Nano Hydroxyapatite in Oral Care: A Scientific and Clinical Overview

An Educational Resource for Dental Professionals

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Nano hydroxyapatite (nHA) has become a widely discussed ingredient in modern oral care, and as its use has grown, so have questions about how it works, how safe it is, and how it compares with other approaches. This overview is intended to give clinicians and informed consumers a clearer scientific framework for evaluating those questions.

A number of claims circulating about nano hydroxyapatite are technically accurate in isolation but are presented without the broader context of how the oral environment actually functions. Without that framework, even accurate statements can lead to conclusions that misrepresent the underlying biology and chemistry. The goal here is to fill in that context.

Starting With the Biology

A helpful place to start is with the structure of enamel itself. The basic building block of enamel is 20–40 nm rod-shaped nanocrystals of hydroxyapatite. The body maintains teeth by keeping them bathed in a supersaturated solution of this mineral. Under physiological conditions, saliva and oral fluids are supersaturated with respect to both hydroxyapatite and fluorapatite. If the oral fluids were unsaturated with respect to apatite, the dental hard tissues would dissolve without any other cause.[1]

These minerals are present in several forms: Ca^{2+} + HPO_4^{2-} ion pairs that are sub-nanometer in size; prenucleation clusters (~0.5–2 nm), which are dynamic and reversible and widely described in non-classical crystallization literature; and amorphous calcium phosphate (ACP)-like nanophases (~1–5 nm, sometimes up to ~10 nm transiently). These forms are kept stable by salivary proteins such as statherin.[2]

These sub-nanometer to small nanosized clusters are responsible for maintaining tooth mineralization. They penetrate the biofilm and act as a reservoir for calcium and phosphate ions, supporting remineralization as pH changes. Oral soft tissues are constantly exposed to these minerals in a range of sizes and structures without evidence of tissue toxicity. This is how the system is designed.

When quality nano hydroxyapatite is introduced through oral care products and formulated correctly, it can bypass mesocrystal growth inhibition, resulting in some particle deposition on enamel and within surface defects, ion reservoir behavior following partial dissolution, and subsequent reprecipitation and growth onto existing enamel mineral. A substantial and growing body of research supports nano hydroxyapatite's effectiveness in this role.[3]

The remainder of this document addresses common claims and concerns raised about nano hydroxyapatite and provides the scientific context for evaluating each.

Technical Review and Response to Common Claims

1. Composition and Structure

a) **Synthetic crystals.** A common framing is that nano hydroxyapatite is a "synthetic" material distinct from the real mineral. This is misleading. Synthesized nano hydroxyapatite is lab-created, but it is nano hydroxyapatite, the real mineral, not some synthetic substitute. Much like nano particles of elemental silver are typically synthesized but are still silver. Hydroxyapatite is the primary mineral in hard tissues and is relatively insoluble. It is soluble with a critical pH of about 5.5.

b) **Nanoscale dimensions.** The gold standard for nano hydroxyapatite is 20–40 nanometers and rod-shaped. Studies indicate that the size[4] is important for remineralization efficiency, and shape[5] for tissue safety.[6] This is the basic building block crystalline structure of enamel and is therefore most biomimetic, which accounts for the non-classical theory of remineralization by oriented attachment of meso-crystals, although the primary remineralization interaction of nano hydroxyapatite is by ionic epitaxial crystal growth on demineralized enamel.[7] Saliva is supersaturated with both hydroxyapatite and fluorapatite. It is how the body maintains the mineralization of teeth.

c) **Chemical stability.** A calcium-to-phosphate ratio of 1.67 is ideal stoichiometric chemistry. Enamel is often contaminated with carbonate, and the ratio is closer to 1.6. Even carbonated hydroxyapatite is relatively insoluble — otherwise enamel would not exist as a durable mineral.[8]

d) **Stabilizing agents.** Typically, potassium chloride salt is utilized to keep the nano particles of hydroxyapatite stable, much like nano particles of elemental silver use a stabilizing agent. Once in the mouth, salivary proteins like statherin adsorb to the surface of the nano crystals and aid in stability and inhibiting agglomeration and aggregation.[9]

2. Intended Use Versus Actual Function

e) **Marketed as remineralization.** There is no clear FDA marketing clearance for nano hydroxyapatite in dentistry oral care products, so most use is based on cosmetic claims: remineralizes enamel, strengthens teeth, reduces sensitivity, whitens. Multiple studies demonstrate its effectiveness at remineralization, strengthening enamel, reducing sensitivity, and providing whitening.[4, 10–24] It cannot be marketed as an anticavity material; only fluoride has that FDA clearance. A product containing both fluoride and nano hydroxyapatite can be marketed as an anticavity product. The evidence for the effectiveness of fluoride-free, hydroxyapatite-containing oral care products in reducing dental caries, both from RCTs and in situ clinical trials, has expanded. More studies now show that hydroxyapatite is effective as an anti-caries active ingredient in the absence of fluoride.[10] However, it is not FDA market cleared for those claims.

