

Response to Nano Hydroxyapatite Claims

Written by Dr. Kim Kutsch

We appreciate the conversation around nano-hydroxyapatite and the opportunity to clarify some important context for those trying to make informed decisions about oral health.

In this case, the video features and promotes the perspectives of Dr. Ryan Nolan, who is also the founder of Elementa, a company that markets elemental silver oral care products. Elementa products are further promoted and recommended within the comments and follow-up discussion. Because this is a directly competing approach to nano-hydroxyapatite, this represents a clear conflict of interest and is an important context to consider when evaluating the claims being made.

This conflict is compounded by an apparent inconsistency in how nanoparticles are characterized. The discussion raises safety concerns about nano-hydroxyapatite and nanoparticles broadly, despite nano-hydroxyapatite having received formal safety approval from the European Union's Scientific Committee on Consumer Safety, while simultaneously promoting a brand built on silver nanoparticles. Silver nanoparticles, by contrast, have not been approved by the EU due to safety concerns and insufficient data.³¹ Questioning the safety of an EU-approved material while advocating for one the EU has restricted reflects a selectivity that is worth noting when weighing the objectivity of these claims.

While several of the individual scientific statements presented are technically accurate, key pieces of context are missing. Without that broader framework, the information can lead to conclusions that don't fully reflect how the oral environment actually functions.

A helpful place to start is with the biology 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 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 the form of $\text{Ca}^{2+} + \text{HPO}_4^{2-}$ 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

Our goal in sharing this is not to dismiss differing viewpoints, but to ensure that the discussion includes the full scientific context so clinicians and consumers can evaluate the information more completely.

Technical Review and Response to Claims:

1. *Composition and Structure*

- a) *Synthetic crystals*. This is a misleading claim. Synthesized nano-hydroxyapatite is lab-created, but it is nano-hydroxyapatite, the real mineral, not some synthetic material. 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 size⁴ is important for remineralization efficiency, and shape⁵ 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. Obviously, even carbonated hydroxyapatite is relatively insoluble, or you wouldn't have enamel.⁸
- d) *Stabilizing agents*: Yes, 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 also aid in stability and inhibiting agglomeration and aggregation.⁹

2. *Intended Use versus Actual Function*

- a) *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.
- b) *Function as an Occluding Agent*: nano-hydroxyapatite does actually participate in remineralization, both by providing ions for epitaxial growth and also 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
- c) *Sand in a pothole*: This is not substantiated by any study. In fact, nano-hydroxyapatite does actually participate in remineralization, both by providing ions for epitaxial growth and also 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*

- a) *Agglomeration (clumping)*: *When dental formulations are exposed to saliva, the salt stabilizers become weakened, and nanoparticles clump together.* 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. And the nano-hydroxyapatite bypasses the inhibition of meso crystal formation and salivary protein adsorbs onto and coats the nano

hydroxyapatite and prevents agglomeration and aggregation just the way they inhibit smaller prenucleation clusters found in saliva.^{2,26,27}

- b) *Biofilm Barrier*: Actually, the biofilm acts as both a barrier and a scaffold. It contains irregular channels, but is a negatively charged material which attracts positively charged calcium, so nanoparticles do penetrate the biofilm to some degree, but also get trapped in the biofilm and become a reservoir for calcium and phosphate ions, as there is 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 the pH is a significant strategy.
- c) *Lack of Permanent Binding*: This is categorically false and not supported by any study. Instead, the mechanism is clear: both epitaxial growth of enamel and mesocrystal growth occur, creating new permanent enamel. Again, the use of “synthetic crystals” is intentionally misleading, as these “synthesized crystals” are actually real hydroxyapatite mineral. The literature is replete with studies indicating the efficacy of nano hydroxyapatite in remineralization of enamel.^{4, 10-18}
- d) *Mineral Reservoir Issues*: Again, this is misleading and ignores dissolution kinetics. It’s not as simple as nano hydroxyapatite survives while enamel dissolves first. 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 the thermochemistry, nano-hydroxyapatite can have faster dissolution kinetics based on surface area, and they dissolve quickly despite being less soluble because of 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 And if the enamel dissolves faster, the nano hydroxyapatite provides a stable source of ions acting as a mineral reservoir.
- e) *An Internal Contradiction on Stability and Sensitivity*: The claim that nano-hydroxyapatite is too chemically stable to dissolve and therefore cannot function as a mineral reservoir is directly undermined by a concession made elsewhere in the same discussion: 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 being dismissed. These two positions cannot coexist: if nano-hydroxyapatite is inert and unable to release ions, it cannot occlude tubules. The acknowledgment of

