

Effectiveness of Silver Diamine Fluoride on *Streptococcus mutans* and *Lactobacillus*: A Systematic Review

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Received 11 July 2025 • Revised 13 December 2025 • Accepted 5 January 2026 • Published online 5 October 2026

Abstract:

Objective: This systematic review evaluated the efficacy of silver diamine fluoride (SDF) at various concentrations, follow-up intervals, and in combination with other agents in reducing *Streptococcus mutans* (*S. mutans*) and *Lactobacillus*, as well as comparing its effectiveness with other antimicrobial agents.

Material and Methods: A systematic search was conducted in Scopus, Web of Science, Cochrane Library, PubMed, and Google Scholar for studies published up to 31 December 2023. Eligible studies included both in vitro and clinical studies evaluating the effects of SDF on *S. mutans* and *Lactobacillus*. Extracted data included SDF concentration, follow-up interval, and antibacterial outcomes. The risk of bias was assessed using the appropriate tools, according to the study design.

Results: Twenty-four studies met the inclusion criteria. In vitro studies consistently demonstrated the strong antibacterial effects of SDF, with increased efficacy at higher concentrations. Clinical studies reported significant reductions in *S. mutans* and *Lactobacillus* for up to six months post-treatment. When compared to other agents, SDF showed comparable or superior antibacterial efficacy. Most studies showed a moderate to high risk of bias.

Conclusion: SDF demonstrated significant antibacterial activity against *S. mutans* and *Lactobacillus* in both laboratory and clinical studies. Its efficacy is influenced by factors such as concentration, follow-up interval, and combination with

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J Health Sci Med Res
doi: 10.31584/jhsmr.20261443
www.jhsmr.org

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other agents. Despite methodological variability limiting the certainty of evidence, the current findings support SDF as an effective antibacterial agent against cariogenic bacteria. Further well-designed and standardised clinical trials with longer follow-up periods are needed to strengthen the evidence base and validate its comparative effectiveness in caries management.

Keywords: antibacterial, dental caries, *Lactobacillus*, silver diamine fluoride, *Streptococcus mutans*

Introduction

Although the prevalence of dental caries has declined in developed countries over recent decades, it remains a widespread global health concern, particularly in low socioeconomic regions and among children¹. Dental caries is a preventable disease when its etiological factors are well understood². It is initiated by acidogenic bacteria that ferment dietary carbohydrates, producing organic acids that demineralise dental hard tissues³.

Minimally invasive dentistry and preventive strategies, including pit and fissure sealants and fluoride applications, are widely adopted in clinical practice and have shown high efficacy^{1,2}. More recently, silver diamine fluoride (SDF) has garnered attention due to its ability to arrest caries progression without removing the lesion. SDF is a colourless compound containing silver and fluoride, known for its enamel-strengthening properties and long-standing use as an antimicrobial agent⁴. It is considered a simple, cost-effective, and non-invasive method for caries management⁴. Studies have indicated that SDF can arrest and prevent coronal and dentine caries in primary and permanent teeth^{5,6}.

Streptococcus mutans (*S. mutans*) is a key pathogen in dental caries due to its ability to produce large quantities of extracellular polysaccharides and acids that exceed the salivary buffering capacity³. Additionally, it strongly adheres to tooth surfaces and initiates plaque formation. In contrast, *Lactobacillus* species have a limited ability to initiate biofilm formation independently but rely on *S. mutans*-derived

polysaccharides for colonization^{5,7}. Consequently, *S. mutans* facilitates the adherence and proliferation of *Lactobacillus* on tooth surfaces. The presence of fermentable carbohydrates further promotes the growth of these bacteria, supporting caries progression⁷. *Lactobacillus* species are commonly found in both superficial and deep carious lesions⁵. Both *S. mutans* and *Lactobacillus* can survive in highly acidic environments enriched with fermentable sugars, which favor *Lactobacillus* growth and accelerate the progression of dental caries^{5,7}.

In vitro studies indicate that SDF inhibits *S. mutans* and *Lactobacillus* biofilm formation, disrupts multispecies cariogenic biofilms on dentin surfaces, and reduces demineralization^{1,5}. The anticaries mechanism of SDF is primarily attributed to the positively charged silver ions, which adhere to bacterial cell walls and inhibit bacterial aggregation. These ions interact with essential bacterial enzymes, blocking the electron transport chain or reacting with thiol groups to deactivate enzymatic functions, ultimately leading to bacterial cell death. Additionally, silver ions can electrostatically bind to the anionic components of bacterial membranes, resulting in membrane leakage or rupture, and may react with phosphorous and sulfur-containing proteins, causing cytoplasmic extrusion. Another mechanism involves the interaction of silver ions with bacterial DNA, leading to mutations or inhibition of replication. Moreover, binding of silver ions to bacterial amino acids can form organometallic complexes that further enhance antibacterial activity⁸.

Although Khurshid et al.⁸ provided robust evidence supporting the antibacterial efficacy of SDF and its role in dentin caries arrest, knowledge gaps remain regarding its clinical effectiveness across different concentrations and follow-up intervals. Moreover, while the addition of potassium iodide (KI) has been proposed to counteract the undesirable black staining associated with SDF⁸, its synergistic effect on cariogenic bacteria remains inconclusive, warranting further investigation. To date, no systematic review has comprehensively evaluated the antibacterial effects of SDF against *S. mutans* and *Lactobacillus*. This systematic review, therefore, evaluated the antibacterial efficacy of SDF at different concentrations, follow-up intervals, and in combination with other agents against *S. mutans* and *Lactobacillus* levels, and compared its effectiveness with that of other antimicrobial agents.

Material and Methods

Study design

This systematic review followed the PRISMA guidelines and was registered with PROSPERO (Reg ID: CRD42024502846). The research question was developed using the Population, Intervention, Comparator, Outcomes, and Study Design (PICOS) framework as follows: What is the effectiveness of SDF at different concentrations, follow-up interval, and in combination with other agents in reducing *S. mutans* and *Lactobacillus*/*L. acidophilus* level compared to other antimicrobial agents in both paediatric and adult populations?

The PICOS elements were defined as follows: Population (P), children or adults; Intervention (I), SDF applied at different concentrations, follow-up intervals, and in combination with other agents; Comparison (C), other antimicrobial agents; Outcome (O), reduction in *S. mutans* and *Lactobacillus*/*L. acidophilus* count; Study design (S): in vitro and in vivo studies.

Eligibility criteria

Studies were eligible for inclusion if they evaluated the antibacterial effects of SDF on *S. mutans* or *Lactobacillus*. Eligible studies were required to report the SDF concentration and post-treatment intervals, with or without comparator groups. Comparators interventions included other antimicrobial agents, a negative control such as distilled water, or untreated groups. Studies were required to report quantitative outcomes for *S. mutans* or *Lactobacillus* counts, regardless of the measurement method. Eligible study designs included randomised controlled trials, non-randomised controlled trials, cohort studies, observational studies, and in-vitro experiments. Only full-text articles published in English were included, with no restriction on publication date. Animal studies and those lacking relevant microbiological outcomes were excluded. In addition, case reports, case series, review articles, theses/dissertations, and conference abstracts were also excluded.

Search strategy

A comprehensive search was conducted in four electronic databases (Scopus, Web of Science, Cochrane Library, and PubMed) for articles published up to December 31, 2023, on the effectiveness of SDF in inhibiting *S. mutans* and *Lactobacillus*. Additional searches of grey literature were performed using Google Scholar. The search included and combined several keywords, synonyms, and free terms. The search strategy and limits for each database were as follows: For Scopus, the search string was TITLE-ABS-KEY ("silver diamine fluoride" OR "SDF") AND ("streptococcus mutans" OR "lactobacillus" OR "mutans" OR "S. mutans") AND ("caries" OR "dental decay" OR "cavity" OR "dentin* caries" OR "dental caries" OR "cariou") AND NOT DOCTYPE (ab AND bk AND ch AND re). For Web of Science, the query was ALL=((("silver diamine fluoride" OR "SDF") AND ("streptococcus mutans" OR "lactobacillus"

OR "mutans" OR "*S. mutans*") AND ("caries" OR "dental decay" OR "cavity" OR "dentin* caries" OR "dental caries" OR "cariou*"), and Review Article (Exclude – Document Types) and Book Chapters or Proceeding Papers (Exclude – Document types). In PubMed, the search was (((silver diamine fluoride[Title/Abstract]) OR (SDF[Title/Abstract])) AND ((*Streptococcus mutans*[Title/Abstract]) OR (*S. mutans*[Title/Abstract]) OR (*Lactobacillus*[Title/Abstract])) AND ((dental caries[Title/Abstract]) OR (dental decay[Title/Abstract]) OR (caries[Title/Abstract]))). The Cochrane Library search used "silver diamine fluoride" OR "SDF" in Title Abstract Keyword AND "*Streptococcus mutans*" OR "mutans" OR "*Lactobacillus*" in Title Abstract Keyword AND "caries" OR "dental decay" OR "cavity" in Title Abstract Keyword – in Trials. Finally, Google Scholar was searched using the string: caries OR SDF OR *lactobacillus* OR mutans "silver diamine fluoride" "*streptococcus mutans*" –review. Reference lists of all included full-text articles were manually screened to identify additional relevant studies.

Study screening and selection

Two reviewers (NAA and MMA) independently screened the titles and abstracts of studies identified through electronic database searches. Results were exported to EndNote version 9 (Clarivate Analytics, USA), and duplicates were removed. Full texts were retrieved when abstracts lacked sufficient information to determine eligibility. In the second phase, the full texts were assessed based on the inclusion criteria. Any disagreements were resolved through discussion with a third reviewer (ASH). The study selection process is illustrated in the PRISMA flow diagram (Figure 1).

