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COMPARATIVE EFFECTIVENESS OF NANO-HYDROXYAPATITE AND FLUORIDE-BASED INTERVENTIONS FOR THE MANAGEMENT OF DENTIN HYPERSENSITIVITY: A SYSTEMATIC REVIEW

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Abstract

Background: *Dentin hypersensitivity is a common oral health condition characterized by short, sharp pain arising from exposed dentin in response to thermal, tactile, or evaporative stimuli. Fluoride-based products are widely used for its management, while nano-hydroxyapatite (n-HAP) has emerged as a biomimetic alternative with potential dentinal tubule-occluding and remineralizing properties.*

Objective: *To systematically evaluate the comparative effectiveness of nano-hydroxyapatite and fluoride-based interventions for the management of dentin hypersensitivity.*

Methods: *This systematic review was conducted according to PRISMA 2020 guidelines. PubMed/MEDLINE, Scopus, Embase, Cochrane Library, and Web of Science were searched, along with reference-list screening. Eligible studies evaluated hydroxyapatite-containing toothpaste or dentifrice against fluoride-based interventions and reported clinical outcomes related to dentin hypersensitivity or remineralization. Study characteristics and clinical outcomes were extracted, and risk of bias was assessed using the Cochrane RoB 2 tool.*

Results: *Four randomized clinical trials met the eligibility criteria. Across the included studies, both nano-hydroxyapatite and fluoride-based interventions demonstrated reductions in dentin hypersensitivity. Hydroxyapatite-containing formulations produced clinically meaningful improvements in sensitivity assessed through tactile and air-blast stimulation and patient-reported sensitivity measures. In comparative evaluations, hydroxyapatite demonstrated effects comparable to, and in some outcomes favorable to, fluoride-based interventions. However, differences in hydroxyapatite concentration, formulation, comparator products, assessment methods, and follow-up duration limited direct quantitative comparison. Overall, three studies were judged to have low risk of bias, while one had some concerns related primarily to missing outcome data.*

Conclusion: *Nano-hydroxyapatite appears to be a promising alternative to fluoride-based interventions for reducing dentin hypersensitivity. However, the limited number of studies and methodological heterogeneity highlight the need for larger, well-designed trials with standardized outcome measures and longer follow-up.*

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Introduction

Dentin hypersensitivity (DH) is a common dental condition characterized by short, sharp pain from exposed dentin in response to thermal, tactile, evaporative, osmotic, or chemical stimuli. It commonly occurs following gingival recession, periodontal disease, tooth wear, erosion, abrasion, or non-carious cervical lesions. The hydrodynamic theory explains DH through fluid movement within exposed dentinal tubules, making tubule occlusion an important therapeutic approach. [1,2]

Several desensitizing agents are available, including fluoride, potassium salts, arginine, calcium-based compounds, and hydroxyapatite. Fluoride-based products are widely used because they promote mineral deposition and can reduce dentinal permeability. Clinical studies have demonstrated that fluoride varnishes can effectively reduce DH, although their effectiveness may vary according to formulation and treatment protocol. [3–5]

Nano-hydroxyapatite (n-HAP) has gained attention as a biomimetic treatment because its composition resembles the mineral phase of natural teeth. Its nanoparticles can deposit on exposed dentin and contribute to dentinal tubule occlusion, potentially reducing sensitivity. Clinical studies have reported significant reductions in DH following the use of n-HAP-containing products, with some findings showing effects comparable to conventional desensitizing agents. [6,7]

Comparative studies have suggested that hydroxyapatite-based formulations may provide similar or greater reductions in DH compared with fluoride-based products. However, differences in formulations, concentrations, treatment duration, and methods used to assess sensitivity make direct comparisons difficult. [8–10]

Therefore, comparing nano-hydroxyapatite with fluoride-based interventions is clinically important for determining their relative effectiveness in managing DH. This systematic review aims to compare the effectiveness of nano-hydroxyapatite and fluoride-based interventions in reducing dentin hypersensitivity and to evaluate their comparative clinical outcomes.

Methodology

Study Design and Reporting Guidelines

The present systematic review was conducted to evaluate the clinical outcomes of hydroxyapatite-containing toothpaste compared with fluoride toothpaste, with particular emphasis on remineralization and dentin hypersensitivity. The review was structured and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A predefined eligibility framework based on the Population, Intervention, Comparator, Outcomes, and Study Design (PICOS) approach was used to determine the eligibility of potentially relevant studies.

Eligibility Criteria

Studies were selected according to predefined eligibility criteria based on the PICOS framework. The criteria were established before study selection to ensure consistency in the screening and inclusion process.

Inclusion Criteria

1) Population: Studies involving human participants with dentin hypersensitivity, enamel demineralization, or other clinically relevant conditions requiring remineralization were eligible for inclusion. Adult and adolescent populations were considered when the reported outcomes were relevant to the objectives of the present review.

2) Intervention: The intervention of interest was hydroxyapatite-containing toothpaste or dentifrice, including formulations containing nano-hydroxyapatite (n-Hap), microcrystalline hydroxyapatite, or other clinically applicable hydroxyapatite formulations.

3) Comparator: Studies comparing hydroxyapatite-containing toothpaste with fluoride toothpaste, fluoride dentifrice, fluoride gel, or other established fluoride-based dental products were considered eligible. Studies with an appropriate placebo or alternative desensitizing comparator were also considered when they provided relevant comparative clinical outcomes.

