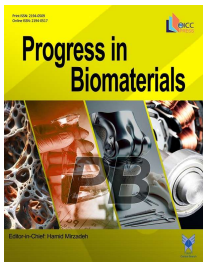

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Strontium-Containing Biomaterials in Dentistry: Mechanisms of Remineralisation and Clinical Translation - A systematic Review

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Review Article

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Abstract

Introduction: Strontium has emerged as a promising component in biomaterials, enhancing remineralisation of dental hard tissues through ionic substitution, bioactivity, and modulation of apatite formation. It has been integrated into strontium-doped nano-hydroxyapatite, bioactive glasses, and fluorophosphates, each exploiting distinct structure–function mechanisms.

Objectives: This systematic review evaluates the efficacy of strontium-containing biomaterials for enamel and dentin remineralisation, with focus on physicochemical properties, mechanisms of action, and translational potential.

Methods: A systematic review of in vitro studies was conducted, including strontium-enriched formulations applied to enamel and/or dentin. Outcomes included changes in surface microhardness (ΔSMH) and lesion depth. Owing to heterogeneity in designs, formulations, and measures, findings were synthesised narratively using SWiM (Synthesis Without Meta-analysis) guidelines**.**

Results: Twenty-one in vitro studies were identified; only one used a bovine tooth model, and no human clinical trials were found. Twelve reported >30% enamel ΔSMH improvement, with Sr-doped nano-hydroxyapatite achieving gains up to 45%. Sr-bioactive glass and Sr–fluoride hybrids reduced lesion depth by 15–25%, with several studies showing synergistic effects with fluoride.

Conclusions: To conclude, strontium-based biomaterials show promising potential for enhancing enamel remineralization and caries prevention; however, current evidence is derived exclusively from in vitro studies. Well-designed in vivo clinical trials are therefore essential before these findings can be reliably translated into clinical practice.

Keywords: Strontium, tooth remineralization, apatite formation, dental biomaterials, caries management

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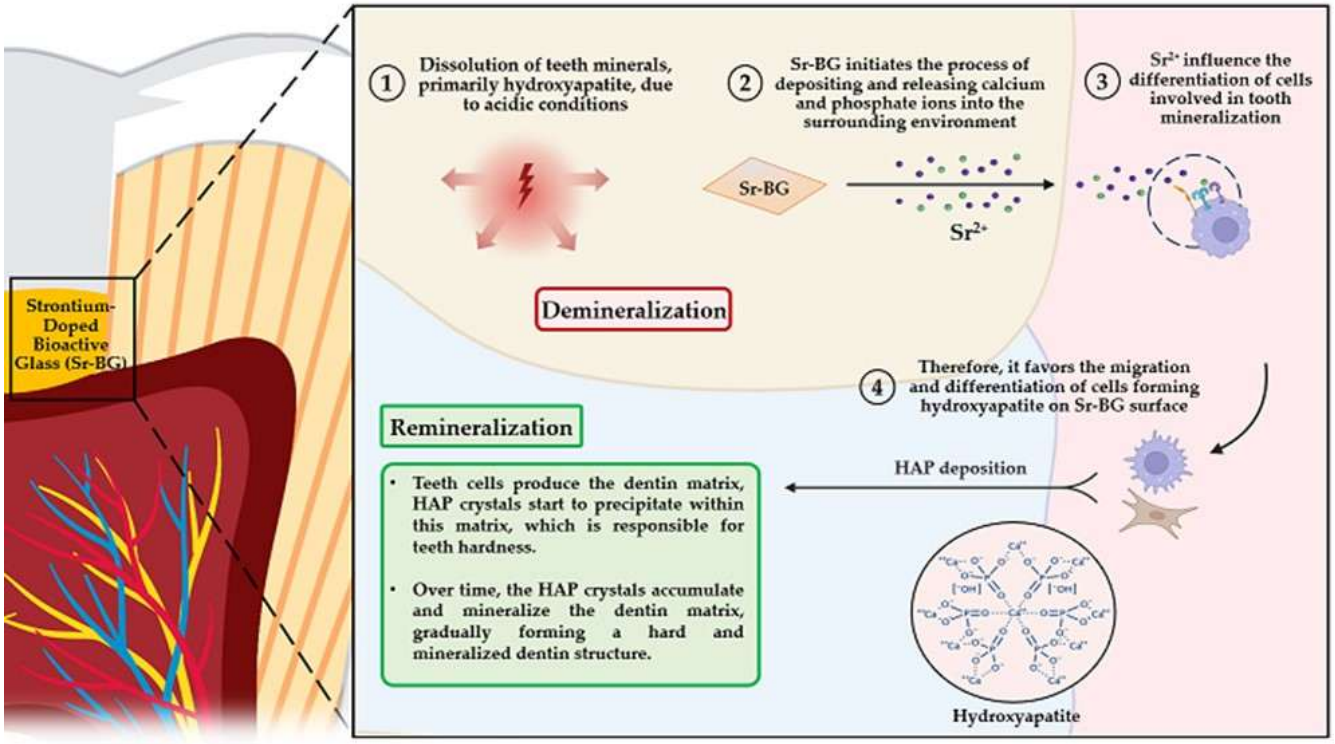
Graphical abstract



1. Introduction

Strontium (Sr), an alkaline earth element chemically similar to calcium (Ca), has been widely applied in dentistry for its radiopacifying, desensitising, and bioactive properties [1,2,3]. It is incorporated into restorative materials, bioactive glasses, and hydroxyapatite-based formulations to enhance mineral deposition, mechanical reinforcement, and osteogenic potential [4, 5] . Despite these promising findings, most studies evaluating strontium-based materials have been limited to in vitro settings, where conditions differ significantly from the oral environment. Consequently, there remains a substantial translational gap between laboratory success and clinical application. Reliable evidence synthesis is therefore essential to determine the reproducibility and relevance of these results under realistic conditions.