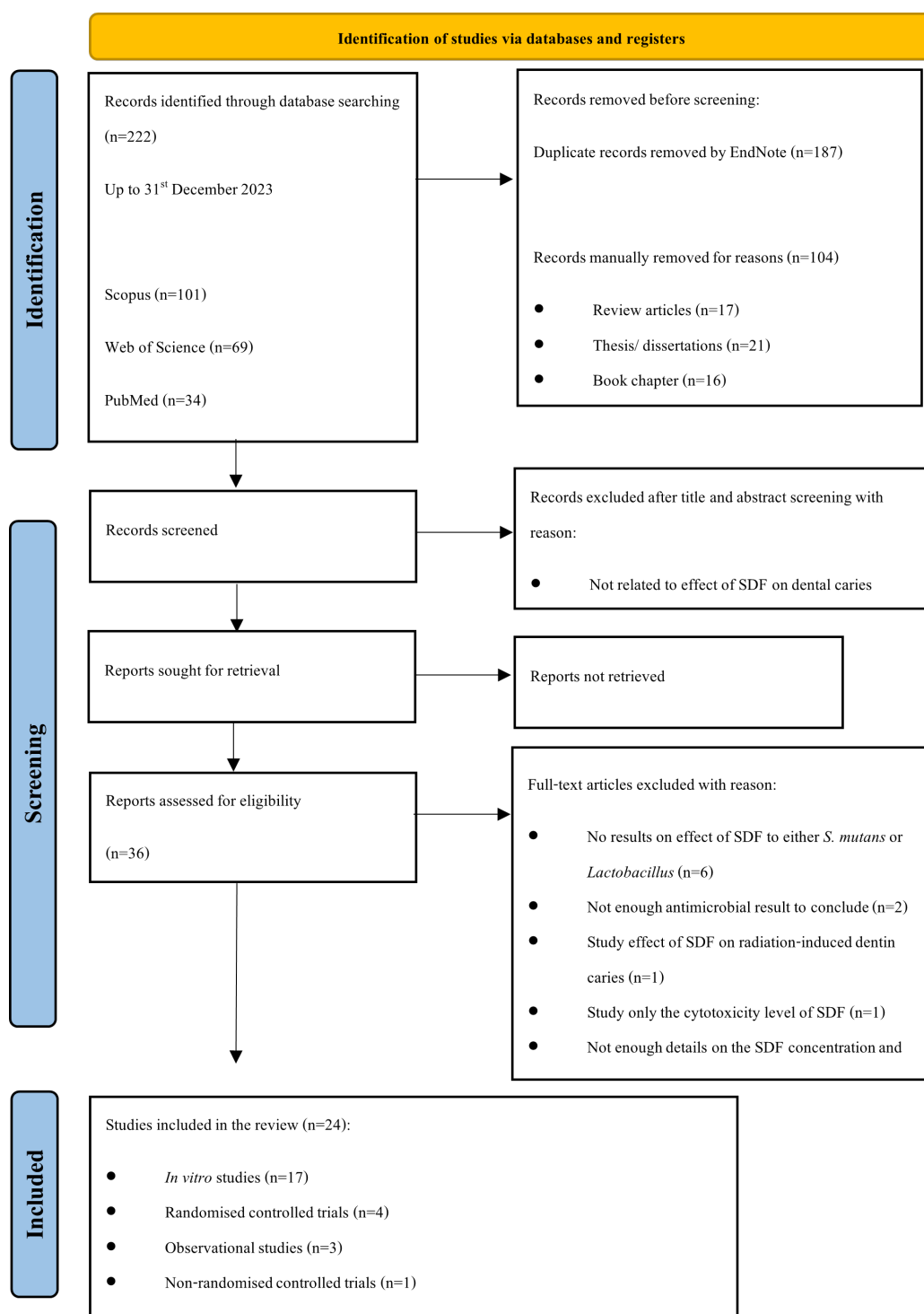
Data extraction and management

For both in vitro and in vivo studies, the extracted data included the first author, year of publication, country of origin, study objective, SDF concentration, comparator

agents (if any), follow-up interval, and bacterial counts of *S. mutans* and *Lactobacillus* before and after treatment. Additional details such as outcome measures, sample size, and type were recorded for in vitro studies, while in vivo studies included participant number and age range, sample type, and study design. Data extraction and verification were independently performed by the same two reviewers (NAA and MMA), with discrepancies resolved through discussion with a third reviewer (ASH). The characteristics and findings related to the antibacterial efficacy of SDF are summarised in Table 1 (in vitro), Table 2 (RCT), and Table 3 (other study designs).

Risk of bias and quality assessment

The quality of the included studies was independently assessed by two reviewers (ASH, MMA), and any discrepancies were resolved through discussion. Due to methodological heterogeneity among the included studies, different assessment tools were applied according to study type. For in vitro studies, the Quality Assessment Tool for In Vitro Studies (QUIN Tool) was used^{9,10}. This tool comprises 12 criteria, each scored as 2 for "adequately specified," 1 for "inadequately specified," and 0 for "not specified"¹¹. The final score for each study was calculated using the formula: $(\text{Total score} \times 100) / (2 \times \text{number of applicable criteria})$. A score >70% indicated low risk of bias, 50–70% represented moderate risk, and <50% indicated high risk of bias. For randomised controlled trials (RCTs), the Risk of Bias 2 (RoB2) tool was used to assess both external and internal validity. The assessment covered the randomisation process, allocation concealment, missing outcome data, outcome measurement, and selective reporting¹¹. Each domain was rated as low risk, some concerns, or high risk of bias. Meanwhile, the ROBINS-I (Risk of Bias in Non-Randomised Studies of Interventions) tool was used for non-randomised studies to evaluate the potential bias due to confounding, bias in the selection of participants into the



PRISMA=preferred reporting items for systematic reviews and meta-analyses, SDF=silver diamine fluoride

Figure 1 PRISMA flow diagram of literature search and study selection

Study, Year	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
Country				<i>S. mutans</i>	<i>Lactobacillus</i>	
Outcome measures: CFU, SEM and CLSM						
Chu et al., 2012 ¹⁹	32 artificially demineralized human dentine samples inoculated with <i>S. mutans</i> (ATCC 35668)	To characterize the effects of 38.0% SDF on dentine caries induced by <i>S. mutans</i>	38.0% SDF vs Water (control)After 7 days	Microbial kinetics with log ₁₀ CFU (mean±S.D.)	log ₁₀ CFU SDF (0.00) water (control) (6.03±0.18) (p-value<0.001)	N/A
Hong Kong				Biofilm Morphology with SEM	SEM images showed that 38.0% SDF disrupted <i>S. mutans</i> biofilm, with very few live bacteria detected	38.0% SDF possesses an antimicrobial activity against <i>S. mutans</i> biofilms
				Biofilm viability with CLSM (dead: live bacteria ratio)	dead-to-live bacteria ratio 38.0% SDF (5.61±2.42) water (control) (0.025±0.01) (p-value<0.01)	
Mei et al., 2013 ⁵	30 human dentine blocks inoculated <i>S. mutans</i> (ATCC 35668) and <i>L. acidophilus</i> (ATCC 9224)	To investigate the anti-microbial effect of SDF on <i>S. mutans</i> and <i>L. acidophilus</i> co-cultured dual-species biofilm	38.0% SDF vs Water (control)After 7 days	Biofilm kinetics with log ₁₀ CFU (mean±S.D.)	mean log ₁₀ CFU 38.0% SDF (4.02±0.35) water (control) (6.72±0.49) (p-value<0.01)	mean log ₁₀ SDF (1.80±0.28) water (control) (3.48±1.14) (p-value<0.01)
Hong Kong				Biofilm viability with CLSM (dead: live bacteria ratio ±S.D.)	Biofilm viability with CLSM (dead: live bacteria ratio ±S.D.)	SDF showed antimicrobial activity against <i>S. mutans</i> and <i>L. acidophilus</i> dual-species biofilms on dentine
					dead-to-live bacteria ratio 38.0% SDF (6.74±5.29) water (control)(0.02±0.002) (p-value=0.03)	dead-to-live bacteria ratio 38.0% SDF (6.74±5.29) water (control) (0.02±0.002) (p-value=0.03)

Table 1 (continued)

Study, Year Country	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Mei et al., 2013 ³¹	72 dentin blocks inoculated with <i>S.</i>	To investigate the mechanism of SDF in arresting dentin caries	38.0% SDF vs Water (control) After, 7, 14, and 21 days	Growth kinetics with $\log_{10}$ CFU (mean $\pm$ S.D.)	Growth kinetics with $\log_{10}$ CFU (mean $\pm$ S.D.)	38.0% SDF had antimicrobial activity against <i>S. mutans</i> and <i>L. acidophilus</i> dual- species cariogenic biofilms on dentine.
Hong Kong	<i>mutans</i> (ATCC 35668), and <i>L. acidophilus</i> (ATCC 9224)			mean $\log_{10}$ CFU (SDF vs control) Day 7 (0.27 $\pm$ 0.65 vs. 5.63 $\pm$ 0.87), Day 14 (3.99 $\pm$ 0.08 vs. 7.71 $\pm$ 0.08) Day 21 (4.39 $\pm$ 0.42 vs. 8.11 $\pm$ 0.11) (p-value<0.01)	$\log_{10}$ CFU (SDF vs control) Day 7 (0.43 $\pm$ 0.37 vs. 7.04 $\pm$ 0.28) Day 14 (4.00 $\pm$ 0.04 vs. 9.56 $\pm$ 0.51) Day 21 (5.42 $\pm$ 0.17 vs. 12.69 $\pm$ 0.39) (p-value<0.01)	38.0% SDF arrests dental caries by reducing the demineralisation process.
				Biofilm viability with CLSM (dead: live bacteria ratio $\pm$ S.D.)	Biofilm viability with CLSM (dead: live bacteria ratio $\pm$ S.D.)	
				dead-to-live bacteria ratios (SDF vs control) Day 7 (2.19 $\pm$ 0.55 vs. 0.22 $\pm$ 0.08) Day 14 (1.64 $\pm$ 0.54 vs. 0.06 $\pm$ 0.02) Day 21 (0.92 $\pm$ 0.36 vs. 0.004 $\pm$ 0.001) (p-value<0.01)	dead-to-live bacteria ratios (SDF vs control) Day 7 (2.19 $\pm$ 0.55 vs. 0.22 $\pm$ 0.08) Day 14 (1.64 $\pm$ 0.54 vs. 0.06 $\pm$ 0.02) Day 21 (0.92 $\pm$ 0.36 vs. 0.004 $\pm$ 0.001) (p-value<0.01)	

Table 1 (continued)

Study, Year Country	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Hamama et al., 2015 ²⁰	45 dentine discs infected with <i>S. mutans</i> isolated from human carious lesions	To evaluate the antimicrobial effect of SDF/KI on the viability of intratubular bacteria	38.0% SDF+KI vs Carisolv vs 2.0% CHX vs Papacarie	Viability of intratubular bacteria using CLSM (mean % dead bacteria $\pm$ S.D.)	N/A	38.0% SDF+KI effectively reduced <i>S. mutans</i> in infected dentinal tubules
Hong Kong				Carisolv (0.4 $\pm$ 0.7%) 2.0% CHX (19.0 $\pm$ 10.8%) Papacarie (19.5 $\pm$ 6.6%) (p-value < 0.001)		
Savas et al., 2015 ²¹	48 enamel blocks inoculated with <i>S. mutans</i> UA159 (ATCC700610)	To evaluate the effectiveness of different antibacterial agents in comparison with SDF against <i>S. mutans</i>	38.0% SDF vs APF vs AHF vs 0.2% CHX After 2 days	Total viable microorganism in the biofilm with mean CFU (mean $\pm$ S.D.)	N/A	38.0% SDF showed highest activity against <i>S. mutans</i> compared with other agents
Turkey				mean CFU 38.0% SDF (0.0)APF (2.62 $\times 10^8 \pm 1.72 \times 10^7$) AHF (2.65 $\times 10^8 \pm 2.04 \times 10^7$) 0.2% CHX (3.21 $\times 10^8 \pm 3.01 \times 10^7$) (p-value < 0.05)		
Vinson et al., 2018 ²²	Six-well plates inoculated with <i>S. mutans</i> UA159 (ATCC700610)	To quantitatively evaluate the effects of SDF with/without using SSKI as reducing agent on the viability of established <i>S. mutans</i> biofilms	38.0% SDF vs KI vs 38.0% SDF+KI After 24 hours	Total bacteria count with log ₁₀ CFU	N/A	38.0% SDF caused the greatest disruption of <i>S. mutans</i> biofilm compared to 38.0% SDF+KI and KI alone.
USA				log ₁₀ CFU 38.0% SDF alone seven-fold log ₁₀ reduction in CFU KI alone two-fold log ₁₀ reduction in CFU 38.0% SDF+KI four-fold reduction in CFU log ₁₀ (p-value < 0.05) % of reduction from negative control (untreated) 38.0% SDF alone and 38.0% SDF+KI reduced <i>S. mutans</i> (>99.9%) compared to KI (97.0%) (p-value < 0.05)		

