

Effectiveness of Nanohydroxyapatite in the Remineralization of Tooth Enamel: Current Evidence and Clinical Perspectives

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Abstract:

Dental caries is one of the most prevalent oral diseases worldwide and is primarily associated with an imbalance between enamel demineralization and remineralization. The development of biomimetic remineralizing agents has therefore become an important area of preventive dentistry. Nanohydroxyapatite (nHAp), a nanoscale form of hydroxyapatite that closely resembles the mineral phase of natural dental enamel, has attracted considerable attention because of its physicochemical properties, biocompatibility, and potential to promote enamel remineralization. This review evaluates the current scientific evidence concerning the effectiveness of nHAp in the remineralization of early enamel lesions and white spot lesions. Evidence from systematic reviews, meta-analyses, and experimental and clinical studies indicates that nHAp can increase enamel surface microhardness, facilitate mineral deposition, reduce mineral loss, and contribute to the repair of early carious lesions. Its proposed mechanisms include direct deposition of apatite nanoparticles, provision of calcium and phosphate ions, formation of a protective apatite-rich layer, and promotion of crystal growth within subsurface enamel lesions. Recent systematic reviews suggest that nHAp may demonstrate remineralizing effects comparable to, and in some experimental conditions greater than, conventional fluoride-based approaches. However, the available evidence remains heterogeneous, with a substantial proportion of studies being in vitro or in situ and relatively few well-designed long-term clinical trials. Therefore, nHAp should currently be regarded as a promising biomimetic remineralizing agent rather than an unequivocally established replacement for fluoride. Further standardized randomized controlled trials are required to determine optimal concentrations, formulations, treatment protocols, and long-term clinical effectiveness.

Keywords: nanohydroxyapatite; nano-hydroxyapatite; enamel remineralization; dental caries; white spot lesions; biomimetic dentistry; preventive dentistry; fluoride.

Introduction

Dental caries is a dynamic, biofilm-mediated disease characterized by alternating periods of mineral loss and mineral gain in dental hard tissues. When the demineralization process predominates, subsurface enamel lesions may develop and clinically appear as white spot lesions (WSLs). At this early stage, the lesion may remain potentially reversible through non-invasive remineralization. Consequently, strategies that promote mineral recovery without mechanical removal of tooth structure have become a major component of minimally invasive dentistry.

Dental enamel is composed predominantly of inorganic mineral, with hydroxyapatite representing the principal crystalline phase. The similarity between synthetic hydroxyapatite and the mineral component of dental tissues has led to extensive investigation of hydroxyapatite-based materials as biomimetic agents. Nanohydroxyapatite possesses nanoscale dimensions, high surface area, increased surface reactivity, and physicochemical characteristics that facilitate interaction with enamel surfaces. These characteristics have generated significant interest in its application in preventive and restorative dentistry. The potential of nHAp is particularly relevant to early caries management. Unlike conventional restorative approaches, remineralization aims to restore mineral content while preserving the original tooth structure. Several experimental studies and clinical investigations have reported beneficial effects of nHAp-containing dentifrices and other formulations on initial enamel lesions. However, the magnitude and clinical relevance of these effects remain subjects of scientific debate.

The purpose of this review is to critically examine the current evidence regarding the effectiveness of nanohydroxyapatite in enamel remineralization, with particular emphasis on its mechanism of action, experimental evidence, clinical outcomes, comparison with fluoride, and limitations of the existing literature.

Physicochemical Characteristics of Nanohydroxyapatite

Hydroxyapatite is a calcium phosphate mineral that constitutes a major component of the inorganic phase of dental hard tissues. Nanohydroxyapatite consists of hydroxyapatite particles at the nanoscale and has attracted interest because its morphology and chemical composition resemble those of biological apatite.

The nanoscale structure provides several potentially advantageous properties. First, nHAp has a high surface-area-to-volume ratio, increasing its ability to interact with the enamel surface. Second, its similarity to enamel apatite may facilitate biomimetic deposition onto demineralized areas. Third, nHAp can function as a source or reservoir of calcium and phosphate ions, which are essential for the formation of new apatite crystals.