4) Outcomes: Studies were included when they reported at least one clinically relevant outcome related to dentin hypersensitivity or

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dental remineralization. Outcomes included changes in sensitivity or pain scores, responses to air-blast or tactile stimulation, clinical measures of hypersensitivity, mineral gain, enamel remineralization, lesion progression or regression, and other validated measures of hard-tissue remineralization.

5) Study Design: Eligible study designs included randomized controlled trials (RCTs), controlled clinical trials, prospective or retrospective observational studies, and cross-sectional studies, provided that they reported relevant clinical outcomes and met the remaining eligibility criteria.

Exclusion Criteria

Studies were excluded if they met any of the following criteria:

1)Animal, in-vitro, laboratory, or experimental studies without clinical human data. 2)Studies that did not evaluate hydroxyapatite-containing toothpaste or dentifrice as an intervention. 3) Studies without an appropriate fluoride-based comparator or relevant comparison group. 4) Studies that did not report outcomes related to dentin hypersensitivity, remineralization, enamel/dentin mineralization, or other predefined dental outcomes. 5) Case reports, case series, narrative reviews, systematic reviews, meta-analyses, editorials, letters, conference abstracts, protocols, and commentaries without sufficient original clinical data. 6) Duplicate publications or multiple reports describing the same study population, where the most complete report was retained. 7) Studies with insufficient information or outcome data required for assessment and extraction. 7) Studies for which the full text could not be obtained for eligibility assessment.

Literature Search Strategy

A comprehensive literature search was conducted in the electronic databases PubMed/MEDLINE, Scopus, Embase, the Cochrane Library, and Web of Science to identify studies evaluating the clinical outcomes of hydroxyapatite-containing toothpaste compared with fluoride toothpaste. The search covered the available literature from database inception to October 2025.

The search strategy incorporated controlled vocabulary and relevant free-text terms related to the intervention, comparator, and clinical outcomes. The principal search terms included "hydroxyapatite," "nano-hydroxyapatite," "microcrystalline hydroxyapatite," "hydroxyapatite toothpaste," "hydroxyapatite dentifrice," "fluoride toothpaste," "fluoride dentifrice," "dentin hypersensitivity," "dental sensitivity," "tooth sensitivity," "remineralization," "remineralisation," "enamel remineralization," and "dental hard tissue." Boolean operators (AND/OR) were used to combine the search terms appropriately.

Reference lists of the included studies and relevant review articles were also manually screened to identify additional potentially eligible studies. Records retrieved from all databases and other sources were compiled, and duplicate records were removed before the screening process.

Study Selection and Data Extraction

All records identified through the database searches were screened according to the predefined eligibility criteria. After removal of duplicate records, titles and abstracts were assessed for relevance. Potentially eligible studies were retrieved in full text and evaluated against the inclusion and exclusion criteria. Studies that did not meet the predefined eligibility requirements were excluded, with the reasons for exclusion documented. The study selection process is presented in the PRISMA 2020 flow diagram.

Data from the four included studies were extracted using a standardized data extraction format. The extracted information included first author and publication year, country, study design, sample size, participant population and clinical condition, hydroxyapatite intervention, fluoride comparator, duration of follow-up, outcome assessment methods, and reported clinical outcomes.

For dentin hypersensitivity outcomes, information regarding air-blast and tactile stimulation, pain or sensitivity scores, and validated clinical sensitivity scales was extracted where available. For remineralization-related outcomes, relevant measures of mineralization, enamel or dentin surface changes, and remineralization effects were recorded. Any relevant safety or adverse-event information

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reported by the included studies was also extracted.

Risk of Bias and Quality Assessment

The methodological quality and risk of bias of the included studies were assessed according to their study design. As the four included studies were randomized clinical trials, the Cochrane Risk of Bias 2 (RoB 2) tool was used for risk-of-bias assessment.

The RoB 2 assessment considered five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Each domain was assessed and categorized as low risk of bias, some concerns, or high risk of bias according to the RoB 2 framework.

The domain-level assessments were considered collectively when determining the overall risk of bias for each study. The risk-of-bias findings were subsequently incorporated into the interpretation of the systematic review results.

Data Synthesis

Because of the differences among the included studies in terms of participant characteristics, hydroxyapatite formulations and concentrations, fluoride comparators, treatment protocols, outcome assessment methods, and follow-up periods, the findings were synthesized narratively.

The results were organized according to the two principal outcomes of the review: dentin hypersensitivity and remineralization. For dentin hypersensitivity, changes in clinical sensitivity and pain responses following air-blast or tactile stimulation were compared between hydroxyapatite and fluoride-based interventions. For remineralization outcomes, reported changes in mineralization and dental hard-tissue characteristics were summarized.

Where studies used different measurement scales or assessment methods, the findings were described according to the individual study's reported measures rather than combining them quantitatively. The overall interpretation considered the direction and consistency of findings across the four included studies, together with their methodological quality and risk-of-bias assessments.