Table 1 (continued)

Study, Year Country	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Yu et al., 2018 ²³ Hong Kong	104 dentine blocks from 26 human molars inoculated with <i>S. mutans</i> (ATCC 35668)	To investigate the bacterial growth inhibition of 38.0% SDF solution and 5% NaF varnish on artificial dentine caries lesions	38.0% SDF + NaF vs 38.0% SDF vs NaF After 7 days	Growth kinetics by log ₁₀ CFU (mean±S.D.)	N/A	38.0% SDF showed the highest antibacterial activity against the <i>S. mutans</i> biofilm compared to NaF and SDF+NaF.
				mean log ₁₀ CFU 38.0% SDF (4.49±0.57) NaF (6.56±0.39) 38.0%SDF+NaF (5.75±0.56) (p-value<0.001)		
Zhao et al., 2021 ² China	24 enamel blocks used to test the inhibition against <i>S. mutans</i> (ATCC 35668)	To investigate the effects of a SDF, CO ₂ laser, and CO ₂ laser+ SDF on the inhibition of <i>S.</i> <i>mutans</i>	38.0% SDF vs CO ₂ laser vs 38.0% SDF+CO ₂ After 24 hours	Microbial viability by CLSM (dead: live ratio±S.D.)		38.0% SDF and 38.0% SDF+CO ₂ laser significantly inhibited <i>S.</i> <i>mutans</i> growth.
				dead-to-live bacteria ratio 38.0% SDF (1.42±0.11) NaF (0.58±0.04) 38.0% SDF+NaF (0.91±0.09) (p-value=N/A)	N/A	
				Growth kinetics by log ₁₀ CFU (mean±S.D.)		
				mean log ₁₀ CFU 38.0% SDF (2.9±0.8) CO ₂ laser alone (6.2±0.6) SDF+CO ₂ laser (2.2±1.1) (p-value<0.05)		
				Biofilm morphology by SEM	SEM images showed that 38.0% SDF and 38.0% SDF+CO ₂ laser disrupted <i>S.</i> <i>mutans</i> biofilms, with few intact bacteria observed	
				Bacteria viability by CLSM	Most dead cells were observed on enamel surfaces treated with 38.0% SDF alone or 38.0% SDF+CO ₂	

Table 1 (continued)

Study, Year Country	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Xue et al., 2022 ²⁴ China	33 enamel slices immersed in <i>S. mutans</i> (ATCC 35668)	To study the effects of a 445 nm diode laser and SDF on preventing enamel demineralization and inhibiting cariogenic bacteria	38.0% SDF vs 445 nm diode laser vs SDF+ 445 nm diode laser After 1 day incubation	Growth kinetics By log ₁₀ CFU (mean±S.D.)	mean log ₁₀ CFU 38.0% SDF alone (4.54±0.15) 445 nm laser alone (7.89±0.26) (p-value<0.001). SDF+laser (4.21±0.26) (p-value<0.05)	The 445 nm diode laser enhanced the antibacterial effect of 38.0% SDF against <i>S. mutans</i> . Combined treatment showed superior caries prevention.
				Morphology by SEM	Bacterial growth inhibition and cell damage were observed on enamel surfaces treated with 38.0% SDF and SDF+445 nm diode laser	
Ali et al., 2023 ¹³ Saudi Arabia	Biofilm caries model with 27 saliva-coated dentine blocks inoculated with <i>S. mutans</i> (ATCC 700610)	To compare the antibacterial efficacy of 38.0% SDF with that of CPP-ACP against <i>S.</i> <i>mutans</i> using a biofilm caries model	38.0% SDF vs CPP- ACP After 48 hours	Microbial viability by CLSM (dead: live bacteria ratio)	Few live bacteria seen in the 38.0% SDF group; fewer live bacteria observed in the SDF+445 nm diode laser group	38.0% SDF showed superior bactericidal activity against <i>S. mutans</i> biofilm compared to CPP- ACP.
				Total viable counts with CFU (mean±S.D.)	mean CFU 38.0% SDF (0.00) CPP-ACP (96x10 ⁶ ±34.64x10 ⁶) (p-value<0.05)	

Table 1 (continued)

Study, Year	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Outcome measure: MID, MIC, MBC, ZOI						
De Almeida et al., 2011 ¹⁴	<i>S. mutans</i> (ATCC 25175) and clinical isolates from saliva and buccal mucosa of six patients	To evaluate the antibacterial activity of different concentration SDF and CHX against <i>S. mutans</i>	12.0% SDF vs 30.0% SDF vs 0.12% CHX Contact time after: 30sec, 30min, 60min, 90min, 24hrs	MID (mm)	mean MID 12.0% SDF (9.70) 30.0% SDF (11.00) 0.12.0% CHX (9.20)	N/A
Brazil						30.0% SDF showed higher antibacterial activity against <i>S. mutans</i> at all contact times than 12.0% SDF and 0.12% CHX.
Targino et al., 2014 ¹⁵	<i>S. mutans</i> (ATCC 25175)	To evaluate the antimicrobial activity of NSF, against <i>S. mutans</i> in comparison to CHX and SDF	38.0% SDF vs NSF vs 0.12% CHX	MIC (µg/mL)	MICs SDF (33.33±14.43) NSF (33.54±14.52) CHX (3.30±0.5) (p-value<0.05)	N/A
Brazil				MBC (µg/mL)	MBCs SDF (50.00) NSF (50.32) CHX (6.00) (p-value<0.05)	SDF and NSF have shown a significant antimicrobial effect against <i>S. mutans</i> , with NSF potentially more effective at lower doses.
Annis et al., 2017 ¹⁶	38.0% SDF applied to agar cultures of <i>S. mutans</i> (ATCC 25175)	To study the effect of SDF and AHF on inhibiting the growth of <i>S. mutans</i>	38.0% SDF vs AHF vs NaF	ZOI mean (mm)	mean ZOI SDF (9.55 mm) AHF (8.86 mm) NaF (4.13 mm) (p-value=N/A)	N/A
Indonesia						38.0% SDF more effectively inhibits the growth of <i>S. mutans</i> compared to AHF.
Lou et al., 2018 ¹⁷	Test solutions applied to agar cultures of <i>S. mutans</i> (ATCC 35668) and <i>L. acidophilus</i> (ATCC 9224)	To identify the possible antimicrobial activity of SDF, AgF, and AgNO ₃ on <i>S. mutans</i> and <i>L. acidophilus</i>	38.0% SDF vs AgF vs AgNO ₃	ZOI mm ² (mean±S.D.)	mean ZOI 38.0% SDF (395.8±15.1) AgF 423.6±82.4 AgNO ₃ 177.8±14.9 (p-value<0.005)	mean ZOI 38.0% SDF 362.6±23.7 AgF 208.7±13.9 AgNO ₃ 171.2±20.8 (p-value<0.005)
USA						38.0% SDF is most effective against <i>S. mutans</i> and <i>L. acidophilus</i> compared to other silver and fluoride agents.

Table 1 (continued)

Study, Year Country	Number and type of sample	Objective	SDF vs comparator/ Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Karched et al., 2019 ²	Dentin samples inoculated with <i>S. mutans</i> (CCUG 11877)	To assess the antimicrobial efficacy of SDF and SDF+KI by comparing total viable counts before and after antimicrobial treatment	38.0% SDF vs 38.0% SDF+KI vs 2.0% CHX	ZOI mm (mean±S.D.) mean ZOI 38.0% SDF (25.7±0.84) 38.0% SDF+KI (15.15±0.9) 2.0% CHX (23.05±0.21)	N/A	<i>S. mutans</i> growth was most inhibited by 38.0% SDF compared to 38.0% SDF+KI and 2.0% CHX.
Kuwait						
Preethy et al., 2020 ⁸	60 sterile Petri dishes inoculated with <i>S. mutans</i> (NCTC10449)	To evaluate the antibacterial effectiveness of 38.0% SDF and chitosan in combination against <i>S. mutans</i>	38.0% SDF vs 2.0% chitosan vs 3.0% chitosan vs 38.0% SDF+2.0% chitosan vs 38.0% SDF+3.0% chitosan	ZOI mm (mean) mean ZOI 38.0% SDF 24.36 mm (30 µL) 38.55 mm (60 µL) 40.22 mm (90 µL) SDF+3.0% chitosan 23.23 mm (30 µL) 26.18 mm (60 µL) 31.32 mm (90 µL) SDF+2.0% chitosan 21.34 mm (30 µL) 12.25 mm (60 µL) 25.44 mm (90 µL) Chitosan alone (2.0% and 3.0%) 11.24;11.14 (30 µL) 12.12; 13.21(60 µL) 14.14; 14.24(90 µL) (p-value=NR)	N/A	38.0% SDF alone exhibited the highest ZOI compared to other test agents, indicating strong antibacterial activity against <i>S. mutans</i> .
India						
Favaro et al., 2022 ⁴	Microdilution techniques and agar medium inoculated with <i>S. mutans</i> (ATCC 35668)	To evaluate antimicrobial activity of silver nanoparticles and fluoride anticaries agent	30.0% SDF vs CHX vs AgF vs Ag	ZOI (mm) median ZOI 30.0% SDF (5.94) CHX (5.11) AgF (2.67) Ag alone (2.66) (p-value<0.05)	N/A	30.0% SDF showed the largest inhibition zone against <i>S. mutans</i> , followed by CHX and AgF.
Brazil						

AgF=silver fluoride, AgNO3=silver nitrate, AHF=ammonium hexafluoroarsenate, APF=acidulated phosphate fluoride, ATCC=American Type Culture Collection, CCUG=Culture Collection University of Gothenburg, CFU=colony forming units, CHX=chlorhexidine, CLSM=confocal laser scanning microscope, CO2=carbon dioxide, KI=potassium iodide, MBC=minimum bactericidal concentrations, MIC=minimum inhibitory concentration, MID=maximum inhibitory dilution, ZOI=zone of inhibition, NaF=sodium fluoride varnish, NCTC=National Collection of Type Cultures, NSF=nano silver fluoride, SDF=silver diamine fluoride, SEM=scanning electron microscope, NR=not reported.