The biological compatibility of hydroxyapatite is another important characteristic. Because hydroxyapatite is naturally present in mineralized tissues, nHAp has been investigated as a biomimetic material in several dental applications, including caries prevention, enamel remineralization, dentinal hypersensitivity management, and restorative materials.

Mechanisms of Enamel Remineralization by Nanohydroxyapatite

The remineralizing activity of nHAp appears to involve several complementary mechanisms.

Direct deposition of apatite nanoparticles

Demineralized enamel contains microscopic pores and regions of reduced mineral density. Because of their small dimensions, nHAp particles may penetrate or accumulate within these defects and serve as nucleation sites for subsequent mineral deposition. This process can result in the formation of an apatite-rich layer on the enamel surface and within superficial lesion

Calcium and phosphate ion delivery

Remineralization requires adequate availability of calcium and phosphate ions. nHAp can provide these mineral components at the enamel interface. Under favorable conditions, released ions contribute to supersaturation with respect to enamel apatite and promote precipitation of new mineral.

Biomimetic crystal growth

The structural similarity between nHAp and biological apatite allows nHAp particles to act as templates for crystal growth. Newly deposited mineral may become integrated with existing enamel crystals, potentially increasing mineral density and mechanical resistance.

Surface protection

In addition to promoting mineral deposition, nHAp may produce a mineral-rich protective layer on the enamel surface. Such a layer may reduce exposure of the underlying enamel to acidic challenges and contribute to the inhibition of subsequent demineralization.

Evidence from Experimental Studies

A substantial body of laboratory research has demonstrated the remineralization potential of nHAp. Experimental models have reported increases in enamel surface microhardness, reductions in mineral loss, and morphological changes consistent with mineral deposition.

A scoping review examining nHAp-containing dentifrices concluded that available studies generally support a role for nHAp in the remineralization of initial carious

lesions and reduction of enamel demineralization. The review also emphasized that the evidence base includes a considerable number of in vitro and in situ investigations, which limits direct extrapolation to clinical practice

An important experimental observation concerns concentration. Research summarized in the literature suggests that a 10% nHAp suspension may provide substantial remineralization of early enamel lesions, whereas increasing the concentration beyond this level does not necessarily produce proportional improvements. One proposed explanation is that excessive deposition on the external enamel surface may reduce penetration of nanoparticles into deeper porous areas of the lesion.

These findings demonstrate that the therapeutic effect of nHAp is not determined solely by the presence of the material. Particle size, concentration, formulation, exposure time, and physicochemical characteristics may substantially influence its effectiveness.

Evidence from Systematic Reviews and Meta-Analyses

Higher-level evidence provides a more balanced interpretation of the effectiveness of nHAp.

A systematic review and meta-analysis investigating the efficacy of nHAp for caries prevention included in vivo and in situ studies and identified five in vivo and five in situ studies involving more than 600 teeth and over 1,000 specimens. The authors concluded that the available evidence supported the potential of nHAp to reduce caries development and promote remineralization; however, considerable heterogeneity prevented a quantitative meta-analysis of the in vivo studies.

More recent evidence specifically addressing white spot lesions is also encouraging. A systematic review and meta-analysis published in 2024 included 14 studies, of which three were in vivo, one was in situ, and ten were in vitro. The analysis reported that pure nHAp was associated with significantly greater enamel surface microhardness and mineral gain compared with fluoride alone in the included studies. Nevertheless, the authors emphasized that the relatively small number of clinical studies, methodological limitations, high risk of bias in some studies, and short follow-up periods prevent definitive conclusions regarding long-term clinical effectiveness.

These findings are important because they demonstrate a distinction between **experimental efficacy** and **clinical effectiveness**. While nHAp consistently demonstrates remineralizing potential under laboratory conditions, stronger clinical evidence is necessary before it can be considered an established substitute for fluoride in all clinical circumstances.

Fluoride remains one of the most extensively studied and widely accepted agents for caries prevention. Its principal anticaries effects include enhancement of remineralization and formation of more acid-resistant fluoridated apatite phases.

nHAp differs mechanistically from fluoride because it can directly supply calcium-phosphate mineral and produce a biomimetic apatite layer. Consequently, the two approaches may be complementary rather than mutually exclusive.

