesions, advancing patient outcomes.

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