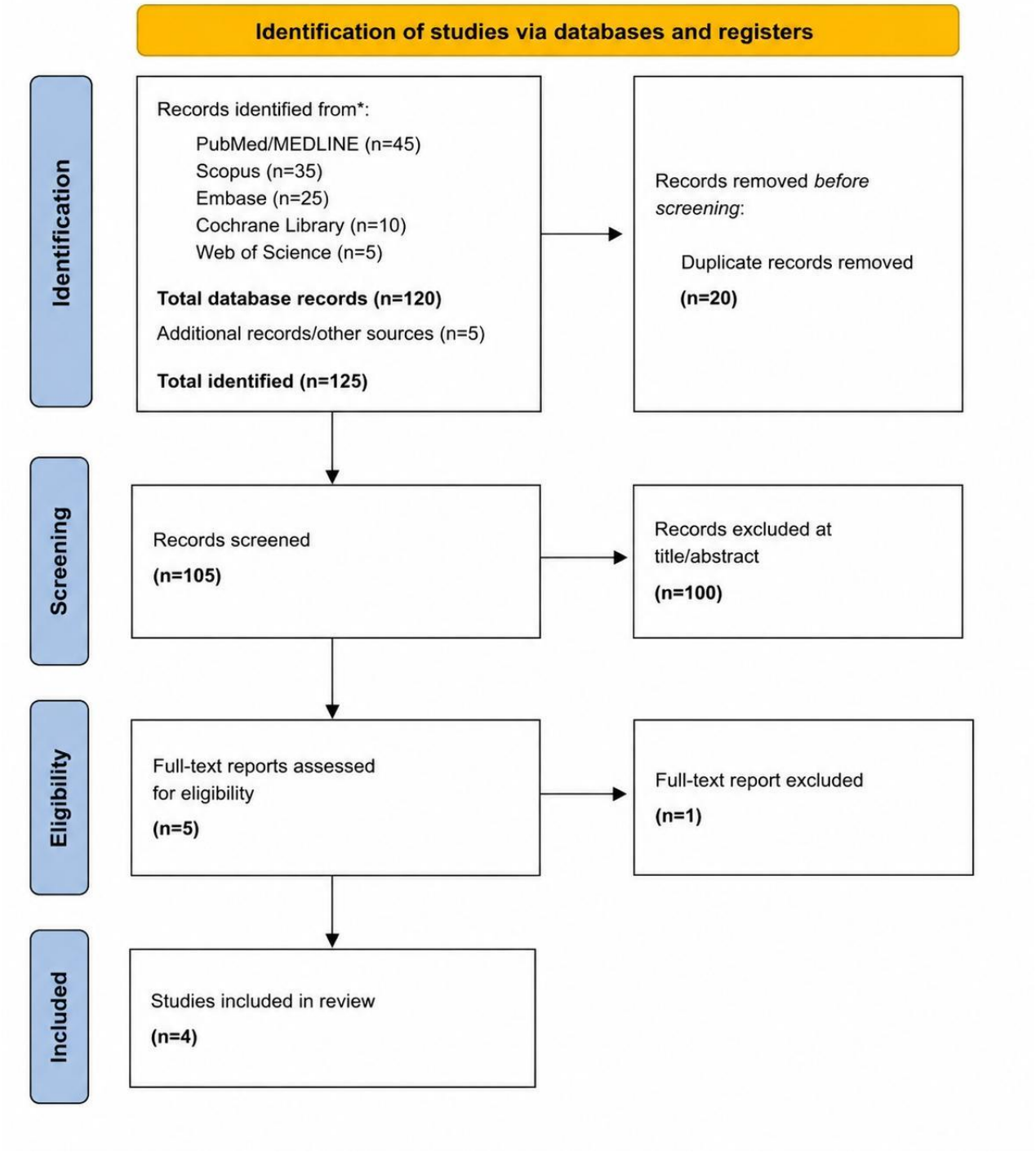
Results

Study Selection Process

The database search identified a total of 125 records, including 45 records from PubMed/MEDLINE, 35 from Scopus, 25 from Embase, 10 from the Cochrane Library, and 5 from Web of Science. An additional 5 records were identified through other sources. After removing 20 duplicate records, a total of 105 records were screened based on their titles and abstracts. Of these, 100 records were excluded as they did not meet the eligibility criteria. The remaining 5 full-text reports were assessed for eligibility, of which 1 report was excluded. Finally, 4 studies were included in the systematic review. (Figure 1)

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Baseline Characteristics and Study Characteristics

A total of 4 randomized controlled trials were included in the systematic review, evaluating the clinical effects of hydroxyapatite-containing toothpastes on dentin hypersensitivity and related remineralization outcomes. The included studies comprised at least 252 recruited participants across the four trials, although the number completing follow-up varied between studies. Vano et al. (2014) included 105 adults and compared 15% nano-hydroxyapatite toothpaste with fluoride toothpaste and placebo, with outcomes assessed at baseline, 2 weeks, and 4 weeks [11]. Vano et al. (2018) also recruited 105 adults and evaluated a 2% nano-hydroxyapatite gel toothpaste against fluoride gel toothpaste and

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placebo over 4 weeks [12]. Ehlers et al. (2021) enrolled 21 children aged 6–16 years with molar-incisor hypomineralization (MIH), comparing microcrystalline hydroxyapatite toothpaste with amine fluoride toothpaste over 56 days [13]. Amaechi et al. (2021) recruited 105 adults, of whom 85 completed the study, and compared 10% and 15% nano-hydroxyapatite formulations, including a potassium-nitrate supplemented formulation, with a calcium sodium phosphosilicate toothpaste over 8 weeks [14]. Across the studies, dentin hypersensitivity was assessed using clinical stimuli including air-blast and tactile stimulation, together with VAS or other validated pain/sensitivity scales (Table 1).