A 2024 systematic review specifically evaluated products combining nHAp and fluoride for the treatment of initial enamel lesions. Five studies were included: four clinical studies and one in situ study, involving 151 white spot lesions. The studies varied substantially in treatment duration, protocols, and control groups, preventing quantitative meta-analysis. Nevertheless, most studies reported potentially favorable results for the combination of nHAp and fluoride, while the overall level of evidence was considered moderate. The authors concluded that the clinical evidence was promising but insufficient to recommend widespread use based solely on the current evidence. An updated systematic review and meta-analysis of hydroxyapatite-containing oral-care products also reported clinical evidence supporting hydroxyapatite as an effective caries-preventive agent. This emerging evidence strengthens the rationale for considering hydroxyapatite-based formulations within modern preventive dentistry. **Clinical Implications**

The potential clinical applications of nHAp are particularly relevant to patients with early enamel lesions, high caries risk, orthodontic white spot lesions, and conditions characterized by repeated episodes of enamel demineralization.

The main advantages of nHAp include its biomimetic nature, biocompatibility, capacity for mineral deposition, and ability to increase enamel surface hardness. Its incorporation into toothpastes, gels, mouthrinses, and other oral-care formulations provides opportunities for non-invasive management of early lesions.

However, clinicians should distinguish between the ability of nHAp to improve laboratory measures of remineralization and its capacity to produce clinically meaningful prevention of cavitation. Early intervention, adequate oral hygiene, dietary control, plaque management, and appropriate fluoride exposure remain fundamental components of caries prevention.

Limitations of the Current Evidence

Despite promising results, several limitations affect the interpretation of current research.

First, a substantial proportion of published studies are in vitro or in situ. Such experimental models cannot completely reproduce the complex oral environment,

including saliva, biofilm, dietary acids, mechanical abrasion, and individual patient behavior.

Second, substantial methodological heterogeneity exists among studies. Differences have been reported in particle size, nHAp concentration, formulation, application frequency, exposure time, enamel substrate, artificial lesion model, and outcome assessment methods.

Third, clinical trials are relatively limited compared with laboratory studies. The 2024 systematic review of WSLs, for example, identified only three in vivo studies among 14 eligible investigations.

Finally, long-term clinical outcomes remain insufficiently characterized. More studies are required to determine whether improvements in surface microhardness and mineral content translate into reduced incidence of cavitation and clinically measurable long-term caries prevention.

Future Research Directions

Future investigations should prioritize well-designed randomized controlled clinical trials with sufficiently large sample sizes and standardized outcome measures. Research should also establish optimal nHAp particle size, concentration, delivery system, and frequency of application.

Longitudinal studies comparing nHAp directly with conventional fluoride products would be particularly valuable. In addition, studies evaluating combinations of nHAp with fluoride, calcium-phosphate technologies, or other biomimetic agents may help identify synergistic approaches to enamel remineralization.

Advanced imaging and analytical techniques, including scanning electron microscopy, energy-dispersive X-ray spectroscopy, micro-computed tomography, and quantitative microhardness testing, should be combined with clinically relevant endpoints to provide a more comprehensive assessment of remineralization.

Conclusion:

Nanohydroxyapatite represents a promising biomimetic approach to the prevention and management of early enamel demineralization. Its chemical and structural similarity to natural enamel apatite, high surface reactivity, and ability to provide calcium and phosphate make it a biologically plausible remineralizing agent.

Current experimental evidence indicates that nHAp can increase enamel surface microhardness, promote mineral deposition, reduce mineral loss, and facilitate remineralization of early carious and white spot lesions. Systematic reviews and meta-analyses provide encouraging evidence, including findings suggesting that pure nHAp may perform favorably compared with fluoride in certain experimental outcomes.

Nevertheless, the clinical evidence remains less conclusive than the laboratory evidence. The relatively small number of clinical trials, methodological heterogeneity, short follow-up periods, and risk of bias limit the certainty of current conclusions. Therefore, nHAp should be considered a promising adjunct or alternative remineralizing technology, while fluoride remains an established component of evidence-based caries prevention.

Overall, nanohydroxyapatite has considerable potential within minimally invasive and biomimetic dentistry. Further high-quality randomized controlled trials and long-term clinical investigations are necessary to establish standardized treatment protocols and determine its precise position in contemporary preventive dentistry.

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