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The effect of nanohydroxyapatite on the remineralization of demineralized tooth enamel

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Abstract: Dental enamel is the hardest tissue in the human body; however, it is susceptible to mineral loss caused by cariogenic acids, dietary factors, and oral environmental conditions. The remineralization of demineralized enamel is therefore an important approach in the prevention and early management of dental caries. Nanohydroxyapatite (nHAp), due to its chemical similarity to the mineral component of natural tooth enamel and its nanoscale particle size, has attracted considerable attention as a promising remineralizing agent. The present study aims to evaluate the effect of nanohydroxyapatite on the remineralization of demineralized tooth enamel. The study focuses on the potential of nanohydroxyapatite to restore mineral content, improve enamel surface characteristics, and enhance the structural integrity of demineralized enamel. The application of nanohydroxyapatite may facilitate the deposition of calcium and phosphate ions onto the enamel surface, promoting the formation of a mineral layer similar to the natural enamel structure. The findings are expected to demonstrate the potential effectiveness of nanohydroxyapatite as a biomimetic agent for enamel remineralization and to support its possible application in preventive dentistry and caries management. Further research is required to determine the optimal concentration, application time, and clinical effectiveness of nanohydroxyapatite-based remineralizing materials.

Keywords: nanohydroxyapatite, tooth enamel, remineralization, demineralization, dental caries, biomimetic remineralization, preventive dentistry.

Main body:

1. Dental Enamel Demineralization and the Need for Remineralization

Dental caries remains one of the most prevalent oral diseases worldwide and represents a major public health concern. According to the World Health Organization (WHO), approximately 2.5 billion people worldwide are affected by untreated dental caries in permanent teeth. In addition, untreated caries in primary teeth affects approximately 514 million children globally. Overall, oral diseases affect nearly 45% of the world's population, corresponding to approximately 3.5 billion people. These figures demonstrate the substantial global burden of dental diseases and emphasize the importance of effective preventive and remineralization strategies.

Dental enamel is the hardest and most highly mineralized tissue in the human body. It is composed predominantly of hydroxyapatite crystals and is continuously exposed to fluctuations in the oral environment. When the pH of dental plaque decreases as a result of bacterial metabolism of

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fermentable carbohydrates, calcium and phosphate ions are released from the enamel surface. This process, known as demineralization, can lead to the development of subsurface enamel lesions and clinically visible white spot lesions. If the balance between mineral loss and mineral gain remains unfavorable, the lesion may progress to irreversible cavitation.

Remineralization is the natural process by which calcium and phosphate ions are redeposited into partially demineralized enamel. Enhancing this process during the early stages of caries development is therefore an important objective of preventive dentistry. Nanohydroxyapatite (nHAp) has received increasing attention because its chemical composition is similar to that of the mineral phase of natural enamel.

2. Mechanism of Action of Nanohydroxyapatite

Nanohydroxyapatite is composed primarily of calcium and phosphate ions and has a particle size within the nanometer range. Its nanoscale dimensions provide a relatively large surface area and allow the particles to interact closely with irregularities and microporosities present on the demineralized enamel surface.

Experimental studies indicate that nHAp can contribute to remineralization through both particle-mediated and ion-mediated mechanisms. Nanoparticles can directly deposit onto the enamel surface and form a mineral-like protective layer, while calcium and phosphate ions released from the particles may contribute to the reconstruction of the mineral phase of enamel.

An in vitro study investigating different concentrations of nano-hydroxyapatite (1%, 5%, 10%, and 15%) under pH-cycling conditions demonstrated that all nHAp groups showed significantly greater surface microhardness recovery than the negative control. Furthermore, at concentrations below 10%, increasing the concentration of nHAp was associated with an increase in surface microhardness and percentage surface microhardness recovery. The study identified 10% nHAp as a potentially optimal concentration for the remineralization of early enamel lesions. Scanning electron microscopy also demonstrated that nHAp particles were deposited on the demineralized enamel surface and appeared to form a new mineral layer.

3. Evidence from Experimental Studies

The effectiveness of nHAp has been investigated using several laboratory indicators, including surface microhardness, calcium-to-phosphorus ratio, scanning electron microscopy, atomic force microscopy, and lesion-depth measurements.

In one study involving 30 human premolars, specimens were divided into a nano-hydroxyapatite group (n=15) and a sodium fluoride group (n=15). The enamel specimens were artificially demineralized and subsequently treated with a 10% aqueous suspension of 20-nm nano-hydroxyapatite or 2% sodium fluoride. The nHAp group demonstrated a significant increase in mineral content, as assessed by the Ca/P ratio, and surface microhardness recovery was significantly closer to the baseline level compared with the control condition. The investigators also reported that the surface morphology following nHAp treatment became similar to that of biological enamel.

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Another in vitro investigation compared nano-hydroxyapatite with micro-hydroxyapatite in demineralized enamel. The results demonstrated that nano-hydroxyapatite produced greater remineralization than micro-hydroxyapatite according to surface and cross-sectional microhardness measurements. However, mineral deposition was predominantly observed in the outer part of the lesion, indicating that the ability of nHAp to reduce lesion depth may be limited. The remineralization effect was also reported to increase under acidic conditions, suggesting that nHAp may have particular relevance during episodes of enamel demineralization.

Further evidence comes from a study comparing 10% nano-hydroxyapatite, 10% casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), sodium fluoride, and deionized water. The percentage of surface microhardness recovery in the nHAp and fluoride groups was significantly greater than that observed in the CPP-ACP and negative-control groups. Scanning electron microscopy demonstrated deposition of nHAp particles on the demineralized enamel surface, resulting in the formation of a new surface layer. No statistically significant difference in surface microhardness recovery was observed between the nHAp and fluoride groups during the experimental period.