Table 1. Characteristics of Included Studies

Study	Country	Study Design	Sample Size	Population / Condition	HAP Intervention	Fluoride / Comparator	Frequency / Protocol	Follow-up	Remineralization Outcome	Dentin Hypersensitivity Outcome / Assessment	Main Findings	Adverse Events	Comparator Eligibility
Vano et al., 2014	Italy	Double-blind randomized controlled clinical trial; 3 parallel groups	105 total; 35/group	Adults with dentin hypersensitivity; 2 hypersensitive teeth meeting tactile and airblast criteria	15% nano-hydroxyapatite toothpaste; fluoride-free	Fluoride toothpaste; commercially available fluoride dentifrice	Brush 2 min, twice daily	Baseline, 2 and 4 weeks	NR; remineralization was discussed mechanistically but not directly measured as a clinical endpoint	Airblast sensitivity, tactile sensitivity, VAS	HAP group showed significantly lower airblast, tactile and VAS sensitivity than fluoride/placebo at 2 and 4 weeks (P<0.001)	No adverse events reported after 4 weeks	Direct HAP vs fluoride comparison; strong match
Vano et al., 2018	Italy	Double-blind randomized controlled clinical	105 total; 35/group	Adults with dentin hypersensitivity; 2 hypersensitive teeth	2% nano-hydroxyapatite gel toothpaste; fluoride-free	Fluoride gel toothpaste; plus placebo group	Apply/treat teeth for 10 min, twice daily	Baseline, 2 and 4 weeks	NR; not directly assessed as a clinical remineralization	Airblast, tactile sensitivity and VAS	Nano-HAP significantly reduced dentin hypersensitivity at 2 and 4 weeks; significant	No clinically important adverse events reported	Direct HAP vs fluoride comparison; strong matc

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Study	Country	Study Design	Sample Size	Population / Condition	HAP Intervention	Fluoride / Comparator	Frequency / Protocol	Follow-up	Remineralization Outcome	Dentin Hypersensitivity Outcome / Assessment	Main Findings	Adverse Events	Comparator Eligibility
		trial; 3 parallel groups							endpoint		effects were observed across multiple sensitivity tests		h
Ehlers et al., 2021	Germany	Randomized controlled clinical trial; double-blind	21 randomized; HAP n=10, fluoride n=11; 14 completed per-protocol analysis	Children/adolescents (6–16 years) with hypersensitive molars affected by molar-incisor hypomineralization (MIH)	10% microcrystalline hydroxyapatite toothpaste	Amine fluoride toothpaste; 1400 ppm fluoride	Brush 2 min morning and 2 min evening	28 and 56 days	NR; remineralization not directly measured as the primary clinical outcome	Tactile stimulus with Wong-Baker FACES; air-blast with Schiff Cold Air Sensitivity Scale	HAP was non-inferior to amine fluoride in the intention-to-treat analysis; non-inferiority was not demonstrated in the per-protocol analysis	One adverse event in fluoride group; none in HAP group; no serious adverse events	Direct HAP vs fluoride comparison; strong match
Amaechi et al., 2021	USA	Double-blind randomized parallel-grou	105 recruited; 85 completed;	Healthy adults with dentin hypersensitivity	10% nano-HAP; 15% nano-HAP; 10% nano-HAP + potassi	Calcium sodium phosphosilicate (CSPS) desens	Routine toothbrushing twice daily	2, 4, 6 and 8 weeks	NR; remineralization not directly assessed in this	Cold-stimulus VAS and air-stimulus VAS	All products significantly reduced DHS from baseline ($P<0.001$). 15%	No adverse events or compromised oral	Not a strict HAP-vs-conventional-fluoride comp

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Study	Country	Study Design	Sample Size	Population / Condition	HAP Intervention	Fluoride / Comparator	Frequency / Protocol	Follow-up	Remineralization Outcome	Dentin Hypersensitivity Outcome / Assessment	Main Findings	Adverse Events	Comparator Eligibility
		p clinical trial; 4 groups	10% HAP n=22, 15% HAP n=19, 10% HAP+KNO3 n=24, CSPS n=20		um nitrate	itizing tooth paste; commercial comparator			trial		HAP and 10% HAP+KNO3 were generally comparable with CSPS	health reported	arator; eligibility should be reviewed

Risk of Bias Assessment Using RoB 2.0

The risk of bias assessment was conducted for all four randomized clinical trials included in this systematic review using the Cochrane Risk of Bias 2 (RoB 2.0) tool. The assessment covered five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Overall, Vano et al. (2014) [11], Vano et al. (2018) [12], and Amaechi et al. (2021) [14] were considered to have a low overall risk of bias across all assessed domains. These studies demonstrated appropriate randomization procedures, adequate blinding, standardized outcome assessment, and generally complete outcome data, supporting the methodological reliability of their findings. Ehlers et al. (2021) [13] was judged to have some concerns regarding the overall risk of bias, primarily because of concerns related to missing outcome data. Participant attrition resulted in a smaller number of participants completing the study, which may have reduced statistical power and potentially influenced the estimated treatment effect. Nevertheless, the study retained appropriate randomization and blinding procedures, and no major concerns were identified regarding deviations from the intended intervention or outcome measurement. Across the individual domains, randomization, deviations from intended interventions, measurement of outcomes, and selection of reported results were predominantly judged as low risk, while missing outcome data represented the principal methodological concern. Overall, the RoB 2.0

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assessment indicates that the included evidence was of generally good methodological quality, with only limited concerns arising from participant attrition in one study. These findings support the reliability of the overall conclusions while indicating that the results of Ehlers et al. [3] should be interpreted with some caution. (Figure 2 and Figure 3)