f) **Function as an occluding agent.** Nano hydroxyapatite does actively participate in remineralization, both by providing ions for epitaxial growth and by supplying mesocrystals for oriented attachment of new crystal growth. It occludes dentinal tubules and creates new permanent layers of mineral, and is superior to fluoride for reducing dentin hypersensitivity and may be superior to other desensitizing agents.[20]

g) **"Sand in a pothole."** The characterization of nano hydroxyapatite as merely sitting in surface defects like sand in a pothole is not substantiated by any study. Nano hydroxyapatite participates in remineralization by providing ions for epitaxial growth and mesocrystals for oriented attachment of new crystal growth. It occludes dentinal tubules and creates new permanent layers of mineral, and is superior to fluoride for reducing dentin hypersensitivity and may be superior to other desensitizing agents.[20]

3. Technical Challenges and Criticisms

h) **Agglomeration (clumping).** A common concern is that when dental formulations are exposed to saliva, the salt stabilizers become weakened and nanoparticles clump together. This is not substantiated by any study. A stable dental formulation may exhibit some agglomeration in the mouth during use, but agglomeration is held together by weak forces. nHA formulations in the mouth are not likely to remain as a fully monodisperse nano suspension; they probably become a mixed population of small particles, clusters, and enamel/pellicle-bound deposits, all of which contribute positively to remineralization. The nano hydroxyapatite bypasses the inhibition of meso-crystal formation, and salivary proteins adsorb onto and coat the nano hydroxyapatite, preventing agglomeration and aggregation in the same way they inhibit the smaller prenucleation clusters found in saliva. [2,26,27]

i) **Biofilm barrier.** It is sometimes argued that biofilm acts purely as a barrier to nano hydroxyapatite. In reality, biofilm acts as both a barrier and a scaffold. It contains irregular channels and is a negatively charged material, which attracts positively charged calcium. Nanoparticles do penetrate the biofilm to some degree, and they also get trapped in the biofilm and become a reservoir for calcium and phosphate ions during an acid challenge. Ions are easily transported through the biofilm channels, so the biofilm transports ions to the enamel surface and traps nanoparticles that are too large to be transported, serving as a future reservoir. For remineralization to occur, the pH must be above the critical pH of 5.5, so modulating pH is a significant strategy.

j) **Lack of permanent binding.** The claim that nano hydroxyapatite never permanently binds to enamel is categorically false and not supported by any study. The mechanism is well established: both epitaxial growth of enamel and mesocrystal growth occur, creating new permanent enamel. The use of "synthetic crystals" as a dismissive label is misleading, as these synthesized crystals are real hydroxyapatite mineral. The literature is replete with studies indicating the efficacy of nano hydroxyapatite in remineralization of enamel.[4, 10–18]

k) **Mineral reservoir issues.** A related claim is that nano hydroxyapatite "survives" while enamel dissolves first, and therefore cannot serve as a mineral reservoir. This ignores dissolution kinetics. Kinetics matter more than thermochemistry. Nano particles have a very high surface area compared to the enamel surface, so while enamel can and often does dissolve faster because of thermochemistry, nano hydroxyapatite can have faster dissolution kinetics based on surface area, and these particles dissolve quickly despite being slightly less soluble due to their slightly higher calcium-to-phosphate ratio. Thermodynamics (calcium-phosphate ratio) sets the direction and ultimate equilibrium, but kinetics (surface reactivity, structure, transport, protein/biofilm interactions, and surface area) overwhelmingly determine which phase dissolves first and how fast in the oral environment.[28] If the enamel does dissolve faster, the nano hydroxyapatite then provides a stable source of ions, acting as a mineral reservoir.

l) **An internal contradiction on stability and sensitivity.** The argument that nano hydroxyapatite is too chemically stable to dissolve, and therefore cannot function as a mineral reservoir, is directly undermined by another commonly accepted point: that nano hydroxyapatite is effective for dentin hypersensitivity. Sensitivity relief cannot occur without mineral deposition into dentinal tubules, which requires precisely the kind of dissolution and reprecipitation dynamics that the "too stable to function" argument dismisses. These two positions cannot coexist. If nano hydroxyapatite were inert and unable to release ions, it could not occlude tubules. Acknowledging sensitivity efficacy is, in effect, acknowledging that the mineral reservoir argument fails.

4. Safety and Comparison to Natural Enamel

m) **Toxicity concerns.** General concerns are sometimes raised about the safety of nano hydroxyapatite, often without identification of specific peer-reviewed sources. The most rigorously studied material in this category, the Fluidinova nanoXIM® hydroxyapatite, has gone through extensive toxicity testing and was reviewed and approved by the European Union’s Scientific Committee on Consumer Safety (SCCS). An excerpt from that review is included below for reference.