sensitivity efficacy is, in effect, an acknowledgment that the mineral reservoir argument fails.

4. *Safety and Comparison to Natural Enamel*

- a) *Toxicity Concerns*: What are the “sources”? Not supported by studies. The Fluidinova nanoXIM® material has gone through extensive toxicity testing and won approval from the Scientific Committee on Consumer Safety of the EU. Excerpt here:

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

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 NPs 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, and no permeation into the deeper layers of the epithelium in either tissue model was observed.

Absorption by the gastric compartment (from SCCS/1624/20): The stability of nanoXIM.CarePaste HAP-nano was assessed in a stability study in simulated gastric fluid (SGF) by determination of calcium content at different time points (7.5, 15 and 30 mins). The results have confirmed that the material would solubilise in the gastric fluid if ingested. Therefore, there should not be any issue of nano-related concerns over its safety following ingestion. As it was concluded that systemic exposure to HAP-nano following cosmetic use in oral care products was not significant, only local toxicity and genotoxicity have to be assessed.

34 SCCS/1648/22 Final Opinion on Hydroxyapatite (nano)

Toxicological Evaluation:

Local toxicity (from SCCS/1624/20): To determine the biocompatibility / oral irritation test on human oral epithelium of HAP-nano, an in vitro model of

reconstructed human oral epithelium was used after exposure to nanoXIM nanoparticles (SkinEthic reconstructed Human Oral Epithelium). Most probably, it was a non-keratinizing model that was taken as the worst case scenario, as no toxicity was revealed using this model, one should not assume any toxic effects in a keratinized model, which has an additional protective layers of stratum corneum. Also, the data showed that 3.1% HAP-nano after an incubation period of 48 hr was not cytotoxic to the mucosal cells. Cellular internalization uptake 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. The uptake by CHO-K1 cells was demonstrated at all tested concentrations. However, the uptake of HAP-nano by L5178Y TK+/- mouse lymphoma cells was marginal and only observed at one concentration, the highest one tested, after 24 h treatment.

Mutagenicity/genotoxicity: The genotoxicity of HAP-nano was investigated in three endpoints: gene mutations (by the mammalian gene mutation test), structural chromosome aberrations, and aneuploidy (by the micronucleus assay). The genotoxicity studies were performed along with characterization in culture media and uptake of HAP-nano by cells. Stability of the dispersion of the test nanomaterial in cell culture medium prior to and after the experiment was provided. The Notifier used appropriate methodologies according to OECD TGs, the SCCS Guidance on the safety assessment of nanomaterials in cosmetics (SCCS/1611/19), and the current state of knowledge.

The 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 study results on gene mutations and micronucleus tests, the SCCS is of the opinion that HAP-nano does not pose a genotoxicity hazard.

35 CCS/1648/22 Final Opinion on Hydroxyapatite (nano)

Conclusion: In view of the above, and taking into account the scientific data provided and reasonably foreseeable exposure conditions, does the SCCS consider hydroxyapatite (nano) safe when used in oral cosmetic products according to the maximum concentrations and specifications as reported in the submission? 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 only applies to the 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; - the particles are not coated or surface modified. This product went through extensive toxicity/safety studies. Yet another study indicates that nano particles of hydroxyapatite in oral health products do not pose a risk to oral soft tissues.⁶ Another study examined particle shape and penetration of renal tissue, with round spherical shaped particles being the biggest concern followed by needle shaped, and lastly by rod shaped.⁵ Rod shape is the material in nanoXIM.