This systematic review aims to critically appraise and consolidate available data on the remineralisation potential of strontium-containing biomaterials for enamel and dentine. By comparing outcomes across formulations and experimental models, this review identifies key mechanisms and limitations that influence translational viability. Strontium's biological rationale lies in its ionic substitution capacity: Sr^{2+} can replace Ca^{2+} within the hydroxyapatite lattice, altering lattice dimensions, enhancing solubility, and promoting apatite nucleation [6, 7, 8]. These effects improve ion exchange, bioactivity, and mineral recovery of enamel and dentin, while also contributing to mechanical reinforcement [5,9]. Understanding these mechanisms provides a foundation for optimising Sr-based biomaterials for effective clinical translation in preventive and restorative dentistry.

2. Methods

Due to substantial heterogeneity in study designs, intervention formulations, lesion models, and outcome measures (e.g., variations in surface microhardness testing and remineralisation protocols), a formal meta-analysis was deemed inappropriate. Instead, a structured narrative synthesis was adopted in accordance with the SWiM (Synthesis Without Meta-analysis) reporting guidelines [10].

2.1. Synthesis Approach and Grouping Logic

The included studies were grouped according to biomaterial type and composition, allowing comparison across distinct formulation classes with shared mechanisms of action. Five primary synthesis groups were established based on material characteristics and ionic components:

1. Strontium-doped nano-hydroxyapatite (nHAp),

2. Strontium-doped bioactive glasses (BG),

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3. Strontium–fluoride hybrids,
4. Strontium-doped fluorophosphate and amorphous calcium phosphate (ACP) systems, and
5. Strontium carbonates and other Sr-based acidic formulations.

Within each group, findings were summarised by quantitative outcome measures, specifically percentage change in surface microhardness (ΔSMH) and lesion depth reduction (%). These data were compared narratively to determine the relative efficacy of each biomaterial type. Supporting physicochemical data (e.g., XRD, FTIR, SEM/EDX, ion release) were integrated to explain structure–function relationships and identify recurring mechanistic patterns. To enhance comparability, results were combined according to:

- **Shared biological endpoints** (enamel vs. dentine remineralisation),
- **Consistent measurement methods** (ΔSMH, lesion depth, mineral uptake).

This structured synthesis enabled identification of consistent trends while maintaining transparency regarding heterogeneity and study limitations. The research topic was registered in PROSPERO with the registration ID 554126. This review focused on experimental and quasi-experimental studies published within the last decade, aimed at investigating the remineralization potential, biocompatibility, and efficacy of strontium-based materials in promoting the remineralization of dental hard tissues. The study selection followed the PICOS framework, including in vitro studies on strontium-enriched dental biomaterials. Forty-five eligible studies were identified, and their findings were presented in a PRISMA flow diagram for transparency analyses [10, 11]. A. Relevant data were extracted from the full-text articles and summarized in Table 1, providing details on the experimental methods and statistically significant outcomes. A thorough electronic search was performed in scientific databases including PubMed-MEDLINE, Scopus, and Web of Science, using a combination of relevant keywords and MeSH terms. The search was conducted to identify studies published between January 2014 and December 2024, ensuring the inclusion of the most up-to-date research on strontium-based materials for dental applications. The search terms included (“Strontium”) AND (“dental caries” [MeSH Terms]) OR ((“Tooth remineralisation” [MeSH Terms]) OR (“Tooth repair” [MeSH Terms])). All retrieved studies were screened based on predefined eligibility criteria, and relevant data were extracted to assess the effectiveness of strontium-based materials in promoting remineralisation and their potential benefits in dental care. The initial search yielded a total of 3,140 articles, which were imported into Endnote (Endnote X20, Clarivate Analytics, Philadelphia, USA). Two independent reviewers screened the titles and abstracts using Rayyan QCRI (Rayyan, Doha, Qatar) to assess the relevance of the articles. During the first phase of evaluation, duplicate articles were removed. The title and abstracts of the remaining 3,118 papers were carefully reviewed, resulting in exclusion of 2,588 papers that did not meet the inclusion criteria. Subsequently, 45 relevant papers were thoroughly examined by downloading and reading the full text. Additionally, 1 paper was discovered through the references of the 45 selected papers and was assessed in a similar manner. Both authors reached a consensus on which studies fully satisfied the selection criteria. After reading the full text, 24 papers were excluded, details of which are given in Figure 1. Ultimately, this review includes 21 articles. The inclusion and exclusion criteria for this systematic review were established using the PICOS framework to ensure the relevance and quality of the studies reviewed [12] We only incorporated the studies that:

1) Investigated strontium as part of biomaterials (e.g., Sr-doped hydroxyapatite, bioactive glass, fluorophosphate, ACP, composites).
2) Reported SEM/TEM, XRD, FTIR, EDX, ion release, or micro-CT to establish structure function relationships.
3) Focused on enamel/dentin remineralisation outcomes (ΔSMH, lesion depth reduction, mineral uptake, apatite formation).
4) Evaluated remineralization of enamel and/or dentin in human and bovine teet
5) Were limited to experimental/quasi-experimental studies (2014–2024)

We henceforth excluded studies that:

1) Reported Bone regeneration
2) Assessed enamel erosion
3) Assessed enamel bleaching
4) Tested Dentin Hypersensitivity
5) Assessed dentin tubule occlusion
6) Conducted on cells

2.2. Use of artificial intelligence tools

Generative artificial intelligence (AI) was used solely for linguistic and editorial refinement of the manuscript draft, including grammar, flow, and clarity improvement. No AI tools were used for data analysis, literature screening, or interpretation of findings.