Table 2 Study characteristics and reported results of the antimicrobial efficacy of SDF from RCT studies

Study, Year Country	Number and age range of participants Type of sample	Objective	SDF vs competitor Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Garrastazu et al., 2020 ²⁵ Brazil	64 children (6–10 years old) using stimulated saliva samples	To evaluate the longitudinal effect of SDF on salivary levels of <i>S. mutans</i> in oral cavity compared with CHX	30.0% SDF vs 1.0% CHX After 1 month and 3 months	mean CFU at baseline: 38.0% SDF (8.79x10 ⁷ ±4.62x10 ⁶). 1.0% CHX (6.35x10 ⁷ ±2. 28x10 ⁸). (p-value>0.05) after 1 month: 38.0% SDF (3.06x10 ⁶ ±3.09x10 ⁴) 1.0% CHX (3.07x10 ⁴ ±2.86x10 ⁴) (p-value>0.05) after 3 months: 38.0% SDF (2.94x10 ⁶ ±5.97x10 ⁶) 1.0% CHX (2.92x10 ⁶ ±3.48x10 ⁶) (p-value>0.05)	N/A	30.0% SDF showed similar antimicrobial effects to 1.0% CHX over time.
				Total viable counts with CFU (mean±S.D.)		
Ammar et al., 2022 ¹ Egypt	50 children (4–6 years old) with active dentin caries (59 teeth in SDF group / 71 in NSF group)	To compare <i>S. mutans</i> and lactobacilli counts in dentin caries after one month of treatment with NSF or SDF	38% SDF vs NSF After 1 month	median log ₁₀ CFU SDF at baseline: 4.85(0.52) after 1 month: 4.30(0.48) (p-value<0.0001)	median log ₁₀ CFU SDF at baseline: 4.48(1.00) after 1 month: 3.95(4.70) (p-value<0.0001)	Both SDF and NSF significantly reduced of <i>S. mutans</i> and lactobacilli counts within 1 month, with no significant differences between groups.
				Total viable counts with log ₁₀ CFU median (IQR)	Total viable counts with log ₁₀ CFU median (IQR)	
				NSF at baseline: 4.70 (0.70) after 1 month: 3.70(4.30) (p-value<0.0001)	NSF at baseline: 4.70 (0.90) after 1 month: 0.00(4.30) (p-value<0.0001)	

Table 2 (continued)

Study, Year Country	Number and age range of participants Type of sample	Objective	SDF vs competitor Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Langpoklakpam et al., 2022 ²⁶	87 children (3–9 years old) using unstimulated saliva samples	To compare the efficacy of SDF and SDF with KI on <i>Lactobacillus</i> count	38.0% SDF vs 38.0% SDF+KI Immediately, 1 month, and 3 months post application	N/A	mean CFU at baseline: 38.0% SDF (120.87±83.39) SDF+KI (97.93±92.18) (p-value>0.05) immediately: 38.0% SDF (2.13±3.11) SDF+KI (1.80±2.73) (p-value>0.05)after 1 month: 38.0% SDF (11.67±9.36) SDF+KI (9.40±8.71) (p-value>0.05) after 3 months: 38.0% SDF (22.47±18.26) SDF+KI (18.00±15.95) (p-value>0.05)	Both 38.0% SDF and SDF+KI were effective against <i>Lactobacillus</i> over 3 months, with no significant difference between groups at any time point.

Table 2 (continued)

Study, Year Country	Number and age range of participants Type of sample	Objective	SDF vs competitor Follow-up interval	Results		Effect/Conclusion
				<i>S. mutans</i>	<i>Lactobacillus</i>	
Verma et al., 2022 ²⁷ India	54 children (12–14 years old) using unstimulated saliva samples	To evaluate antibacterial, antiplaque and anticaries effects of SDF and NaF in children	38.0% SDF vs NaF At baseline, after 3 days, 3 months and 6 months, post application	Total viable counts with CFU (mean difference±SE) Mean difference between SDF and NaF group: at baseline: (392.222±91.195) (p-value<0.001) after 3 days: (57.333±69.262) (p-value=0.688) after 3 months: (15.889±27.148) (p-value=0.829) after 6 months: (5.278±29.899) (p-value=0.983)	N/A	Both SDF and NaF significantly reduced <i>S. mutans</i> counts over time, with no significant difference between them.

CFU=colony forming units, CHX=chlorhexidine, KI=potassium iodide, NaF=sodium fluoride varnish, SE=standard error, NSF=nano silver fluoride, SDF=silver diamine fluoride, IQR=interquartile range, N/A=not applicable, S.D.=standard deviation

Table 3 Study characteristics and reported results of the antimicrobial efficacy of SDF from other types of studies

Study, Year Country	Number and age range of participants	Type of study	Objective	SDF vs competitor Follow-up interval	Results		Effect/Conclusion
					<i>S. mutans</i>	<i>Lactobacillus</i>	
Karched et al., 2019 ¹² Kuwait	5 adults with at least 5 carious lesions. Dentin samples collected before and after treatment	Non-randomized controlled trial	To assess the antimicrobial efficacy of SDF and SDF+KI by comparing total viable counts before and after antimicrobial treatment	38% SDF vs SDF+KI vs 2.0% CHX	median CFU 38.0% SDF at baseline: (3.5×10 ³) post-treatment: (0.0) (p-value<0.05)	N/A	38.0% SDF and SDF+KI showed greater antimicrobial effect against <i>S. mutans</i> than 2.0% CHX.
		In vivo		Immediately	38.0% SDF+KI at baseline: (6.78×10 ³) post-treatment: (0.0) (p-value<0.05)		
Mitwalli et al., 2019 ²⁹ USA	20 patients with at least one cavitated root/cervical carious lesion, supragingival plaque collected	In vivo study	To assess the effect of SDF on microbial profiles present in plaque from root/cervical carious lesions before and one month post treatment	38.0% SDF After 1 month	2.0% CHX at baseline: (1.66×10 ³) post-treatment: (1.16×10 ³) (p-value>0.05)	The relative abundance of <i>S. mutans</i> decreased from 10.0% to 6.0% one-month post treatment (p-value=N/A)	The relative abundance of some acid-producing species, particularly <i>S. mutans</i> , was reduced after SDF treatment.
					16S rDNA sequencing	N/A	

Table 3 (continued)

Study, Year Country	Number and age range of participants Type of sample	Type of study	Objective	SDF vs competitor Follow-up interval	Results		Effect/Conclusion
					<i>S. mutans</i>	<i>Lactobacillus</i>	
Mei et al.,2020 ³⁰ Hong Kong	14 children (5 years old) with early childhood caries, plaque from carious lesions collected	In vivo study	To investigate the microbiome profile and relative abundance changes in plaque following SDF treatment	38.0% SDF At baseline, after 2 weeks and 12 weeks post application	16S rRNA gene sequences to operational taxonomic units (OTUs) OTUs In arrested caries, at baseline: 30,944 at week 2: 36,946 at week12: 13,047 In active caries, at baseline: 30,944 at week 2: 20,869 at week 12: 12,405	16S rRNA gene sequences to operational taxonomic units (OTUs) OTUs In arrested caries, at baseline: 22 at week 2: 10 at week 12: 23 In active caries at baseline: 22 at week 2: 10,891 at week 12: 4,229	After SDF treatment, <i>S. mutans</i> levels decreased in both arrested and active caries, while <i>Lactobacillus</i> decreased in arrested caries but increased in active caries.
Chakraborty et al.,2021 ²⁸ India	20 children (3–10 years old), unstimulated saliva samples collected	In vivo study	To assess the efficacy and performance of SDF in inhibiting the <i>S. mutans</i> count in saliva immediately after application of SDF, and after 1, 3, and 6 months of each patient	38.0% SDF Immediately, after treatment, and at 1-, 3-, and 6-months post treatment	Total viable counts with CFU (mean±S.D.) mean CFU 38.0% SDF at baseline: (406.80±120.92) immediately: (178.85±66.66) after 1 month: (243.40±71.90) after 3 months: (292.35±89.15) after 6 months (341.75±103.61) (p-value<0.05)	N/A	The best inhibitory effect was observed in 3 months, suggesting the quarterly application of SDF is an optimal choice.

CFU=colony forming units, CHX=chlorhexidine, KI=potassium iodide, NaF=sodium fluoride varnish, NCTC=National Collection of Type Cultures, NSF=nano silver fluoride, SDF=silver diamine fluoride, N/A=not applicable, OTU=operational taxonomic unit, rDNA=ribosomal deoxyribonucleic acid, rRNA=ribosomal ribonucleic acid

study, bias in the classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in the measurement of outcomes, and bias in the selection of the reported results¹¹. Each domain was rated as having a low, moderate, or serious risk of bias. Where insufficient methodological information was provided, the domain was rated as no information. The overall risk of bias of each study was determined using the highest level of risk identified among the domains.

Results

Selection and characteristics of included studies

A total of 361 records were retrieved from the electronic database search. After removing the duplicates, 174 articles remained. Of these, 104 were excluded during the initial screening for not meeting the inclusion criteria, and 32 more were excluded after reviewing titles and abstracts. Two full-text articles were unavailable. After the full-text screening of 36 articles, six were excluded for lacking data on the effects of SDF on *S. mutans* or *Lactobacillus*, and two were excluded due to insufficient antimicrobial outcomes. One focused on radiation-induced caries, while another assessed only the cytotoxicity of SDF. Four studies lacking details on the SDF concentration and follow-up interval were also excluded. Ultimately, 24 studies met the inclusion criteria and were included in this review. One study¹² employed both an in vitro design and a non-randomised controlled trial (Figure 1).

Seventeen in vitro studies^{2,4,5,12-24} examined the antibacterial effects of SDF compared with various agents against *S. mutans*, with some also evaluating *Lactobacillus* or *L. acidophilus*. The agents included silver fluoride (AgF), silver nitrate (AgNO₃), chlorhexidine (CHX), sodium fluoride varnish (NaF), ammonium hexafluorosilicate (AHF), and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). Outcomes assessed including colony forming units (CFU), biofilm viability, zone of inhibition

(ZOI), minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and bacterial growth via microscopy. SDF concentrations, exposure times, and evaluation time points of the test agents varied across studies (Table 1).

The review also covered the antibacterial effectiveness of SDF in vivo studies, comprising four^{1,25-27} (Table 2), one non-randomised controlled trial¹², and three observational²⁸⁻³⁰ (Table 3). These studies involved children aged 3–14 years with some adult participants. Sample sizes ranged from five to 87. Various biological samples were analysed, including saliva and dental plaque, following treatment with 38.0% SDF either alone or in combination with KI. Comparators (control) included nano silver fluoride (NSF), CHX, and NaF varnish. The time interval between treatment and outcome measurement varied from immediately post-treatment to 6 months, with most studies reporting outcomes at 1-, 3-, and 6-month intervals.