- b) *Mismatch and Human Teeth:* Again, this information is inaccurate, and the conclusions are false and not substantiated by any study. Most human enamel has a calcium to phosphate ratio of 1.60 to 1.67 as determined by EDS.³⁰ The 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

References:

1. Fejerskov O, Kidd E. Dental Caries: The Disease and its Clinical Management. Blackwell Munksgaard 2003. pp: 56.
2. Schlesinger, D. H., Hay, D. I. Complete covalent structure of statherin, a tyrosine-rich acidic peptide which inhibits calcium phosphate precipitation from human parotid saliva. J. Biol. Chem. 252: 1689-1695, 1977
3. Chen L, Al-Bayatee S, Khurshid Z, Shavandi A, Brunton P, Ratnayake J. Hydroxyapatite in Oral Care Products-A Review. Materials (Basel). 2021 Aug 27;14(17):4865. doi: 10.3390/ma14174865. PMID: 34500955; PMCID: PMC8432723.
4. Imran E, Cooper PR, Ratnayake J, Ekambaram M, Mei ML. Potential Beneficial Effects of Hydroxyapatite Nanoparticles on Caries Lesions In Vitro-A Review of the Literature. Dent J (Basel). 2023 Feb 7;11(2):40.

5. Rao CY, Sun XY, Ouyang JM. Effects of physical properties of nano-sized hydroxyapatite crystals on cellular toxicity in renal epithelial cells. *Mater Sci Eng C Mater Biol Appl.* 2019 Oct;103:109807.
6. Komiyama S, Miyasaka R, Kikukawa K, Hayman R. Can nano-hydroxyapatite permeate the oral mucosa? A histological study using three-dimensional tissue models. *PLoS One.* 2019 Apr 23;14(4):e0215681
7. Liu Y, Mai S, Li N, Yiu CK, Mao J, Pashley DH, Tay FR. Differences between top-down and bottom-up approaches in mineralizing thick, partially demineralized collagen scaffolds. *Acta Biomater.* 2011 Apr;7(4):1742-51
8. Changyu Shao et al. ,Repair of tooth enamel by a biomimetic mineralization frontier ensuring epitaxial growth.*Sci. Adv.*5,eaaw9569(2019).
9. Schestakow A, Riegelmann M, Hannig M. Exploratory study of nanoparticle interaction with intraorally formed dental biofilms. *BMC Oral Health.* 2025 Aug 22;25(1):1355.
10. Haghgoo R, Rezvani MB, Salehi Zeinabadi M. Comparison of nano-hydroxyapatite and sodium fluoride mouthrinse for remineralization of incipient carious lesions. *J Dent (Tehran).* 2014 Jul;11(4):406-10
11. Roveri N, Battistella E, Bianchi CL, et al. Surface enamel remineralization: biomimetic apatite nanocrystals and fluoride ions different effects. *Journal of Nanomaterials* 2009, article ID 746383, 9 pages.
12. Kutsch VK, Kois JC, Chaiyabutr Y, Milicich GW. Reconsidering remineralization strategies to include nanoparticle hydroxyapatite. *Compendium* March 2013. 34(3):170-177.
13. Gore AB, Patel SP, Gulve MN, Aher GB. Comparative evaluation of the remineralizing potential of different calcium and fluoride-based delivery systems on artificially demineralized enamel surface; an in vitro study. *J Conserv Dent.* 2022 May-Jun;25(3):292-296
14. Pepla E, Besharat LK, Palaia G, Tenore G, Migliau G. Nano-hydroxyapatite and its applications in preventive, restorative and regenerative dentistry: a review of literature. *Ann Stomatol (Roma).* 2014 Nov 20;5(3):108-14.
15. Vyavhare S, Sharma DS, Kulkarni VK. Effect of three different pastes on remineralization of initial enamel lesion: an in vitro study. *J Clin Pediatr Dent.* 2015 Winter;39(2):149-60.
16. Manchery N, John J, Nagappan N, Subbiah GK, Premnath P. Remineralization potential of dentifrice containing nanohydroxyapatite on artificial carious lesions of enamel: A comparative in vitro study. *Dent Res J (Isfahan).* 2019 Sep 5;16(5):310-317.