All methodological and analytical decisions were made by the authors, and the integrity of data synthesis was preserved.

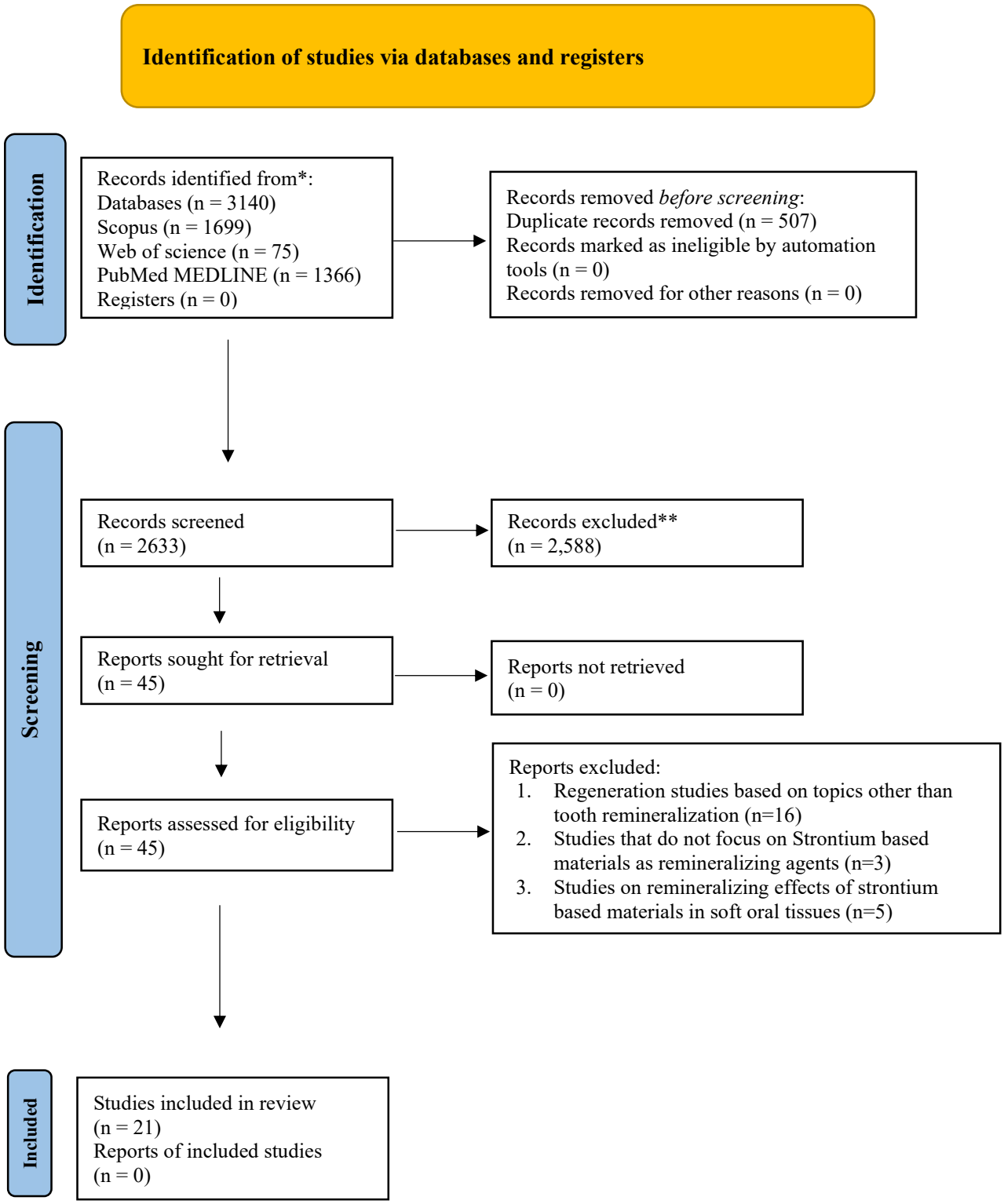

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of this selected study

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3. Risk of bias (RoB) analysis

The risk of bias for the included studies was assessed using the RoBDEMAT tool [13], which is specifically designed for in vitro dental material research.

The tool evaluates potential sources of bias across four domains:

1. Planning and allocation – adequacy of randomisation, group allocation, and sample size calculation.

2. Sample or specimen preparation – standardisation and reproducibility of materials and methods.

3. Outcome assessment – reliability and consistency of outcome measurements across studies.

4. Data treatment and outcome reporting – transparency and appropriateness of data analysis and result presentation. Each domain was evaluated using signalling questions, with responses categorised as *"sufficiently reported," "insufficiently reported," "not reported,"* or *"not applicable."* A rating of *"sufficiently reported"* indicated adequate methodological transparency, whereas *"insufficiently reported"* reflected partial information, and *"not reported"* indicated a complete lack of relevant detail. Items deemed *"not applicable"* were excluded from domain scoring.