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Vano et al. (2014)	+	+	+	+	+	+
Vano et al. (2018)	+	+	+	+	+	+
Ehlers et al. (2021)	+	+	!	+	+	!
Amaechi et al. (2021)	+	+	+	+	+	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
+ Low
! Some concerns
− High

Figure 2: Traffic Light Plot of Domains Showing Risk of Bias for Included Studies Using RoB 2.0

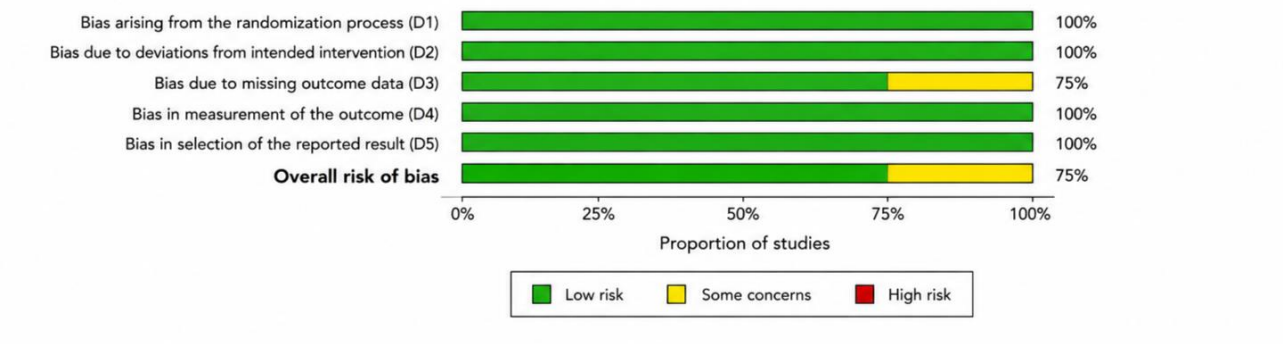


Figure 3: Traffic Light Plot Summary for Included Studies Using RoB 2.0

Systematic Review of Outcomes

Outcome summeries in table 2

Dentin Hypersensitivity

The primary clinical outcome assessed across the included studies was dentin hypersensitivity. Different studies used objective and subjective methods, including cold-air/airblast stimulation, tactile stimulation, visual analogue scale (VAS), and pain-rating scales. Overall, the included studies demonstrated that hydroxyapatite-containing toothpastes were effective in reducing dentin hypersensitivity, although the magnitude of benefit varied according to hydroxyapatite concentration, patient population, comparator, and follow-up period.

Cold-Air and Air-Blast Sensitivity

Vano et al. (2014) reported significantly lower cold-air sensitivity in participants using 15% nano-hydroxyapatite toothpaste compared with the fluoride toothpaste and placebo groups at both 2 and 4 weeks ($P < 0.001$). Similarly, Vano et al. (2018) demonstrated significantly lower cold-air sensitivity with 2% nano-hydroxyapatite gel toothpaste at 2 and 4 weeks compared with the fluoride and placebo groups ($P < 0.05$).

Amaechi et al. (2021) also assessed sensitivity using an evaporative air stimulus. The hydroxyapatite-containing formulations produced significant reductions in sensitivity over the follow-up period, although the magnitude of reduction differed between formulations and the CSPS comparator.

Tactile Sensitivity

Tactile sensitivity was evaluated in the two Vano trials. In the 2014 trial, the 15% nano-hydroxyapatite toothpaste produced significantly lower tactile sensitivity at 2 and 4 weeks compared with the control groups ($P < 0.001$). The 2018 trial using 2% nano-hydroxyapatite similarly reported significantly lower tactile sensitivity at 2 and 4 weeks compared with fluoride and placebo ($P < 0.05$).

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Subjective Pain and VAS Outcomes

Subjective sensitivity was assessed using the visual analogue scale (VAS) in the Vano trials. In the 2014 study, VAS scores were significantly lower in the nano-hydroxyapatite group at both 2 and 4 weeks compared with baseline and the control groups ($P < 0.001$). Vano et al. (2018) also demonstrated significantly lower VAS scores in the nano-hydroxyapatite group at 2 and 4 weeks ($P < 0.05$).

Hypersensitivity Associated with Molar-Incisor Hypomineralization

Ehlers et al. (2021) investigated hydroxyapatite toothpaste in children and adolescents with molar-incisor hypomineralization (MIH)-associated hypersensitivity. The study compared 10% microcrystalline hydroxyapatite toothpaste with amine fluoride toothpaste.

In the intention-to-treat analysis, hydroxyapatite demonstrated non-inferiority to amine fluoride at the assessed follow-up. However, non-inferiority was not demonstrated in the per-protocol analysis, indicating that the findings should be interpreted cautiously.

Remineralization Outcomes

Although remineralization is a major component of the review question, none of the four retained clinical trials directly measured clinical remineralization as an outcome. Therefore, these studies cannot be used to establish a direct clinical effect of hydroxyapatite toothpaste on enamel or dentin remineralization.

The available studies primarily evaluated dentin hypersensitivity and desensitizing effects. Consequently, outcomes such as mineral gain, lesion depth, fluorescence changes, or other validated measures of enamel remineralization should only be included if additional eligible studies directly report these endpoints.