Most of the studies were conducted in Hong Kong^{5,19,20,23,30,31}, followed by Brazil^{4,14,15,25} and India^{18,26-28}, the USA^{17,22,29}, China^{2,24}, Egypt¹, Saudi Arabia¹³, Kuwait¹², Turkey²¹, and Indonesia¹⁶. The outcome measures evaluated the antibacterial efficacy of SDF and other agents using bacterial count, ZOI, MIC, MBC, bacterial sequencing, dead/live cell ratio, and bacterial morphology analyses. The most common measure was the evaluation of the mean log CFU^{1,2,5,12,13,19,21-28}, followed by ZOI^{4,12,16-18}, while some studies examined the dead/live bacteria^{2,5,19,20,23,24,31}, MIC/MBC¹⁵, MID¹⁴, cell morphological changes^{2,19,24}, and relative abundance of bacteria^{29,30}.

The antibacterial efficacy of SDF

Concentration of SDF

The antibacterial efficacy of SDF varied with concentration across the included studies. De Almeida et al.¹⁴ compared 12.0% and 30.0% SDF and found that 30.0% SDF exhibited a greater inhibition zone against *S.*

mutans (11.00 mm) than 12% SDF (9.70 mm) and 0.12% CHX (9.20 mm) at all tested contact times, indicating a concentration-dependent effect. Similarly, Favaro et al.⁴ reported that 30.0% SDF exhibited the largest inhibition zone compared with CHX, AgF, and Ag alone, confirming its superior antibacterial potential among tested agents. In contrast, most in vitro^{2,5,12,13,15–24,30,31} and clinical studies^{1,12,26–30} investigated 38.0% SDF concentration, which consistently demonstrated the strongest antibacterial activity against *S. mutans* and *Lactobacillus*. This concentration resulted in significant reductions in bacterial viability and CFU counts, as well as visible biofilm disruption and higher dead-to-live bacterial ratios under microscopy. These findings suggest that increasing SDF concentration enhances its antibacterial efficacy, with 38.0% SDF exhibiting stronger antibacterial effects against *S. mutans* and *Lactobacillus*, and support its clinical preference in the dental practice.

Follow-up interval post SDF application

Several studies have investigated the antibacterial efficacy of SDF based on the time interval between its application and post-treatment assessments. Short-term outcomes were observed immediately¹² to 1 month post-treatment^{1,29}, while longer-term follow-ups ranged from 3 to 6 months^{25–28,30}. In an in vitro study, Mei et al.³¹ observed that SDF inhibited cariogenic biofilm formation. The inhibition of *S. mutans* growth was obvious in the first 7 days after SDF application based on a very low CFU count. However, the CFU increased over time, indicating that repeated SDF application may be necessary to maintain its inhibitory effect on biofilm formation. In clinical settings, Mei et al.³⁰ found the relative abundance of *S. mutans* and *Lactobacillus* decreased from week 2 to week 12 following SDF application in the arrested caries group, whereas *Lactobacillus* levels increased in active caries after 12 weeks post-treatment. Furthermore, Garrastazu et al.²⁵ and Verma et al.²⁷ also reported significant reductions in *S. mutans* counts from 1 to 6 months after SDF application.

However, Chakraborty et al.²⁸ observed a gradual decline in the inhibitory effect over time (mean CFU: 243.40±71.90 at 1 month, 292.35±89.15 at 3 months; 341.75±103.61 at 6 months). Overall, a single application of 38.0% SDF demonstrated sustained antimicrobial effects for up to 3–6 months, although reapplications may be required to optimise the long-term efficacy.

Combination and comparison of SDF with other antimicrobial agents

Numerous studies have investigated the antibacterial efficacy of SDF, either in combination with or in comparison to other antimicrobial agents, as summarised below.

SDF vs Chlorhexidine (CHX)

In vitro studies demonstrated that SDF had greater antibacterial activity than 0.12–0.2% CHX, showing larger inhibition zones, lower MIC/MBC values, and greater reductions in *S. mutans* counts^{4,12,15,21}. Hamama et al.²⁰ reported that 38.0% SDF significantly increased the percentage of dead bacteria in dentine (56.1±13.0%) compared to 2.0% CHX (19.0±10.8%). However, clinical findings are mixed. Garrastazu et al.²⁵ found no significant difference between 30.0% SDF and 1.0% CHX gel in reducing salivary *S. mutans* in children over 30 and 90 days. While Karched et al.¹² observed greater bacterial reduction with 38.0% SDF than 2.0% CHX in adult carious lesions. Overall, while laboratory data strongly support the enhanced antibacterial potency of SDF, clinical evidence remains limited and inconclusive, highlighting the need for further well-designed trials.

SDF vs Sodium Fluoride varnish and Fluoride gel (NaF and APF)

Several studies have compared the effectiveness of SDF with NaF and APF gel against *S. mutans* and *Lactobacillus*. Savas et al.²¹ reported that 38% SDF exhibited significantly higher antibacterial activity against *S. mutans*

biofilms on enamel in vitro than APF gel, reducing the mean CFU to zero compared with 2.62×10^8 . Yu et al.²³ similarly found that SDF reduced mean $\log_{10}$ CFU to 4.49 ± 0.57 on dentin blocks, compared with 6.56 ± 0.39 for 5% NaF varnish. Annisa et al.¹⁶ also reported a larger inhibition zone for SDF against *S. mutans* (9.55 mm) than 5%NaF (4.13 mm). However, an in vivo study by Verma et al.²⁷ found no significant differences between 38.0% SDF and 5%NaF varnish in reducing salivary *S. mutans* counts over six months in children, indicating similar clinical effectiveness despite in vitro superiority. These findings highlight the need for further in vivo studies to confirm the advantages of SDF.

SDF vs Casein phosphopeptide–amorphous calcium phosphate (CPP–ACP)

Limited evidence from a single in vitro study by Ali et al.¹³ compared 38.0% SDF with CPP–ACP using an *S. mutans* biofilm–caries model. SDF showed complete eradication of *S. mutans* (mean CFU: 0.00), while CPP–ACP had a significantly higher mean CFU ($96 \times 10^6 \pm 34.64 \times 10^6$). The study indicated superior antibacterial efficacy of SDF, while the action of CPP–ACP was attributed to its remineralising effect rather than antibacterial action. Further studies are warranted to explore the potential synergistic effect of combining SDF with CPP–ACP.

SDF vs other silver components: Nano Silver Fluoride (NSF), Silver Fluoride (AgF), and Silver Nitrate (AgNO₃)

Several studies have compared the antimicrobial efficacy of SDF with other silver compounds, such as NSF, AgF, and AgNO₃, against cariogenic bacteria and reported mixed results^{4,15,17}. Targino et al.¹⁵ found no significant difference between 38.0% SDF and NSF against *S. mutans* (MICs: 33.33 ± 14.43 and 33.54 ± 14.52 , respectively; MBCs: 50 for both; p–value <0.005). Lou et al.¹⁷ reported larger inhibition zones for 38.0% SDF against both *S. mutans* and *L. acidophilus* (mean(±S.D.): 395.8 ± 15.1 mm²; 362.6 ± 23.7

mm² respectively) compared with AgF (423.6 ± 82.4 mm²; 208.7 ± 13.9 mm² respectively) and AgNO₃ (177.8 ± 14.90 mm²; 171.2 ± 20.8 mm² respectively with p–value<0.005). Similarly, Favaro et al.⁴ observed larger zones for 30.0% SDF against *S. mutans* (5.94 mm) than AgF (2.67 mm) and Ag nanoparticles (2.66 mm) (p–value<0.05). Clinical findings from Ammar et al.¹ showed significant reductions in *S. mutans* and *Lactobacillus* counts in dentin caries after one month of treatment with both SDF and NSF, with median $\log_{10}$ CFU decreasing from 4.85 to 4.30 (*S. mutans*) and 4.48 to 3.95 (*Lactobacillus*) in the SDF group, and from 4.70 to 3.70 (*S. mutans*) and 4.70 to 0.00 (*Lactobacillus*) in the NSF group, indicating comparable antibacterial efficacy.

SDF vs Ammonium Hexafluorosilicate (AHF)

Evidence comparing the antibacterial efficacy of SDF and AHF against *S. mutans* remains limited. Annisa et al.¹⁶ using the agar disk diffusion method found that 38.0% SDF produced a larger mean ZOI diameter (9.55 mm) against *S. mutans* compared to AHF (8.86 mm), indicating greater antibacterial activity. Savas et al.²¹ found that SDF completely inhibited bacterial growth (mean CFU=0.0), whereas AHF exhibited higher bacterial counts (2.65×10^8). However, these findings are based on two studies, underscoring the need for further investigations to confirm these results and explore potential synergistic effects between SDF and AHF.

SDF vs laser treatment

Research has shown that combining SDF with laser treatment can enhance its antibacterial efficacy against cariogenic bacteria^{2,24}. Two in vitro studies investigated the effects of SDF used with CO₂ and 445 nm diode lasers against *S. mutans* biofilms. Zhao et al.² reported a greater reduction in *S. mutans* CFUs with 38.0% SDF combined with CO₂ laser (mean $\log_{10}$ CFU: 2.2 ± 1.1) compared to the SDF alone (mean $\log_{10}$ CFU: 2.9 ± 0.8). Similarly, Xue et al.²⁴ found that the combination of SDF with a 445–nm

diode laser yielded a lower mean $\log_{10}$ CFU of *S. mutans* (4.21 ± 0.26) than SDF alone (4.54 ± 0.15). SEM and CLSM analyses corroborated these findings, showing marked disruption of bacterial biofilms and a higher proportion of non-viable cells in the combined treatment groups.

SDF vs Potassium Iodide (KI)

Studies evaluating the combination of SDF with potassium iodide (KI) against cariogenic bacteria have reported inconsistent findings. In vitro, Hamama et al.²⁰ stated that SDF+KI effectively reduced *S. mutans* in infected dentinal tubules. In contrast, Vinson et al.²² reported higher *S. mutans* biofilm disruption with SDF alone compared to SDF+KI. An in vivo study by Langpoklakpam et al.²⁶ found no difference in *Lactobacillus* counts between the SDF and SDF+KI groups after three months, and Karched et al.¹² similarly reported comparable *S. mutans* reductions between groups. Overall, the added benefit of KI remains inconclusive.

SDF vs Chitosan

One in vitro study investigated the effectiveness of 38.0% SDF and chitosan, and in combination against *S. mutans*¹⁸. Different volumes (30 μ l, 60 μ l, 90 μ l) of 38.0% SDF, and 2.0% and 3.0% chitosan were used; 38.0% SDF alone at 90 μ l showed the highest mean ZOI (40.22 mm), followed by (38.55 mm) at 60 μ l and (24.36 mm) at 30 μ l. Chitosan alone showed the lowest mean ZOI at 2.0% and 3.0%. at all volumes¹⁸. However, there was a comparable mean ZOI between the group of 38.0% SDF alone at 30 μ l and the group of 3.0% chitosan and 38.0% SDF in combination at 30 μ l (23.23 mm)¹⁸.