A detailed summary of the RoB assessment for each study is presented in Table 1. Figure 2 illustrates the study-level "traffic light" plot, while Figure 3 provides the overall weighted bar chart. Most studies demonstrated adequate reporting of control group use, specimen preparation, statistical analysis, and outcome reporting. However, aspects such as randomisation procedures, sample size justification, and operator blinding were commonly underreported or insufficiently described. Overall, the majority of studies exhibited a low to moderate risk of bias, indicating reasonable methodological reliability but highlighting the need for improved reporting of study design parameters to strengthen reproducibility and comparability in future research.

Table 1: Risk of Bias Assesment using RobDEMAT tool

Study ID	Bias in planning and allocation (Domain 1)			Bias in sample/specimen preparation (Domain 2)		Bias in outcome assessment (Domain 3)		Bias in data treatment and outcome reporting (Domain 4)		Overall
	1.1. Control group	1.2. Randomization of samples	1.3. Sample size rationale and reporting	2.1. Standardization of samples and materials	2.2. Identical experimental conditions across groups	3.1. Adequate and standardized testing procedures and outcomes	3.2. Blinding of the test operator	4.1. Statistical analysis	4.2. Reporting study outcomes	
Lin Lu Dai et al 2021	◉	⊗	◍	◉	◉	⊗	◍	◉	◉	Moderate
Lin Lu Dai et al 2022	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Ijima et al	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Oranich Thngsri et al	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Rajendran et al 2020	◉	◍	◍	⊗	◉	⊗	◍	◉	◉	Moderate
Rajendran et al 2021	◉	◍	◍	⊗	◉	◉	◍	◉	◉	Low
Rajendran et al 2022	◉	◍	◍	⊗	◉	⊗	◍	◉	◉	Moderate
Rajendran et al 2023	◉	◍	◍	⊗	◉	◉	◍	◉	◉	Moderate
Krishnan et al 2016	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Sherin et al 2021	◉	◍	◉	◉	◉	◉	◍	◉	◉	Low
Jayasree et al 2017	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Kirti et al 2024	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Frank Lippert 2020	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
May Mei et al 2021	◉	◉	◍	◉	◉	◉	◍	◉	◉	Low
Vita et al 2022	◉	◍	◍	⊗	◉	◉	◍	◉	◉	Moderate
Abdallah et al 2023	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Dhivya et al 2021	◉	◉	◍	◉	◉	◉	◍	◉	◉	Low
Lorenzo et al 2022	◉	◉	◍	◉	◉	◉	◍	◉	◉	Low
Dotta et al 2022	◍	◍	◍	◉	◉	◉	◍	◉	◉	Low
Kuniko et al 2016	◉	◍	◍	◉	◉	◉	◍	◉	◉	Low
Wang et al 2018	◍	◍	◍	⊗	◉	◉	◍	◉	◉	Moderate

◉ Sufficiently reported ⊗ Insufficiently reported ◍ Not reported

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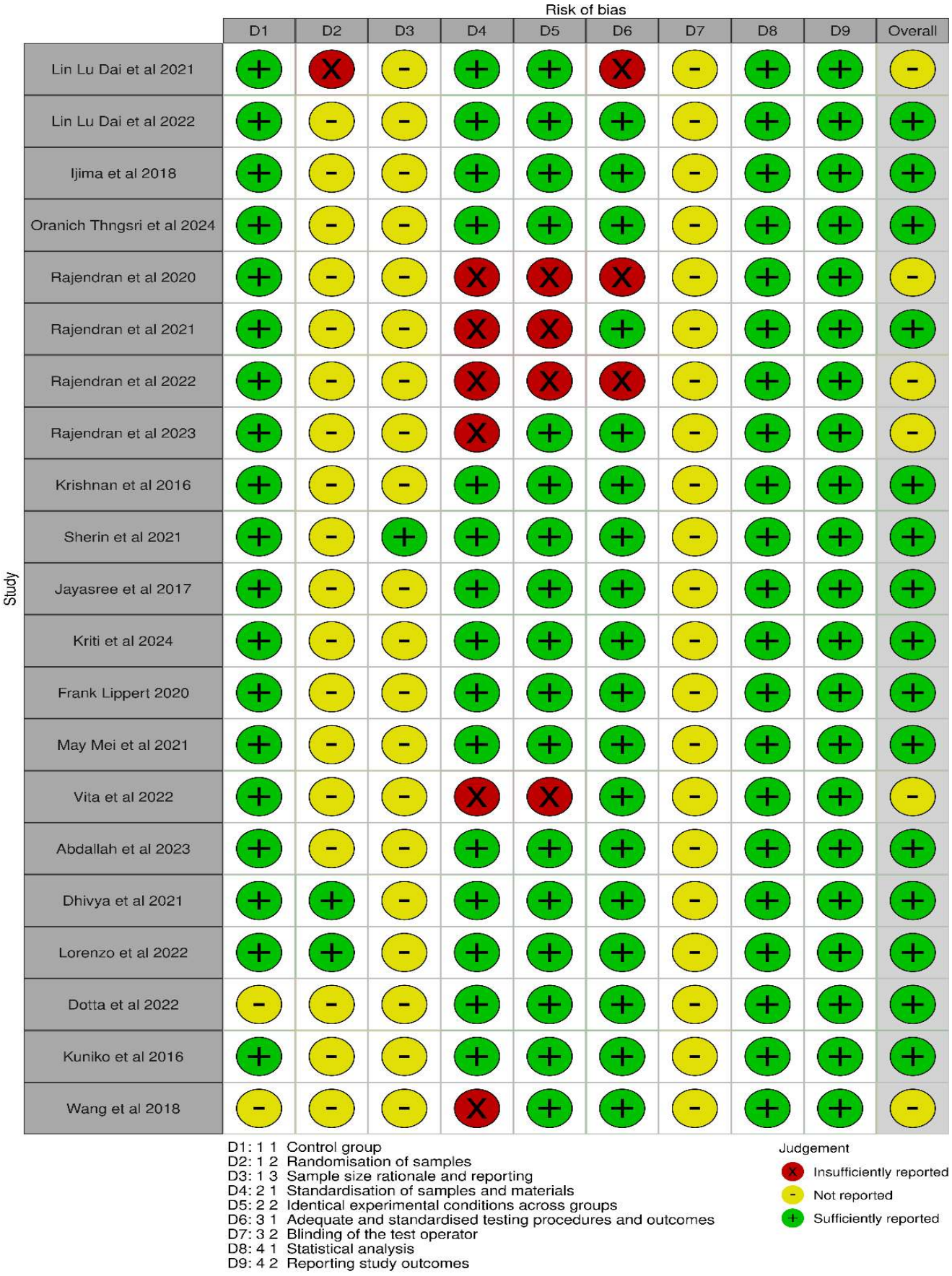