17. Ghiorghe CA, Tărăboanță I, Andrian S, Pancu G, Munteanu C, Istrate B, Lupu FC, Maxim C, Barna AS. Enamel Remineralization Potential of Conventional and Biomimetic Toothpaste Formulations: A Comparative In Vitro Study. *Dent J (Basel)*. 2026 Feb 2;14(2):82.
18. Randorn C, Kaewdee P, Rujijanagul G, Tandorn S. A Qualitative In Vitro SEM Study on the Protective Effects of a Self-Antibacterial Nano-Hydroxyapatite Toothpaste Against Acid-Induced Enamel Surface Erosion. *Int J Mol Sci*. 2026 Mar 19;27(6):2796.
19. Oglakci Ozkoc B, Tunc Dicle A, Alkan E, Yılmaz Atalı P, Eliguzeloglu Dalkilic E, Tağtekin D. The effectiveness of novel remineralising agents in white spot lesion treatment after microabrasion. *BMC Oral Health*. 2026 Jan 8;26(1):244.
20. Limeback H, Enax J, Meyer F. Clinical Evidence of Biomimetic Hydroxyapatite in Oral Care Products for Reducing Dentin Hypersensitivity: An Updated Systematic Review and Meta-Analysis. *Biomimetics (Basel)*. 2023 Jan 6;8(1):23.
21. Limeback H, Meyer F, Enax J. Tooth Whitening with Hydroxyapatite: A Systematic Review. *Dent J (Basel)*. 2023 Feb 12;11(2):50.
22. El Mansy MM, Saleh RS, Rashed MF, El-Motayam AK. Effect of nanohydroxyapatite paste after different pretreatment techniques on remineralization and color change of white spot lesions in children: a randomized control study. *BMC Oral Health*. 2026 Jan 13;26(1):102.
23. Amaechi BT, Alshareif DO, Azees PAA, Shehata MA, Lima PP, Abdollahi A, Kalkhorani PS, Evans V, Bagheri A, Okoye LO. Anti-caries evaluation of a nano-hydroxyapatite dental lotion for use after toothbrushing: An in situ study. *J Dent*. 2021 Dec;115:103863
24. Thomas G, Badrock T, Thompson C. An In Vitro Study to Evaluate the Ability of a Toothpaste Formulation to Repair and Protect Demineralized Enamel Samples. Interteck CRS. December 2022. S/N150-LAB-SMH-22-002.
25. Pawinska M, Paszynska E, Amaechi BT, Meyer F, Enax J, Limeback H. Clinical evidence of caries prevention by hydroxyapatite: An updated systematic review and meta-analysis. *J Dent*. 2024 Dec;151:105429.
26. Goobes R, Goobes G, Campbell CT, Stayton PS. Thermodynamics of statherin adsorption onto hydroxyapatite. *Biochemistry*. 2006 May 2;45(17):5576-86. doi: 10.1021/bi052321z. Erratum in: *Biochemistry*. 2006 Aug 22;45(33):10161. PMID: 16634639.
27. Lehnfeld J, Dukashin Y, Mark J, et al. Saliva and Serum Protein Adsorption on Chemically Modified Silica Surfaces. *Journal of Dental Research*. 2021;100(10):1047-1054

28. Shellis RP; Featherstone JDB; Lussi A. Monographs in oral Science. Chapter 8: The Chemistry of Dental Erosion and Determination of Erosion Potential. 2025
29. SCCS/1648/22 Final Opinion Fluidinova nanoXIM®
30. Uskokovic V. Non-Metallic Biomaterials for Tooth Repair and Replacement, Textbook Chapter 2. 2013
31. SCCS (Scientific Committee on Consumer Safety), *Opinion on Colloidal Silver (nano)*, SCCS/1596/18, adopted October 2018.