Quantitative analysis

Quantitative assessment of in vitro studies revealed that 38.0% SDF demonstrated strong antibacterial activity against *S. mutans*. Across nine studies, *S. mutans* CFU counts ranged from 0.0 to $4.54 \pm 0.15 \log_{10}$ ^{2,5,13,19,21–24,31}.

The ZOI ranged between 9.55 mm and 40.22 mm (mean $\approx 24.9 \pm 10.5$ mm)^{4,12,16–18}, while the MIC and MBC averaged $33.3 \pm 14.4 \mu\text{g/mL}$ and $50 \mu\text{g/mL}$, respectively¹⁵. The CLSM analyses indicated a dead: live bacterial ratio between 1.42 ± 0.11 and 6.74 ± 5.29 ^{2,5,19,20,23,31}. Whereas for *Lactobacillus*, CFU counts across two studies ranged from 0.43 ± 0.37 to $1.80 \pm 0.28 \log_{10}$ ^{5,31}. CLSM ratios ranged between 2.19 ± 0.55 and 6.74 ± 5.29 , confirming substantial bacterial inactivation^{5,31}.

In vivo studies similarly demonstrated pronounced suppression of *S. mutans* following 38.0% SDF application. CFU values ranged from 0.0 (post-treatment) to $2.94 \times 10^6 \pm 3.09$ at three months, with a median of 4.30 (0.48) $\log_{10}$ CFU at one month^{1,12,25,27,28}. Sequencing-based relative abundance analyses showed a decline from 10% to 6% (OTUs=13.047), indicating persistent antibacterial effects^{29,30}. While for *Lactobacillus*, initial suppression was observed at one month (11.67 ± 9.36), followed by an increase at three months (22.47 ± 18.26), with a median of 3.95 (4.70) $\log_{10}$ CFU at one month^{1,26}. Sequencing data (OTUs=23 at three months) indicated minimal long-term alteration in microbial diversity, suggesting partial resistance and recolonization³⁰.

Due to heterogeneity in study designs, outcome measures, and reporting formats, data were summarized descriptively using ranges and mean estimates rather than quantitative meta-analysis as presented in Table 4.

Risk of bias within the studies

The methodological quality of the included in vitro studies was evaluated using the QUIN tool. Overall, the studies demonstrated a moderate risk of bias, with total scores ranging from 46% to 88%. Most studies clearly stated their objectives and used appropriate methodologies; however, sample size justification, operator calibration, blinding, and assessor details were frequently underreported. These limitations are common in in vitro designs where randomisation and blinding are often impractical. Remarkably, Xue et al.²⁴, Favaro et al.⁴, and

Tables 4 Quantitative summary of SDF antibacterial efficacy against *S. mutans* and *Lactobacillus*

Bacteria	Study design	Outcome Measure	Number of studies	Range (Mean±S.D.)	Median (IQR)
<i>S. mutans</i>	in vitro	CFU	9	0.0–4.54±0.15	NR
		ZOI (mm)	5	9.55–40.22	5.94
		MIC (µg/mL)	1	33.3±14.4	NR
		MBC (µg/mL)	1	50	NR
		CLSM (dead:live ratio)	6	1.42±0.11–6.74±5.29	NR
		MID (mm ²)	1	9.0 (12% SDF), 11.0 (30 % SDF)	NR
<i>Lactobacillus</i>	in vitro	CFU	2	0.43±0.37–1.80±0.28	NR
		CLSM (dead:live ratio)	2	2.19±0.55–6.74±5.29	NR
<i>S. mutans</i>	in vivo	CFU	5	0.0 (post treatment) – 2.94x10 ⁶ ±3.09 (at 3 months)	4.30 (0.48) at 1 month
		Relative abundance (sequencing)	2	↓10% to 6%; OTUs=13.047	NR
<i>Lactobacillus</i>	in vivo	CFU	2	11.67±9.36 (at 1 month) – 22.47±18.26 (at 3 months)	3.95 (4.70) at 1 month
		Relative abundance (sequencing)	1	OTUs=23 (at 3 months)	NR

CFU=colony-forming units, CLSM=confocal laser scanning microscopy, IQR=interquartile range, MBC=minimum bactericidal concentration, MIC=minimum inhibitory concentration, MID=maximum inhibitory dilution, NR=not reported, OTU=operational taxonomic unit, S.D.=standard deviation, SDF=silver diamine fluoride, ZOI=zone of inhibition

Zhao et al.² achieved a low risk of bias (88%, 88%, 71% respectively) due to comprehensive reporting and robust analyses. Conversely, de Almeida et al.¹⁴ and Annisa et al.¹⁶ scored below 50%, reflecting a high risk of bias due to limited methodological transparency and inadequate statistical analysis (Table 5).

The risk of bias for the included RCTs was assessed using the ROB 2.0 tool across five domains. Overall, the trials demonstrated low to high risk of bias, with variability observed among domains. Only Ammar et al.¹ exhibited a low risk of bias in all domains, reflecting strong methodological quality. Garrastazu et al.²⁵ showed some concerns related to incomplete reporting of allocation procedures, although other domains were at low risk. In contrast, Langpoklakpam et al.²⁶ and Verma et al.²⁷ were rated as high risk of bias due to missing information on randomisation procedures, deviations from intended interventions, and selective outcome reporting (Figure 2).

The non-randomised studies were evaluated using the ROBINS-I tool. The overall assessment showed a serious risk of bias across all included studies. Each study showed serious bias due to confounding and moderate bias in participant selection and outcome measurement, which were the most common sources of concern. Other domains, such as classification of interventions, deviations from intended interventions, and handling of missing data, were generally rated low risk, indicating adequate procedural control. All four studies (Karched et al.¹², Mitwalli et al.²⁹, Mei et al.³⁰, Chakraborty et al.)²⁸ received an overall “serious” judgment owing to incomplete control of confounders and insufficient reporting of participant selection methods (Figure 3).

Discussion

In this systematic review, the antimicrobial efficacy of SDF against *S. mutans* and *Lactobacillus* was assessed

Table 5 Risk of bias of included in vitro studies

Study	Clear aims/ objectives	Sample size calculation	Sampling technique	Comparison group (s)	Methodology detail & standardization	Operator details	Randomisation	Measurement method (validated tools)	Outcome assessor details	Blinding	Statistical analysis	Presentation of results	Total score	Final score (%)
De Almeida et al., 2011 ¹⁴	2	0	1	2	2	0	0	1	0	0	1	2	11	46 ^c
Chu et al., 2012 ¹⁹	2	2	2	2	2	0	0	2	0	0	2	2	16	67 ^b
Mei et al., 2013 ³¹	2	0	1	2	2	1	0	2	1	1	2	2	16	67 ^b
Mei et al., 2013 ⁵	2	0	2	2	2	0	0	2	0	0	2	2	14	58 ^b
Targino et al., 2014 ¹⁵	2	0	2	2	2	0	0	2	0	0	2	2	14	58 ^b
Hamama et al., 2015 ²⁰	2	0	2	2	2	0	0	2	0	0	2	2	14	58 ^b
Savas et al., 2015 ²¹	2	0	1	2	2	0	1	2	0	0	2	2	14	58 ^b
Annisa et al., 2017 ¹⁶	2	0	1	2	1	1	0	2	0	0	1	2	11	46 ^c
Vinson et al., 2018 ²²	2	0	1	2	2	0	0	2	0	0	2	2	13	54 ^b
Lou et al., 2018 ¹⁷	2	0	2	2	2	0	0	2	0	0	2	2	14	58 ^b
Yu et al., 2018 ²³	2	0	2	2	2	0	2	2	0	0	2	2	16	67 ^b
Karched et al., 2019 ¹²	2	0	1	2	2	1	0	1	1	0	1	2	13	54 ^b
Preethy et al., 2020 ¹⁸	2	0	1	2	2	0	0	2	0	0	1	2	12	50 ^b
Zhao et al., 2021 ²	2	1	2	2	2	0	2	2	0	0	2	2	17	71 ^a
Xue et al., 2022 ²⁴	2	2	2	2	2	1	2	2	1	1	2	2	21	88 ^a
Favaro et al., 2022 ⁴	2	2	2	2	2	1	0	2	2	2	2	2	21	88 ^a
Ali et al., 2023 ¹³	2	2	2	2	2	0	0	1	0	0	2	2	15	63 ^b

Criteria: adequately specified=2 points, inadequately specified=1 point, not specified=0 points, not applicable=excluded from the calculation
 Risk-of-bias grade judgment was based on the QUIN tool by Sheth et al.⁹ and Kendell-Wall et al.¹⁰, Final score (%)=(total score×100)/
 (2×number of applicable criteria). Risk-of-bias categories: ^alow (final score >70%), ^bmoderate (final score 50–70%), ^chigh (final score <50%).

		Risk of bias domain					
		D1	D2	D3	D4	D5	Overall
Study	Garrastazu et al., 2020						
	Langpoklakpam et al., 2022						
	Verma et al., 2022						
	Anmmar et al., 2022						
Domains		Judgement					
D1: Bias arising from the randomization process		High					
D2: Bias due to deviations from intended interventions		Some concerns					
D3: Bias due to missing outcome data		Some concerns					
D4: Bias in measurement of the outcome		Some concerns					
D5: Bias in selection of the reported result		Low					

RoB 2=Risk of Bias 2

Figure 2 Summary of risk of bias assessment using RoB2 for randomised controlled trials

		Risk of bias domain							
		D1	D2	D3	D4	D5	D6	D7	Overall
Study	Karched et al., 2019								
	Mitwalli et al., 2019								
	Mei et al., 2020								
	Chakraborty et al., 2021								
Domains		Judgement							
D1: Bias due to confounding		Serious							
D2: Bias due to selection of participants		Moderate							
D3: Bias in classification of interventions		Moderate							
D4: Bias due to deviations from intended interventions		Moderate							
D5: Bias due to missing data		Moderate							
D6: Bias in measurement of outcomes		Low							
D7: Bias in selection of reported results		Low							

ROBINS-I=Risk of Bias in non-randomized studies of Interventions

Figure 3 Summary of risk of bias assessment using ROBINS-I for non-randomised studies

and compared with other antimicrobial agents through both in vitro and in vivo studies. Outcome measures included quantitative and qualitative assessments, such as CFU counts, MIC, MBC, and ZOI. Additionally, molecular techniques like 16S rDNA and rRNA sequencing were included to identify and classify the bacteria at the genetic level. The reviewed studies indicated that SDF inhibits the growth of cariogenic bacteria, both in the planktonic and the biofilm¹³⁻¹⁵.

Presently, SDF is considered a therapeutic agent for arresting and preventing dental caries³². SDF is very easy to apply to the tooth structure with no pain. Its application does not require any specific devices or equipment¹⁸. Additionally, it is noted that SDF promotes calcium fluoride and silver phosphate, thereby helping to strengthen dental structures¹⁸.