Figure 2. Traffic light plot of the studies' risk of bias (RoB) analysis

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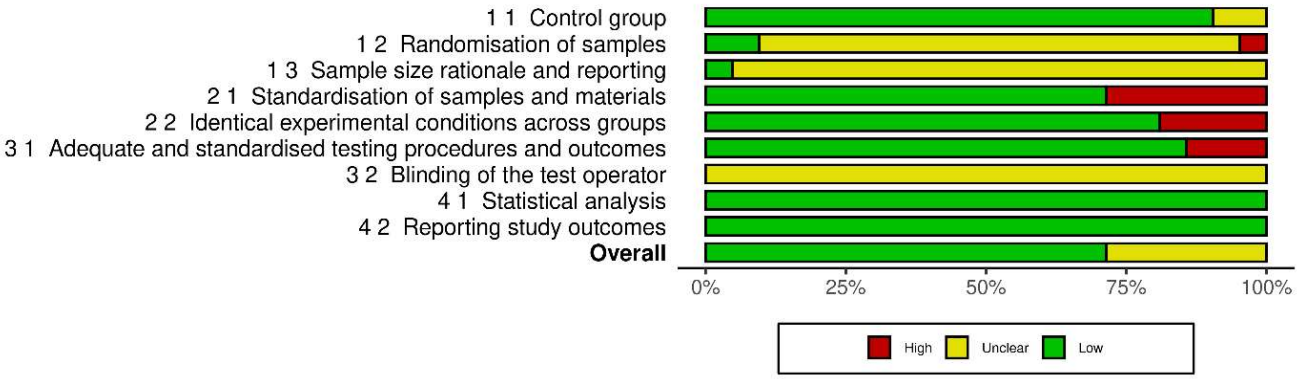

Figure 3. Summary plot of the studies' risk of bias (RoB) analysis

4. Result

To address the variability in strontium formulations, experimental protocols, and endpoints, results have been stratified by material type. Relative efficacies are compared using standardized metrics - primarily Δ surface microhardness (ΔSMH) and lesion depth reduction - where reported. Across material types, studies reported that Sr incorporation modified the crystal lattice, enhanced solubility, and increased Sr^{2+} ion release, thereby accelerating apatite nucleation and improving overall bioactivity as summarized in Table 2.

To provide a clearer synthesis, Table 3 summarizes the quantitative outcomes across material types. Overall, Sr-doped nano-hydroxyapatite demonstrated the highest surface microhardness recovery (ΔSMH 25–45 %) and lesion depth reduction (18–25 %), followed by Sr-doped bioactive glasses and Sr–fluoride hybrids, while Sr-ACP and Sr-carbonate systems showed moderate to minimal effects. Variations in lesion models, ion concentrations, and measurement methods contributed to substantial heterogeneity across studies, limiting direct quantitative comparison but supporting a consistent trend of improved bioactivity with Sr incorporation.

Table 2. Summary of in vitro studies on strontium-based materials for enamel and dentine remineralisation

Sr. No	Material Type	Author and Study (Year)	Formulation	Tissue	Assessment Methods	Biological Endpoints (ΔSMH % / Lesion Depth %)	Physicochemical Modifications / Ion Release	Bioactivity Mechanisms / Key Findings
1.	Sr-doped nano-hydroxyapatite (nHAp)	[14]	Sr-nHAp paste	Enamel	SEM, EDX	ΔSMH ↑ 25–35 %	Sr^{2+} substitution in HA lattice; increased solubility	Enhanced remineralisation compared with conventional toothpaste
		[15]	Sr-nHAp vs CPP-ACP	Enamel	SEM, EDX	ΔSMH ↑ 30–40 %	Lattice substitution; Ca/P enrichment	Sr-nHAp achieved greater remineralisation than CPP-ACP
		[16]	Sr-nHAp vs BG, CPP-ACP	Enamel	SEM, EDX	ΔSMH ↑ 35–45 %	Increased Ca/P ratio; improved crystallinity	Highest remineralisation efficacy among groups
		[17]	Sr-nHAp vs CPP-ACP	Enamel	SEM, EDX	ΔSMH ↑ 32 %	Enhanced ion exchange	Superior remineralisation capacity
		[7]	25 % / 50 % Sr-nHAp	Enamel	AFM, SEM	ΔSMH ↑ dose-dependent (20–40 %)	Lattice expansion; increased solubility	Higher Sr content improved acid resistance