Overall Clinical Outcome

Overall, the included studies provide evidence that hydroxyapatite-containing toothpastes can reduce dentin hypersensitivity, with benefits demonstrated using objective sensitivity tests and subjective pain measures. The strongest direct HAP-versus-fluoride evidence comes from the Vano et al. trials, while the Ehlers et al. study supports comparable effectiveness to amine fluoride in MIH-associated hypersensitivity.

However, the evidence for clinical remineralization remains insufficient within the currently retained studies, and the Amaechi et al. study should be interpreted separately because its comparator was a CSPS desensitizing toothpaste rather than a conventional fluoride-only toothpaste.

Table 2

Summary of Clinical Outcomes Reported in the Included Studies

Study	Outcome Domain	Assessment Method	Follow-up	Findings	Statistical Result	Remineralization
Vano et al., 2014	Dentin hypersensitivity	Cold-air/airblast, tactile test, VAS	2 and 4 weeks	15% nano-HAP produced greater reduction in sensitivity than fluoride and placebo.	$P < 0.001$	Not directly assessed
Vano et al., 2018	Dentin hypersensitivity	Cold-air/airblast, tactile test, VAS	2 and 4 weeks	2% nano-HAP significantly reduced cold-air, tactile and VAS sensitivity.	$P < 0.05$	Not directly assessed
Ehlers et al., 2021	MIH-associated hypersensitivity	Wong-Baker FACES; air-blast/Schiff assessment	28 and 56 days	HAP demonstrated comparable effectiveness to amine fluoride in ITT analysis.	MD −0.75; one-sided 95% CI −∞ to 0.49	Not directly assessed
Amaechi et al.,	Dentin hypersens	Cold-stimulus VAS;	2, 4, 6 and 8	All HAP formulations reduced sensitivity;	Significant differences at	Not directly

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Study	Outcome Domain	Assessment Method	Follo w-up	Findings	Statistical Result	Remineral ization
2021	itivity	evaporative air-stimulus VAS	weeks	effects varied between formulations.	selected time points	assessed

Discussion

Principal Findings

The present systematic review evaluated the clinical outcomes associated with hydroxyapatite-containing toothpastes, with particular emphasis on dentin hypersensitivity and remineralization-related effects. Overall, the included clinical evidence suggests that hydroxyapatite-containing toothpastes are effective in reducing dentin hypersensitivity across different populations and assessment methods. The randomized clinical trials by Vano et al. demonstrated significant reductions in cold-air, tactile, and subjective visual analogue scale (VAS) sensitivity following the use of nano-hydroxyapatite toothpaste compared with fluoride toothpaste and placebo [11,12].

These findings are consistent with previous systematic-review evidence. An updated systematic review and meta-analysis including 44 clinical trials reported that hydroxyapatite-containing oral-care products significantly reduced dentin hypersensitivity compared with placebo and fluoride-containing products. The pooled analysis showed an estimated 23% reduction in dentin hypersensitivity compared with fluoride, supporting the overall direction of the findings observed in the present review [13].

Interpretation of Dentin Hypersensitivity Outcomes

The consistent reduction in dentin hypersensitivity may be explained by the biomimetic properties of hydroxyapatite. Hydroxyapatite particles can deposit on exposed dentinal surfaces and contribute to dentinal tubule occlusion, thereby reducing dentinal fluid movement and limiting stimulation of pulpal nerve endings [13,14].

The findings of the present review are particularly relevant because improvement was observed across multiple methods of sensitivity assessment. The Vano trials demonstrated reductions using both objective stimuli, including air-blast and tactile testing, and subjective VAS measurements [11,12]. This consistency across different outcome measures strengthens the interpretation that hydroxyapatite has a genuine desensitizing effect rather than an effect limited to a single assessment technique.

Previous meta-analytic evidence has also demonstrated that nano-hydroxyapatite is effective in reducing dentin hypersensitivity, although the magnitude of effect may differ according to the type of stimulus used for assessment [14]. Therefore, differences in outcome measurement should be considered when comparing results across clinical trials.

Comparison with Fluoride Toothpaste

An important finding of this review is that hydroxyapatite-containing toothpaste demonstrated comparable or, in some studies, greater effectiveness than fluoride toothpaste for reducing dentin hypersensitivity [11–13]. In the Vano trials, nano-hydroxyapatite formulations produced significantly greater reductions in several hypersensitivity outcomes than fluoride-containing toothpaste and placebo [11,12].

The updated systematic review and meta-analysis by Schlee et al. further supports this observation, reporting a significant reduction in dentin hypersensitivity with hydroxyapatite compared with fluoride-containing oral-care products [15]. These findings suggest that hydroxyapatite may represent a viable desensitizing alternative, particularly for patients whose principal clinical concern is dentin hypersensitivity.

However, these results should not be interpreted as evidence that hydroxyapatite universally replaces fluoride in preventive dentistry. Fluoride has a well-established role in caries prevention, whereas hydroxyapatite may provide additional benefits through biomimetic mineral deposition and dentinal tubule occlusion [13,15]. Therefore, the choice of toothpaste should consider the patient's caries risk, severity of dentin hypersensitivity, oral hygiene needs, and specific formulation.

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Evidence in Molar-Incisor Hypomineralization

The findings of Ehlers et al. provide additional evidence regarding hydroxyapatite use in children and adolescents with molar-incisor hypomineralization (MIH)-associated hypersensitivity. The study compared 10% microcrystalline hydroxyapatite toothpaste with amine fluoride toothpaste and found that hydroxyapatite demonstrated non-inferiority to amine fluoride in the intention-to-treat analysis. However, non-inferiority was not demonstrated in the per-protocol analysis. This discrepancy indicates that although hydroxyapatite appears promising for the management of MIH-associated hypersensitivity, the available evidence remains insufficient to establish clear superiority over fluoride-based treatment.