It is well-documented that silver compounds have superior antimicrobial properties³³. Silver has a broad-spectrum effect with excellent anti-biofilm properties. Therefore, silver ions have been incorporated into some dental materials³³. In fact, various mechanisms were proposed regarding the antimicrobial properties of silver³⁴. Silver ions can interact with the thiol group of enzymes, leading to enzyme deactivation, resulting in bacterial cell death. Further, silver ions interact with the DNA of bacterial cells, causing DNA mutation, eventually causing bacterial death³⁴. Another mechanism was proposed related to binding silver ions with bacterial cells, causing leakage or rupture of the bacterial cell membrane and subsequent bacterial death^{33,34}. Additionally, silver can form a protein-metallic complex by binding with the bacterial amino acids, leading to the accumulation of silver ions inside the bacterial cell, finally causing DNA and RNA inactivation³⁴.

According to the reviewed studies, SDF is available in different concentrations, including 12.0%, 30.0%, and 38.0%. The results indicate that the antimicrobial effect of SDF is influenced by its concentration. The results support that increasing silver ions leads to bacterial growth

suppression. The higher the concentration of SDF, the higher the reported antimicrobial effects¹⁸. A 12.0% SDF showed considerable antibacterial effects. However, 38.0% SDF produced a larger ZOI against *S. mutans*, which was even larger than CHX¹⁴.

In this review, the majority of studies tested the antibacterial effect of 38.0% SDF using different methodologies, such as CFU, biofilm imaging, and viability assays. The findings of these studies indicated that 38.0% SDF significantly reduced the viability of *S. mutans* and *Lactobacillus*. This is because SDF can cause membrane damage, the biofilm disruption of bacterial cells, and increase the dead-to-live bacteria ratio. This finding concurs with the proposed antimicrobial mechanism of SDF, where silver ions can cause the rupture of the bacterial cell membrane, leading to bacterial death³⁴. Additionally, the fluoride present in SDF can arrest dental caries by reducing the demineralisation process⁵. Nevertheless, the cytotoxicity of SDF still raises concerns regarding its use. Research showed that SDF was cytotoxic even nine weeks after SDF rinsing. The SDF was toxic to human gingival fibroblasts and could cause long-term effects^{18,35}.

Furthermore, the antibacterial effect of SDF depends not only on its concentration, but also on the interval between applications. Evidence from an in vitro study showed that SDF has an immediate antibacterial effect that is gradually reduced over time⁵. Short-term outcomes of clinical studies have demonstrated a significant antibacterial effect of SDF immediately after application¹², after 3 days²⁷ and up to one month^{1,29}. Additionally, other clinical studies support that SDF has an antibacterial effect that persists from 3 to 6 months^{25,27}. However, results regarding the persistent inhibitory effect of SDF over time were controversial. A study by Mei et al. (2020)³⁰ reported a sustained reduction in *S. mutans* in the caries active group and arrested caries group from week 2 to week 12, indicating that SDF continues to produce its antimicrobial effect against *S. mutans* even

for several weeks post-treatment. Conversely, in the arrested caries group, the level of *Lactobacillus* decreased after 12 weeks, but increased in the active caries group after 12 weeks. A similar finding was reported by^{26,28}. Chakraborty et al.²⁸ reported that *S. mutans* levels were reduced immediately post-SDF application, then gradually the level of *S. mutans* increased over the next 6 months. Langpoklakpam et al.²⁶ found that the counts of *Lactobacillus* declined immediately after SDF application, then started to increase during the next 3 months. This finding suggests that the persistent antibacterial effect of SDF may depend on the type of dental caries, bacterial colonization, and the oral hygiene of the participants. Additionally, it seems that the antibacterial effect of SDF in a single application is limited. Hence, routine reapplication is necessary to maintain its antibacterial effectiveness.

The studies included in this systematic review evaluated a range of antimicrobial agents besides SDF, including CHX, NaF, APF, CPP-ACP, silver components (NSF, AgF, and AgNO₃), AHF, and laser treatments. CHX is a synthetic antimicrobial agent known for its broad-spectrum efficacy against bacteria, fungi, yeasts, and viruses, and is widely used in caries control and periodontal therapy²¹. NaF and APF are fluoride-based agents commonly applied for caries prevention, particularly in early childhood caries¹⁹. CPP-ACP has demonstrated remineralising properties and potential in enamel repair and caries prevention³⁶. Silver-based agents (NSF, AgF, and AgNO₃) and AHF have demonstrated antimicrobial activity against *S. mutans* biofilms³⁷. Additionally, laser treatments have been investigated for their bactericidal potential and may offer a non-invasive adjunctive approach to caries management³⁸.

The findings from this review suggest that combining SDF with agents, such as NSF, KI, chitosan, or diode laser, may enhance its antibacterial efficacy compared to SDF alone^{1,18,24,26}. However, Yu et al.²³ reported that the addition of NaF reduced the antibacterial effects of SDF.

This may be due to the inactivation of bioactive silver ions, as components in the NaF varnish could bind and neutralise silver ions, limiting their interaction with bacterial cells²³. This finding is significant because it suggests that the combination of SDF with NaF may compromise the antimicrobial efficacy of SDF. The application of SDF with or without NaF was found to decrease the demineralisation of dentine caries, but SDF alone exhibited a stronger inhibition of biofilm growth than NaF³⁹. These findings suggest that although NaF may support remineralisation, its combination with SDF could compromise the antimicrobial effectiveness of SDF, potentially reducing its efficacy in caries prevention and management.

Several RCTs have evaluated the efficacy of SDF in caries management. For instance, Chibinski et al.⁴⁰ conducted a systematic review and meta-analysis confirming the effectiveness of SDF in controlling caries progression in primary teeth⁴⁰. Jain et al.³⁹ and Ruff et al.⁴¹ both conducted RCTs comparing SDF and NaF varnish in preventing new carious lesions in preschoolers, offering valuable clinical insights. These studies support the role of SDF in both the prevention and arrest of dental caries^{39,41}.

The use of SDF in caries management has been associated with certain disadvantages. A primary concern is tooth discoloration after SDF application, which has been reported in several studies^{40,42}. This discoloration, commonly observed as black or dark brown staining following application, which can be aesthetically unappealing, particularly in anterior teeth, may be less acceptable to paediatric and geriatric patients⁴². Furthermore, the bitter taste of SDF application has been reported as a disadvantage, especially in children, potentially affecting compliance and willingness for repeated treatments⁴³. Additionally, the need for retreatment to maintain efficacy, as highlighted in multiple studies, may impact long-term adherence and outcomes^{39,44}. Moreover, the potential to stain soft tissues and clothing during SDF application has

been noted as a practical concern that necessitates careful application and patient management³³. These limitations should be weighed when considering the clinical use of SDF for caries prevention and arrest.

The findings of this review should be interpreted carefully, and some limitations should be considered. First, most included studies were in vitro and relied on bacterial cultures rather than clinical trials, limiting direct clinical applicability. Significant heterogeneity was observed across studies in terms of SDF formulations, concentrations, treatment protocols, and outcome assessments. Furthermore, long-term antibacterial substantivity was inadequately addressed, and this review focused solely on *S. mutans* and *Lactobacillus*, excluding other cariogenic bacteria. The methodological quality of the evidence also presents concerns. In vitro studies showed an overall moderate risk of bias due to factors related to the lack of sample size justification, unreported assessor details, and the lack of operator calibration and blinding. Only 3 of 17 in vitro studies were rated as having a low risk of bias with comprehensive reporting^{2,4,24}, while 2 studies were judged to have a high risk of bias^{14,16}. For RCT studies, the quality was variable. Only one study achieved a low risk of bias. Other studies had limitations in the randomisation process and outcome reporting. Lastly, the included non-randomised studies generally showed a serious risk of bias. This bias was indicated due to the presence of confounding and the lack of clearly reported participant selection criteria. Despite these limitations, this review provides a comprehensive summary of the evidence.

Conclusion

This systematic review highlights the significant antibacterial efficacy of SDF against *S. mutans* and *Lactobacillus*. A 38.0% SDF concentration showed the strongest effect, with sustained outcomes of 3 to 6 months, which supports its clinical utility for caries management.

While combining SDF with other agents appears promising, further research is needed to identify optimal formulations and to evaluate the long-term outcomes. In comparative analysis, 38.0% SDF consistently outperformed NaF, CHX, and APF gels, with some evidence suggesting advantages over other silver-based agents. Overall, the strength of evidence remains moderate across most studies. In vitro studies generally exhibited a moderate risk of bias, whereas non-randomised in vivo studies and clinical trials showed higher risks due to limitations in randomisation, blinding, and control of confounding variables. Well-designed, standardised, randomised trials are needed to confirm these outcomes and to establish robust, evidence-based clinical guidelines for SDF use in caries prevention and management.

Acknowledgement

The authors gratefully acknowledge the Universiti Teknologi MARA (UiTM), Cawangan Sungai Buloh, Kampus Sungai Buloh, and the Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia, for their support of this research.

Funding sources

This work was generously supported and funded by the Research Management Institute of Universiti Teknologi MARA (UiTM), Malaysia (600-UiTMSEL (PL 5/4) (132/2022)).

Conflict of interest

None

References

1. Ammar N, El-Tekeya MM, Essa S, Essawy MM, Talaat DM. Antibacterial effect and impact on caries activity of nanosilver fluoride and silver diamine fluoride in dentin caries of primary teeth: a randomized controlled clinical trial. BMC Oral Health 2022;22:1–11. doi: 10.1186/s12903-022-02697-y.