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Sr. No	Material Type	Author and Study (Year)	Formulation	Tissue	Assessment Methods	Biological Endpoints (ΔSMH % / Lesion Depth %)	Physicochemical Modifications / Ion Release	Bioactivity Mechanisms / Key Findings
		[18]	20 % Sr-nHAp + chitosan	Dentine	SEM, Nano-indentation	Lesion depth ↓ 18–25 %	Ion release; chitosan synergy	Synergistic remineralisation and tubule occlusion
		[19]	CDHAp + Sr/F	Enamel	SEM, FTIR	ΔSMH ↑ 20 %	Sr/F co-doping; apatite formation	Formation of a protective enamel-like layer
2.	Sr-doped bioactive glass (BG)	[20]	Sr-BG	Enamel/Dentine	SEM, Micro-CT	Lesion depth ↓ 20–25 %	Sr^{2+} release; apatite precipitation	Reduced lesion formation and enhanced mineral deposition
		[21]	Sr-BG toothpaste (F-free)	Dentine	SEM, Micro-CT	Lesion depth ↓ 15–20 %	Sr^{2+} release without F	Effective remineralisation without fluoride
		[5]	Sr-BG + resin	Enamel	Nano-indentation	ΔSMH ↑ 10–15 %	Improved mechanical strength	Accelerated remineralisation and hardness recovery
		[22]	SrBGF in GIC	Dentine	Micro-CT, SEM	Lesion depth ↓ 15–18 %	Apatite precipitation	Enhanced bioactivity of glass-ionomer cement
3.	Sr–Fluoride hybrids	[23]	SrF_2 in orthodontic adhesive	Enamel	SEM, XRD	ΔSMH ↑ 20 % > F-alone	Sr–F synergy; fluorapatite formation	Superior remineralisation compared to fluoride alone
		[24]	Sr + F solution	Enamel	Knoop hardness	ΔSMH ↑ 15 %	Increased fluoride uptake	Synergistic re-hardening effect
		[25]	Sr-BG + F	Enamel/Dentine	SEM, Micro-CT	ΔSMH ↑ 18 %, Lesion depth ↓ 12 %	Sr^{2+} + F^- release	Dual-ion synergy enhanced remineralisation
		[26]	CSR + NaF varnish	Enamel	Micro-CT	ΔSMH ↑ 18–22 %	Higher F release with CSR	Dose-dependent remineralisation response
4.	Sr-doped fluorophosphate glasses & ACP	[27]	Sr-FPG	Enamel	SEM, EDX	ΔSMH ↑ 12–15 %	Sr incorporation enhanced apatite nucleation	Improved bioactivity and mineral recovery
		[28]	Sr-ACP	Enamel/Dentine	SEM, EDX	Lesion depth ↓ 20 %	Sr^{2+} stabilised ACP; crystal growth	Promoted epitaxial enamel repair

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Sr. No	Material Type	Author and Study (Year)	Formulation	Tissue	Assessment Methods	Biological Endpoints (ΔSMH % / Lesion Depth %)	Physicochemical Modifications / Ion Release	Bioactivity Mechanisms / Key Findings
5.	Sr carbonates & acidic solutions	[29]	$SrCO_3$ / Sr-$CaCO_3$ gel	Dentine	FTIR, EDS	Lesion depth ↓ 15 %	Formation of protective $SrCO_3$ layer	Acid barrier effect; enhanced mineral retention
		[30]	Sr acetate	Dentine	AFM	ΔSMH ↑ 10–12 %	Tubule occlusion	Improved mechanical strength and reduced sensitivity
		[31]	Sr ions in acidic solution	Enamel	Vickers hardness	ΔSMH loss prevented (~0 %)	Sr-induced surface complexation	Protection against acid erosion

Table 3. Summary of quantitative outcomes across material types

Material Type	ΔSMH (%) Range	Lesion Depth Reduction (%) Range	Overall Trend / Interpretation
Sr-doped nano-hydroxyapatite (nHAp)	25–45% increase	18–25% reduction	Consistently high remineralisation and hardness recovery; performance superior to CPP-ACP and fluoride controls.
Sr-doped bioactive glasses (BG)	10–25% increase	15–25% reduction	Effective mineral recovery; Sr release promotes apatite formation even without fluoride.
Sr–Fluoride hybrids	15–22% increase	10–20% reduction	Synergistic effect of Sr and F ions enhances rehardening and subsurface remineralisation.
Sr-doped fluorophosphate glass & amorphous calcium phosphate (ACP)	12–15% increase	20% reduction	Moderate remineralisation with improved crystal nucleation and enamel repair.
Sr carbonates and Sr-based acidic formulations	10–12% increase	10–15% reduction	Provide protective mineral layer and resistance against acid erosion.

5. Discussion

This review aimed to enhance understanding of the supplementary and synergistic effects of strontium (Sr) on tooth remineralisation across various material systems. Analysis of the available studies revealed multiple mechanisms by which Sr promotes mineral recovery and strengthens dental hard tissues. Strontium (atomic number 38), an alkaline earth element positioned below calcium (Ca) in the periodic table, shares similar chemical properties, allowing Sr^{2+} to partially substitute Ca^{2+} in hydroxyapatite (HA) and interact with phosphate to form mineral deposits on enamel and dentine [32]. This substitution enhances solubility and facilitates nucleation of new apatite crystals, contributing to increased mineral deposition and structural integrity of tooth tissues.