As the nanoXIM® ingredient is only intended to be used in oral cosmetic products (toothpastes, mouthwashes, etc.), only exposure via the oral route had to be considered. After entering the mouth, part of the cosmetic formulation will contact the buccal mucosa and part may be ingested. Therefore *systemic exposure to HAP-nano may occur either via uptake by mucosal cells or by crossing the intestinal tract. Both routes were assessed.*

Penetration into buccal mucosal cells (from SCCS/1624/20): As a preliminary step to investigate whether HAP-nano can enter systemic tissues through the oral epithelium, it was histologically studied to what extent HAP-nano could penetrate the stratified layers in two types of three-dimensional (3-D) reconstituted human oral epithelial models, one with and one without a stratum corneum. The results showed that the nanoparticles did not penetrate the stratum corneum in SkinEthic HGE samples and penetrated only the outermost layer of cells in SkinEthic HOE samples without stratum corneum, with no permeation into the deeper layers of the epithelium in either tissue model.

Absorption by the gastric compartment (from SCCS/1624/20): The stability of nanoXIM.CarePaste HAP-nano was assessed in simulated gastric fluid (SGF) by measuring calcium content at 7.5, 15, and 30 minutes. The results confirmed that the material would solubilize in the gastric fluid if ingested, indicating no nano-related concerns over its safety following ingestion. As systemic exposure to HAP-nano following cosmetic use in oral care products was not significant, only local toxicity and genotoxicity needed to be assessed.

Local toxicity (from SCCS/1624/20): To assess the biocompatibility/oral irritation of HAP-nano on human oral epithelium, an in vitro model of reconstructed human oral epithelium was used (SkinEthic Reconstructed Human Oral Epithelium). A non-keratinizing model was used as a worst-case scenario; no toxicity was revealed, so toxic effects in a keratinized model — which has additional protective stratum corneum layers — would not be expected. Data also showed that 3.1% HAP-nano after a 48-hour incubation period was not cytotoxic to mucosal cells. Cellular internalization of HAP-nano by CHO-K1 and L5178Y TK+/− mouse lymphoma cells was tested in all experimental conditions used for the mammalian gene mutation test and the micronucleus assay. Uptake by CHO-K1 cells was demonstrated at all tested concentrations; uptake by L5178Y TK+/− cells was marginal and observed only at the highest concentration after 24 hours.

Mutagenicity / genotoxicity: Genotoxicity of HAP-nano was investigated across three endpoints: gene mutations (mammalian gene mutation test), structural chromosome aberrations, and aneuploidy (micronucleus assay). Studies were performed alongside characterization in culture media and cellular uptake assessment, with stability of the nanomaterial dispersion confirmed before and after experiments. The methodologies followed OECD test guidelines, the SCCS Guidance on the safety assessment of nanomaterials in cosmetics (SCCS/1611/19), and the current state of knowledge.

Results showed that HAP-nano did not induce gene mutation in the mammalian gene mutation test using the thymidine kinase gene in the L5178Y/TK+/− cell line, and did not induce structural or numerical chromosomal damage in CHO-K1 cells when tested up to precipitation concentrations. Based on these valid in vitro results, the SCCS concluded that HAP-nano does not pose a genotoxicity hazard.

Conclusion: Based on the data provided, the SCCS considers hydroxyapatite (nano) safe when used at concentrations up to 10% in toothpaste and up to 0.465% in mouthwash. This safety evaluation applies to hydroxyapatite (nano) with the following characteristics: composed of rod-shaped particles, of which at least 95.8% (in particle number) have an aspect ratio of less than 3, and the remaining 4.2% have an aspect ratio not exceeding 4.9; and the particles are not coated or surface modified.[29]

Beyond the SCCS evaluation, an additional study indicates that nanoparticles of hydroxyapatite in oral health products do not pose a risk to oral soft tissues.[6] Another examined particle shape and tissue penetration, identifying round spherical particles as the greatest concern, followed by needle-shaped particles, and lastly rod-shaped particles.[5] Rod shape is the form used in nanoXIM.

n) **Mismatch with human enamel.** Claims that synthetic nano hydroxyapatite is too chemically mismatched with human enamel to support remineralization are inaccurate and not substantiated by published studies. Most human enamel has a calcium-to-phosphate ratio of 1.60 to 1.67 as determined by EDS.[30] A modest mismatch does not inherently inhibit remineralization. A more biomimetic substituted apatite can sometimes be a closer chemical match to enamel and may influence dissolution rate, adhesion, and crystal perfection, but plain stoichiometric nano hydroxyapatite can still remineralize enamel effectively, which is why multiple reviews conclude it has meaningful remineralizing potential.[3]

Closing Note

Differing viewpoints exist within dentistry on nearly every active ingredient, and that conversation is healthy. Our intent in publishing this overview is not to dismiss alternative perspectives, but to ensure that discussions about nano hydroxyapatite include the full scientific context — the biology of enamel, the chemistry of saliva, the kinetics of dissolution and reprecipitation, and the safety record of the materials in clinical use. With that context in place, clinicians and consumers are better equipped to evaluate the available evidence and make informed decisions for their patients and themselves.

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