4. Quantitative Evidence of Remineralization

More recent research provides additional quantitative evidence regarding the effectiveness of nano-hydroxyapatite. A 2024 in vitro study evaluated 96 extracted human premolars and compared biomimetic nano-hydroxyapatite with fluoride-amorphous calcium phosphate. The mean Vickers microhardness value was 256.99 ± 45.83 VHN in the demineralized group, compared with 408.11 ± 70.16 VHN in the biomimetic nHAp group and 428.61 ± 54.43 VHN in the fluoride-amorphous calcium phosphate group. The difference between the demineralized enamel and the treated groups was statistically significant.

The same study demonstrated substantial differences in lesion depth. The mean lesion depth was approximately 198.83 μm in the untreated demineralized group, whereas it decreased to 60.17 μm following treatment with biomimetic nano-hydroxyapatite. For comparison, the fluoride-amorphous calcium phosphate group demonstrated a mean lesion depth of approximately 26.33 μm. These findings indicate that nHAp treatment can substantially improve the physical characteristics of demineralized enamel, although fluoride-containing remineralization systems may demonstrate stronger effects under certain experimental conditions.

5. Evidence from Recent Systematic Reviews and Meta-analyses

The effectiveness of nHAp has also been assessed at the systematic-review level. A systematic review and meta-analysis published in 2024 evaluated studies investigating nano-hydroxyapatite in the management of white spot lesions. From 422 identified studies, 14 met the inclusion criteria, including 3 in vivo studies, 1 in situ study, and 10 in vitro studies. Twelve studies were sufficiently comparable to be included in the meta-analysis.

The meta-analysis demonstrated that pure nano-hydroxyapatite was associated with a statistically significant improvement in enamel surface microhardness compared with fluoride alone, with a mean

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difference of 9.29 (95% CI: 7.74–10.84; $p < 0.00001$). A significant effect on mineral gain was also reported. However, the authors emphasized that the available clinical evidence remains limited because of the relatively small number of clinical studies, methodological heterogeneity, risk of bias, and short follow-up periods.

A separate systematic review and meta-analysis examining remineralizing agents for initial enamel lesions included 19 studies from 292 identified articles. For nHAp, the pooled estimate based on surface hardness outcomes was 1.40 (95% CI: 0.65–2.15), indicating significant remineralization potential. Nevertheless, the authors noted substantial heterogeneity and methodological limitations and recommended additional well-designed clinical trials before definitive conclusions regarding clinical superiority can be established.

6. Recent Findings and Clinical Perspectives

Recent evidence continues to support the potential of nHAp-based products as remineralizing agents. A 2025 in vitro study evaluated several hydroxyapatite-containing toothpastes using a 14-day pH-cycling model. All tested products produced a statistically significant increase in surface microhardness ($p < 0.001$). One formulation containing 10% nano-HAp demonstrated a mean percentage remineralization of approximately 21.68 ± 6.72%, while another formulation containing a combination of nanoXIM and nano-HAp achieved approximately 39.81 ± 24.07% remineralization. These findings suggest that formulation characteristics and the combination of different calcium-phosphate technologies may influence remineralization performance.

A 2026 in vitro study further investigated formulations containing 2.5% and 5% nano-hydroxyapatite combined with potassium nitrate. Both concentrations improved enamel surface hardness and partially restored mineral levels following demineralization. However, no statistically significant difference was found between the 2.5% and 5% nHAp formulations, suggesting that increasing the concentration above 2.5% does not necessarily result in an additional remineralization benefit under the experimental conditions used.

7. Overall Interpretation

The available evidence indicates that nanohydroxyapatite has considerable potential for promoting the remineralization of demineralized tooth enamel. Its effectiveness is supported by improvements in surface microhardness, mineral deposition, Ca/P ratios, enamel surface morphology, and lesion characteristics. Experimental evidence suggests that nHAp can form a protective mineral-like layer on the enamel surface and contribute to the restoration of mineral content.

However, the current evidence should be interpreted with caution. A substantial proportion of published studies are in vitro, while relatively fewer investigations have evaluated long-term clinical outcomes. Therefore, although nHAp represents a promising biomimetic approach and a potential alternative or adjunct to conventional fluoride-based products, further randomized controlled clinical trials with larger sample sizes and longer follow-up periods are necessary to establish its long-term effectiveness and optimal clinical application.

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Conclusion:

Nanohydroxyapatite demonstrates considerable potential as an effective biomimetic agent for the remineralization of demineralized tooth enamel. The findings of experimental studies indicate that nHAp can improve enamel surface microhardness, promote mineral deposition, restore the calcium-to-phosphorus balance, and contribute to the formation of a protective mineral-like layer on the enamel surface.

Available evidence suggests that the remineralizing effect of nHAp is influenced by particle size, concentration, treatment duration, and the composition of the formulation. Several in vitro studies have demonstrated that nano-hydroxyapatite can produce remineralization effects comparable to conventional fluoride-based agents under specific experimental conditions. In particular, concentrations around 10% have demonstrated promising results in the treatment of early enamel lesions.

Systematic reviews and meta-analyses also support the positive effect of nHAp on enamel surface hardness and mineral recovery. However, the current evidence base is predominantly composed of in vitro studies, while high-quality clinical trials with large sample sizes and long-term follow-up remain limited.

Therefore, nanohydroxyapatite may be considered a promising material for preventive dentistry and the non-invasive management of early enamel demineralization. Further randomized controlled clinical studies are required to establish its optimal concentration, application protocol, long-term clinical effectiveness, and potential advantages compared with established fluoride-based remineralization therapies.

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