Strontium in Bioactive Glasses

Substitution of Ca with Sr in bioactive glass (BG) networks has demonstrated favourable biological outcomes. Most Sr-doped BGs were synthesised via sol gel processing [33, 34], which produces higher surface area and faster dissolution than melt–quench methods [35]. The larger ionic radius of Sr expands lattice parameters, accelerating Sr^{2+} ion release and hydroxyapatite (HA) precipitation [6]. Upon contact with aqueous media, BGs release Na^+, Ca^{2+}, Sr^{2+}, and PO_4^{3-} ions, increasing pH and forming a calcium phosphate layer that crystallizes into HA [6].

Lin Lu Dai and colleagues demonstrated that Sr-enhanced glass (SBAG) effectively reduced mineral loss and promoted apatite formation on dentine, preserving structural integrity [20]. Their subsequent study confirmed that Sr-doped BG, even without fluoride, could effectively remineralise demineralised dentin [21], highlighting its potential in fluoride-free formulations for individuals with sensitivity or fluoride intolerance.

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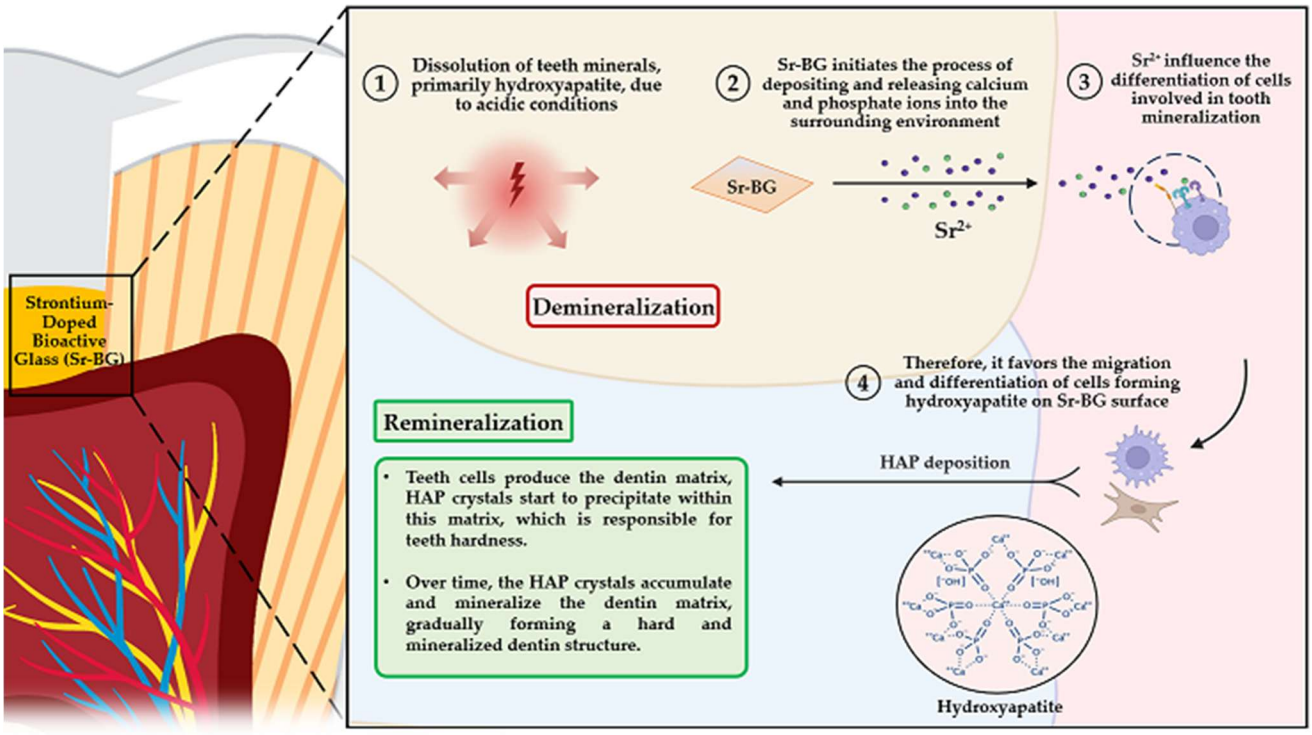

Figure 4. Mechanism of action of Strontium to restore dental hard tissues

Lijima et al. (2018) further reported that Sr incorporation in melt–quenched glass enhanced mechanical stability and elastic modulus by substituting smaller Ca ions with larger Sr ions, improving packing density and structural cohesion [36, 9, 37]. Although silicate-based glasses show excellent bioactivity, they exhibit high melting points and slow degradation. Phosphate-based bioactive glasses (PBGs) have emerged as viable alternatives [38]. PBGs dissolve completely in aqueous media, and their solubility can be tailored by ionic substitution [39]. Fluorophosphate glasses (FPGs), produced by melt–quench methods, permit precise compositional control, and Sr doping increases solubility and apatite nucleation. Dhivya et al. (2021) demonstrated that adding Sr and fluoride ions to PBGs improved their bioactivity and apatite formation, with 6 mol % Sr yielding the highest mineralisation and microhardness improvements, outperforming silica-based gels. Mechanism of action of strontium in promoting remineralisation of dentin is shown in Figure 4.

6. Synergistic effects of strontium and fluoride

The synergistic effects of Sr and fluoride have been extensively studied. Mei et al. (2021) showed that Sr-doped glass combined with fluoride accelerated enamel and dentine remineralisation, producing smoother, more organised enamel surfaces. The dual-ion interaction enhanced fluorapatite formation, improving acid resistance and structural recovery [40]. Abdallah et al. (2023) validated these results by showing that adding calcium strontium silicate (CSR) to NaF varnish increased fluoride release and remineralisation efficacy. Saxena et al. (2024) also found SrF_2 in orthodontic adhesive improved enamel hardness compared with fluoride alone, while Lippert (2017) reported synergistic enamel rehardening. Thongsri et al. (2024) demonstrated that incorporating Sr compounds into glass ionomer matrices enhanced apatite precipitation and dentine density, reinforcing the evidence for Sr–F synergy.