This is clinically relevant because MIH-associated hypersensitivity may interfere with toothbrushing, eating, drinking, and dental treatment. Hydroxyapatite-containing toothpaste may therefore provide a useful option for symptom management in affected patients, although larger pediatric trials with longer follow-up are required.

Remineralization Outcomes

The evidence for remineralization should be interpreted separately from the dentin hypersensitivity findings. Although the primary clinical studies included in the hypersensitivity analysis largely focused on desensitization, previous clinical research has directly evaluated the remineralization potential of hydroxyapatite toothpaste.

Amaechi et al. conducted a double-blind randomized crossover in-situ study comparing 10% hydroxyapatite toothpaste with 500 ppm fluoride toothpaste. Both formulations produced significant remineralization and reductions in lesion depth ($P < 0.0001$). However, there was no statistically significant difference between the hydroxyapatite and fluoride groups, indicating comparable remineralization efficacy [14]. The study also reported that fluoride produced surface lamination whereas hydroxyapatite resulted in a more homogeneous pattern of lesion remineralization [14].

Further clinical evidence is provided by Butera et al., who compared biomimetic hydroxyapatite toothpaste with conventional 1450-ppm fluoride toothpaste in patients with white-spot lesions. The study evaluated sensitivity and clinical lesion-related outcomes over 90 days. Significant reductions in Schiff Air Index and VAS scores were observed in the hydroxyapatite group, supporting its potential desensitizing and remineralization-related clinical benefits [18].

In addition, an in-situ study specifically investigating MIH reported that hydroxyapatite toothpaste promoted remineralization of MIH enamel, providing further evidence for the biomimetic remineralization potential of hydroxyapatite [17].

Taken together, these findings suggest that hydroxyapatite may provide remineralization efficacy comparable to fluoride, although current evidence does not consistently demonstrate superiority. This distinction is important when interpreting the clinical significance of hydroxyapatite-based formulations.

Clinical Implications

The findings of this review have several potential clinical implications. First, hydroxyapatite-containing toothpaste may be considered a useful option for patients experiencing dentin hypersensitivity. The consistent reductions observed across air-blast, tactile, and VAS-based assessments suggest that hydroxyapatite may provide clinically meaningful symptom relief [11–14].

Second, hydroxyapatite may be particularly attractive as a biomimetic oral-care ingredient because of its ability to interact with dental mineral and potentially occlude exposed dentinal tubules [13,14, 15]. This may provide a dual clinical benefit by addressing both sensitivity and mineral loss.

Third, the available evidence suggests that hydroxyapatite can provide remineralization outcomes comparable to fluoride in initial caries lesions [15]. Therefore, hydroxyapatite may be considered a potential alternative or complementary approach in selected patients. Nevertheless, because fluoride remains an established anticaries agent, hydroxyapatite should not automatically be regarded as a replacement for fluoride, particularly in individuals at high risk of dental caries.

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Safety and Tolerability

The available clinical evidence suggests that hydroxyapatite-containing oral-care products are generally well tolerated. The included clinical studies did not identify a consistent pattern of clinically important adverse effects associated with hydroxyapatite toothpaste.

This favorable tolerability profile is also consistent with previous clinical literature evaluating hydroxyapatite-containing oral-care products [13]. Nevertheless, future trials should use standardized adverse-event reporting and longer follow-up periods to establish the long-term safety of different hydroxyapatite formulations.

Strengths and Limitations

A major strength of the present review is its focus on clinical human evidence, particularly randomized clinical trials evaluating hydroxyapatite-containing toothpaste against fluoride or active comparators. The included studies also assessed dentin hypersensitivity using multiple clinical methods, including tactile testing, air-blast stimulation, VAS, and pain-rating scales.

However, several limitations should be considered. First, the number of directly comparable clinical studies was limited. Second, substantial heterogeneity existed in hydroxyapatite concentration, formulation, patient population, comparator composition, follow-up duration, and outcome assessment methods. Third, the available studies did not consistently evaluate direct clinical remineralization endpoints.

Furthermore, [17] used calcium sodium phosphosilicate (CSPS) as the comparator rather than a conventional fluoride-only toothpaste. Therefore, its findings provide supportive evidence regarding the desensitizing potential of hydroxyapatite but should not be interpreted as direct evidence of superiority over conventional fluoride toothpaste.

Recommendations for Future Research

Future randomized controlled trials should use standardized hydroxyapatite formulations and clearly defined fluoride comparators. Longer follow-up periods are also required because many dentin hypersensitivity studies evaluated outcomes over relatively short periods of 2–8 weeks.

Future research should additionally incorporate objective and validated remineralization outcomes, including quantitative mineral loss, lesion depth, fluorescence-based assessment, or microradiographic analysis. Such measures would allow researchers to determine whether hydroxyapatite is genuinely superior to fluoride or primarily provides comparable remineralization.

Large-scale clinical trials involving children, adults with high caries risk, patients with MIH, and patients with established dentin hypersensitivity would further improve the generalizability of the evidence.

Overall Interpretation

Overall, the available evidence supports hydroxyapatite-containing toothpaste as a promising clinical intervention for reducing dentin hypersensitivity, with several randomized trials demonstrating outcomes comparable to or better than fluoride-containing formulations [11–13]. Previous systematic reviews and meta-analyses provide further support for the desensitizing effect of hydroxyapatite [13,14].