2. Zhao IS, Xue VW, Yin IX, Niu JY, Lo ECM, Chu CH. Use of a novel 9.3- μ m carbon dioxide laser and silver diamine fluoride: Prevention of enamel demineralisation and inhibition of cariogenic bacteria. *Dent Mater* 2021;37:940–8. doi:10.1016/j.dental.2021.02.017.
3. Almoudi MM, Hussein AS, Abu Hassan MI, Mohamad Zain N. A systematic review on antibacterial activity of zinc against *Streptococcus mutans*. *Saudi Dent J* 2018;30:283–91. doi: 10.1016/j.sdentj.2018.06.003.
4. Favaro JC, Detomini TR, Maia LP, Poli RC, Guiraldo RD, Lopes MB, et al. Anticaries agent based on silver nanoparticles and fluoride: characterization and biological and remineralizing effects–An in vitro study. *Int J Dent* 2022;19:9483589. doi:10.1155/2022/9483589.
5. Mei ML, Chu C hung, Low K hung, Che C ming, Lo E chin man. Caries arresting effect of silver diamine fluoride on dentine carious lesion with *S. mutans* and *L. acidophilus* dual-species cariogenic biofilm. *Med Oral Patol Oral Cir Bucal* 2013;18:2–9. doi: 10.4317/medoral.18831.
6. Kunlaya K, Nirunsittirat A, Lampang SN, Wattanarat O. Efficacy of Silver Diamine Fluoride for Arresting Non-cavitated Lesions on Approximal Surfaces in Permanent Teeth. *J Heal Sci Med Res* 2025;43:20251176. doi:10.31584/jhsmr.20251176.
7. Wen ZT, Huang X, Ellepola K, Liao S, Li Y. Lactobacilli and human dental caries: more than mechanical retention. *Microbiology* 2022;168:001196. doi: 10.1155/2022/9483589.
8. Khurshid Z, Shabbir J, Al-Otaibi AK, Alsalem AM, Alhamdan AA, Jouhar R, et al. Role of silver diamine fluoride in dentistry. *Eur Dent Res Biomater J* 2020;1:27–31. doi https://doi.org/10.1055/s-0040-1710140.
9. Sheth VH, Shah NP, Jain R, Bhanushali N, Bhatnagar V. Development and validation of a risk-of-bias tool for assessing in vitro studies conducted in dentistry: The QUIN. *J Prosthet Dent* 2024;131:1038–42. doi: 10.1016/j.prosdent.2022.05.019.
10. Kendell-Wall R, Nguyen JT, Salleras F, Kamboj AS, Diwen Tan SA, Manish Trivedi V, et al. Antimicrobial efficacy of Odontopaste in endodontics: a systematic review. *Evid Based Dent* 2024;25:166. doi: 10.1038/s41432-024-01000-y.
11. Vishwanathaiah S, Maganur PC, Syed AA, Kakti A, Hussain Jaafari AH, Albar DH, et al. Effectiveness of silver diamine fluoride (SDF) in arresting coronal dental caries in children and adolescents: a systematic review. *J Clin Pediatr Dent* 2024;48:27–40. doi:10.22514/jocpd.2024.101.
12. Karched M, Ali D, Ngo H. In vivo antimicrobial activity of silver diamine fluoride on carious lesions in dentin. *J Oral Sci* 2019;61:19–24. doi: 10.2334/josnurd.17-0366.
13. Ali SN, Al-Ogayyel S, Farah RI. Antibacterial efficacy of silver diamine fluoride compared to casein phosphopeptide-amorphous calcium phosphate against *streptococcus mutans* in a biofilm caries model. *Pesqui Bras Odontopediatria Clin Integr* 2023;23:e220148. doi:10.1590/pboci.2023.066.
14. de Almeida LF, Cavalcanti YW, Valença AM. In vitro antibacterial activity of silver diamine fluoride in different concentrations. *Acta Odontol Latinoam* 2011;24:127–31. PMID: 22165309.
15. Targino AGR, Flores MAP, Dos Santos Jr. VE, De Godoy Bené Bezerra F, De Luna Freire H, Galembeck A, et al. An innovative approach to treating dental decay in children. A new anti-caries agent. *J Mater Sci Mater Med* 2014;25:2041–7. doi: 10.1007/s10856-014-5221-5.
16. Annisa AN, Andajani T, Sarwono AT. Effect of ammonium hexafluorosilicate on inhibiting growth of *veillonella parvula*. *Int J Appl Pharm* 2017;9:1–2. doi:10.22159/ijap.2017.v9s1.02.
17. Lou Y, Darvell BW, Botelho MG. Antibacterial effect of silver diamine fluoride on cariogenic organisms. *J Contemp Dent Pract* 2018;19:591–8. PMID: 29807972.
18. Preethy NA, Jeevanandan G, Rajeshkumar S, Subramanian EMG. Antimicrobial activity of chitosan in combination with silver diamine fluoride against *streptococcus Mutans*–an in-vitro study. *Int J Res Pharm Sci* 2020;11:5960–4. doi: 10.26452/ijrps.v11i4.3255.
19. Chu CH, Gao SS, Li SK, Wong MCM, Lo ECM. The effectiveness of the biannual application of silver nitrate solution followed by sodium fluoride varnish in arresting early childhood caries in preschool children: study protocol for a randomised controlled trial. *Trials* 2015;16:426. doi: 10.1111/j.1365-263X.2011.01149.x.
20. Hamama HH, Yiu CK, Burrow MF. Effect of silver diamine fluoride and potassium iodide on residual bacteria in dentinal tubules. *Aust Dent J* 2015;60:80–7. doi: 10.1111/adj.12276.
21. Savas S, Kucukyilmaz E, Celik EU, Ates M. Effects of different antibacterial agents on enamel in a biofilm caries model. *J Oral Sci* 2015;57:367–72. doi:10.2334/josnurd.57.367.
22. Vinson LA, Gilbert PR, Sanders BJ, Moser E, Gregory RL. Silver diamine fluoride and potassium iodide disruption of in vitro *Streptococcus mutans* biofilm. *J Dent Child* 2018;85:120–4. PMID: 30869588.

23. Yu OY, Zhao IS, Mei ML, Lo ECM, Chu CH. Caries-arresting effects of silver diamine fluoride and sodium fluoride on dentine caries lesions. *J Dent* 2018;78:65–71. doi: 10.1016/j.jdent.2018.08.007.
24. Xue VW, Yin IX, Niu JY, Lo ECM, Chu CH, Zhao IS. Effects of a 445 nm diode laser and silver diamine fluoride in preventing enamel demineralisation and inhibiting cariogenic bacteria. *J Dent* 2022;126:104309. doi: 10.1016/j.jdent.2022.104309.
25. Garrastazu MD, Mathias-Santamaria IF, Rocha RS, Diniz MB, Caneppele TMF, Bresciani E. Three-month effect of silver diamine fluoride (SDF) in salivary levels of *streptococcus mutans* in children. An exploratory Trial. *Oral Health Prev Dent* 2020;18:a43360. doi: 10.3290/j.ohpd.a43360.
26. Langpoklakpam C, Gambhir N, Gupta N, Singh R, Mittal N, Singh D. Comparative evaluation of antimicrobial efficacy of silver diamine fluoride and silver diamine fluoride with potassium iodide on candida albicans and lactobacilli count and effect on salivary pH in children—An in-vivo study. *J Pharm Negat Results* 2022;13:844–8. doi:10.47750/pnr.2022.13.S07.113.
27. Verma S, Sogi S, Chatterjee S, Sharma P, Dhindsa A, Kapoor R. Antibacterial, antiplaque and anticaries effect of silver diamine fluoride and fluoride varnish in children. *J Pharm Negat Results* 2022;13:1589–94. doi:10.47750/pnr.2022.13.S03.245.
28. Chakraborty S, Gupta N, Gambhir N, Singh R. Efficacy of silver diamine fluoride on *streptococcus mutans* count present in saliva. *Int J Clin Pediatr Dent* 2021;14:700–4. doi: 10.5005/jp-journals-10005-2037.
29. Mitwalli H, Mourao MDA, Dennison J, Yaman P, Paster BJ, Fontana M. Effect of silver diamine fluoride treatment on microbial profiles of plaque biofilms from root/cervical caries lesions. *Caries Res* 2019;53:555–66. doi: 10.1159/000499578.
30. Mei ML, Yan Z, Duangthip D, Niu JY, Yu OY, You M, et al. Effect of silver diamine fluoride on plaque microbiome in children. *J Dent* 2020;102:103479. doi: 10.1016/j.jdent.2020.103479.
31. Mei ML, Li Q li, Chu CH, Lo EM, Samaranayake LP. Antibacterial effects of silver diamine fluoride on multi-species cariogenic biofilm on caries. *Ann Clin Microbiol Antimicrob* 2013;12:1–7. doi: 10.1186/1476-0711-12-4.
32. Worthington H V, Lewis SR, Glenny AM, Huang SS, Innes NP, O'Malley L, et al. Topical silver diamine fluoride (SDF) for preventing and managing dental caries in children and adults. *Cochrane Database Syst Rev* 2024;11:CD012718. doi: 10.1002/14651858.CD012718.pub2.
33. Mungur A, Chen H, Shahid S, Baysan A. A systematic review on the effect of silver diamine fluoride for management of dental caries in permanent teeth. *Clin Exp Dent Res* 2023;9:375–87. doi: 10.1002/cre2.716.
34. Hiraishi N, Sayed M, Takahashi M, Nikaido T, Tagami J. Clinical and primary evidence of silver diamine fluoride on root caries management. *Jpn Dent Sci Rev* 2022;58:1–8. doi: 10.1016/j.jdsr.2021.11.002.
35. Fancher ME, Fournier S, Townsend J, Lallier TE. Cytotoxic effects of silver diamine fluoride. *Am J Dent* 2019 Jun;32:152–6. PMID: 31295398.
36. Manarelli MM, Delbem ACB, Lima TMT de, Castilho FCN, Pessan JP. In vitro remineralizing effect of fluoride varnishes containing sodium trimetaphosphate. *Caries Res* 2014;48:299–305. doi: 10.1159/000356308.
37. Waikhom N, Nidhi, Jabin Z, Anand A. Antimicrobial effectiveness of nano silver fluoride varnish in reducing *streptococcus mutans* in saliva and plaque biofilm when compared with chlorhexidine and sodium fluoride varnishes. *J Clin Exp Dent* 2022;4:e321. doi: 10.4317/jced.59093.
38. Cheng LL. Limited evidence suggesting silver diamine fluoride may arrest dental caries in children. *J Am Dent Assoc* 2017;148:120–2. doi: 10.1016/j.adaj.2016.11.022.
39. Jain A, Deshpande AN, Shah YS, Jaiswal V, Tailor B. Effectiveness of silver diamine fluoride and sodium fluoride varnish in preventing new carious lesion in preschoolers: A randomized clinical trial. *Int J Clin Pediatr Dent* 2023;16:1–8. doi: 10.5005/jp-journals-10005-2488.
40. Chibinski AC, Wambier LM, Feltrin J, Loguercio AD, Wambier DS, Reis A. Silver diamine fluoride has efficacy in controlling caries progression in primary teeth: a systematic review and meta-analysis. *Caries Res* 2017;51:527–41. doi: 10.1159/000478668.
41. Ruff RR, Barry-Godin T, Niederman R. Effect of silver diamine fluoride on caries arrest and prevention: The cariedaway school-based randomized clinical trial. *JAMA Netw Open* 2023;6:e2255458–e2255458. doi: 10.1001/jamanetworkopen.2022.55458.
42. Oliveira BH, Rajendra A, Veitz-Keenan A, Niederman R. The effect of silver diamine fluoride in preventing caries in the primary dentition: a systematic review and meta-analysis. *Caries Res* 2019;53:24–32. doi: 10.1159/000488686.

43. Tan H, Lo ECM, Dyson JE, Luo Y, Corbet EF. A randomized trial on root caries prevention in elders. *J Dent Res* 2010;89:1086–90. doi: 10.1177/0022034510375825.
44. Tirupathi S, Nirmala SVSG, Rajasekhar S, Nuvvula S. Comparative cariostatic efficacy of a novel nano-silver fluoride varnish with 38% silver diamine fluoride varnish a double-blind randomized clinical trial. *J Clin Exp Dent* 2019;11:e105–e112. doi: 10.4317/jced.54995.