7. Strontium-doped hydroxyapatite and related systems

Strontium-doped nano-hydroxyapatite (Sr-nHAp) has gained significant attention for its strong remineralisation potential. Wet chemical synthesis enables precise control of particle size and crystallinity, enhancing ion release kinetics and bioactivity [9,8]. Replacing Ca with Sr increases solubility and reactivity, improving the ability to remineralise subsurface enamel lesions [41,7].

Rajendran and colleagues [14–18] conducted a series of studies demonstrating that Sr-nHAp pastes consistently outperformed conventional toothpaste and CPP-ACP formulations in enhancing remineralisation and surface hardness. Sherin et al. (2021) further showed that incorporating 20 % Sr-nHAp with chitosan significantly increased dentine remineralisation, likely due to synergistic effects on ion exchange and collagen

mineralisation. Vita et al. (2022) developed Sr- and F-modified calcium-deficient hydroxyapatite (CDHAp), which bonded strongly to enamel and formed a protective enamel-like layer. Similarly, Jayasree et al. (2017) found that Sr substitution in tetra calcium phosphate cement elevated pH and elastic modulus, improving dentine remineralisation, while Lorenzo et al. (2022) demonstrated that citrate-stabilised Sr–amorphous calcium phosphate (Sr-ACP) transformed rapidly into apatite, supporting epitaxial enamel repair.

8. Carbonate-based and other strontium compounds

Strontium carbonate and related compounds also show promise for remineralisation and protection. Dotta et al. (2016) reported that $SrCO_3$ and Sr–$CaCO_3$ gels formed mineral-rich layers that shielded dentine from acid erosion while maintaining surface integrity. Sr salts such as $SrCl_2$ and Sr acetate have been used effectively to alleviate dentin hypersensitivity and enhance mechanical properties [30]. Wang et al. (2019) found that Sr ions in acidic environments reduced enamel demineralisation by forming a positively charged Stern layer that repelled hydrogen ions and protected the enamel surface [42]. When considered collectively, the data in Tables 2 and 3 reveal that Sr-doped nano-hydroxyapatite consistently delivers the most effective surface and subsurface remineralisation, driven by lattice substitution–induced solubility and accelerated apatite nucleation.

Sr-doped bioactive glasses and Sr–fluoride hybrids perform comparably well, their efficacy largely mediated by sustained Sr^{2+} and F^- release and enhanced apatite layer formation. In contrast, Sr-doped fluorophosphate, ACP, and carbonate systems demonstrate moderate mineral recovery and greater protective surface effects than deep lesion repair. Mechanistically, these differences highlight that Sr's performance depends on its ionic delivery vehicle, lattice integration, and dissolution kinetics. The collective evidence underscores the need for standardisation of ΔSMH testing protocols, lesion model calibration, and in vivo validation frameworks to ensure reproducibility and facilitate translational comparability across material systems.

9. Limitations and future directions

Although the reviewed evidence demonstrates strong potential for Sr-based materials in enhancing remineralisation, most studies remain in vitro, limiting direct clinical translation. Study heterogeneity across substrates, material types, and experimental protocols makes quantitative comparison challenging. Additionally, long-term data on safety, aesthetic outcomes, and biocompatibility are lacking. Future research should focus on well-designed in vivo and clinical studies that assess outcomes like lesion progression and depth (via OCT-derived ΔZ and lesion depth measurements), changes in enamel microhardness, patient-reported sensitivity, and caries incidence over extended periods.

Future randomised controlled trials comparing Sr-based dentifrices or varnishes with standard fluoride formulations are needed to determine whether Sr provides clinically meaningful benefits beyond fluoride.

Sr-based biomaterials also hold promise as multifunctional systems integrating remineralisation, mechanical reinforcement, ion release, and antimicrobial effects [36, 9]. Their potential applications in pulp–dentine regeneration and bone augmentation further highlight their versatility [43, 44]. However, achieving clinical translation will require standardisation in synthesis, characterisation, and testing protocols, ensuring consistent performance, safety, and long-term efficacy [45].

10. Conclusion

In conclusion, strontium-based biomaterials demonstrate clear promise as multifunctional agents capable of enhancing remineralisation, reinforcing structure, and improving bioactivity of dental hard tissues. Among the evaluated systems, Sr-doped nano-hydroxyapatite and Sr-enriched bioactive glasses show the strongest mechanistic and quantitative performance. However, the transition from laboratory findings to clinical application remains constrained by methodological heterogeneity and the absence of validated in vivo models. Future research should prioritise standardised ΔSMH testing, unified lesion simulation protocols, and long-term in vivo studies to define clinically relevant endpoints. Moving forward, the rational design of Sr-based biomaterials, integrating controlled ion release, mechanical reinforcement, and biocompatibility offers an important pathway toward next-generation restorative and preventive dental materials with genuine clinical translation potential.

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Authors Contribution

Maryam Saeedullah contributed to the methodology, conducted the investigation, curated the data, wrote the original draft, and participated in manuscript preparation. NT contributed to the methodology and manuscript preparation. NAY, Prof Hien, Muaralitharan, and Dr.Arief contributed to the conceptualization, methodology and participated in writing through review and editing. All authors collaboratively revised the manuscript and read and approved the final version.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Conflict of interests

All the authors declare no conflict of interest.

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