For remineralization, the evidence is more nuanced. Clinical studies indicate that hydroxyapatite can promote remineralization and reduce mineral loss, but available evidence does not consistently demonstrate superiority over fluoride [15–17]. Therefore, hydroxyapatite may best be considered a biomimetic alternative or complementary approach, particularly valuable for patients with dentin hypersensitivity, while additional long-term clinical research is required to establish its comparative remineralization efficacy.

REFERENCES

Canadian Advisory Board on Dentin Hypersensitivity. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. J Can Dent Assoc. 2003;69:221–226.

Porto ICCM, Andrade AKM, Montes MAJR. Diagnosis and treatment of dentinal hypersensitivity. J Oral Sci. 2009;51(3):323–332. Doi:10.2334/josnusd.51.323.

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Ritter AV, de L Dias W, Miguez P, Caplan DJ, Swift EJ Jr. Treating cervical dentin hypersensitivity with fluoride varnish: a randomized clinical study. J Am Dent Assoc. 2006;137(7):1013–1020. Doi:10.14219/jada.archive.2006.0324.

Hoang-Dao B-T, Hoang-Tu H, Tran-Thi N-N, Koubi G, Camps J, About I. Clinical efficiency of a natural resin fluoride varnish (Shellac F) in reducing dentin hypersensitivity. J Oral Rehabil. 2009;36(2):124–131. Doi:10.1111/j.1365-2842.2008.01907.x.

Sivaramakrishnan G, Sridharan K. Fluoride varnish versus glutaraldehyde for hypersensitive teeth: a randomized controlled trial, meta-analysis and trial sequential analysis. Clin Oral Investig. 2019;23(1):209–220. Doi:10.1007/s00784-018-2428-8.

Alencar CM, de Paula BLF, Guanipa Ortiz MI, Magno MB, Silva CM, Maia LC. Clinical efficacy of nano-hydroxyapatite in dentin hypersensitivity: a systematic review and meta-analysis. J Dent. 2019;82:11–21. Doi:10.1016/j.jdent.2018.12.014.

Wang L, Magalhães AC, Francisconi-Dos-Rios LF, et al. Treatment of dentin hypersensitivity using nano-hydroxyapatite pastes: a randomized three-month clinical trial. Oper Dent. 2016;41(4):E93–E101. Doi:10.2341/15-145-C.

Orsini G, Procaccini M, Manzoli L, Giuliodori F, Lorenzini A, Putignano A. A double-blind randomized-controlled trial comparing the desensitizing efficacy of a new dentifrice containing carbonate/hydroxyapatite nanocrystals and a sodium fluoride/potassium nitrate dentifrice. J Clin Periodontol. 2010;37(6):510–517. Doi:10.1111/j.1600-051X.2010.01558.x.

Anand S, Rejula F, Sam JVG, Christaline R, Nair MG, Dinakaran S. Comparative evaluation of effect of nano-hydroxyapatite and 8% arginine containing toothpastes in managing dentin hypersensitivity: double blind randomized clinical trial. Acta Med (Hradec Kralove). 2017;60(3):114–119. Doi:10.14712/18059694.2018.3.

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. 2023;8(1):23. Doi:10.3390/biomimetics8010023.

Vano M, Derchi G, Barone A, Covani U. Effectiveness of nano-hydroxyapatite toothpaste in reducing dentin hypersensitivity: a double-blind randomized controlled trial. Quintessence Int. 2014;45(8):703-711.

Vano M, Derchi G, Barone A, Pinna R, Usai P, Covani U. Reducing dentine hypersensitivity with nano-hydroxyapatite toothpaste: a double-blind randomized controlled trial. Clin Oral Investig. 2018;22(1):313-320.

Ehlers V, Reuter AK, Kehl EB, Enax J, Meyer F, Schlecht J, et al. Efficacy of a toothpaste based on microcrystalline hydroxyapatite on children with hypersensitivity caused by MIH: a randomised controlled trial. Oral Health Prev Dent. 2021;19:647-658. Doi:10.3290/j.ohpd.b2403649.

Amaechi BT, Farah R, Liu JA, et al. Remineralization of molar incisor hypomineralization (MIH) with a hydroxyapatite toothpaste: an in-situ study. BDJ Open. 2022;8:33. Doi:10.1038/s41405-022-00126-4

Schlee M, et al. Clinical Evidence of Biomimetic Hydroxyapatite in Oral Care Products for Reducing Dentin Hypersensitivity: An Updated Systematic Review and Meta-Analysis. Biomimetics. 2023;8(1):23.

Hu ML, et al. Clinical efficacy of nano-hydroxyapatite in dentin hypersensitivity: a systematic review and meta-analysis. J Dent. 2019;82:11-21.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Amaechi BT, AbdulAzees PA, Alshareif DO, et al. Comparative efficacy of a hydroxyapatite and a fluoride toothpaste for prevention and remineralization of dental caries in children. BDJ Open. 2019;5:18. Doi:10.1038/s41405-019-0026-8.

Butera A, Gallo S, Pascadopoli M, et al. Home Oral Care with Biomimetic Hydroxyapatite vs. Conventional Fluoridated Toothpaste for the Remineralization and Desensitizing of White Spot Lesions: Randomized Clinical Trial. Int J Environ Res Public Health. 2022;19(14):8676. Doi:10.3390/ijerph19148676