



# The use of silver diamine fluoride to prevent/treat enamel carious lesions: a narrative review

Rasha N. AlSheikh

Restorative Dental Science, College of Dentistry, Imam Abdulrahman bin Faisal University, Dammam, Eastern Province, Saudi Arabia

## ABSTRACT

This comprehensive literature review examines the use of silver diamine fluoride (SDF) for the prevention and treatment of enamel carious lesions. SDF has been approved by different international drug associations as a caries-preventing agent to be used on deep carious lesions (dentin). However, SDF can cause staining of exposed tooth structures. Furthermore, the effect of SDF on the bond of adhesives to the tooth structure is still being determined. This review explores various studies on the use of SDF to treat enamel carious lesions, highlighting its effectiveness and preventive action. The literature suggests that SDF inhibits bacterial growth, promotes remineralization, and does not negatively affect adhesive retentions. Potassium iodide (KI) or glutathione (GSH) can reduce staining and discoloration. However, the reviewed studies have limitations. Further research, including well-designed clinical trials, is necessary to validate the findings and evaluate the long-term implications of SDF treatment. Conclusion: Despite the above-mentioned limitations, SDF shows potential as a therapy for enamel caries prevention, remineralization, and use as an adjuvant to other dental treatments, warranting further investigation and the refinement of application methods.

**Subjects** Dentistry, Drugs and Devices

**Keywords** Silver diamine fluoride, SDF, Enamel carious lesions, Tooth staining

Submitted 18 March 2024

Accepted 19 July 2024

Published 26 August 2024

Corresponding author

Rasha N. AlSheikh,  
ralsheikh@iau.edu.sa

Academic editor

Ajinkya Pawar

Additional Information and  
Declarations can be found on  
page 27

DOI 10.7717/peerj.17897

© Copyright  
2024 AlSheikh

Distributed under  
Creative Commons CC-BY-NC 4.0

OPEN ACCESS

## BACKGROUND

Silver compounds have been used for centuries in treating infections, such as ocular, surgical, oral, and other diseases. Over the last 40+ years, several *in vitro* and *in vivo* studies have investigated using a silver fluoride regimen in dentistry. *In vitro* studies found that silver diamine fluoride (SDF) inhibits plaque metabolic activity, the growth of *Streptococcus mutans*, and carious lesion progression (Thibodeau, Handelman & Marquis, 1978; Ostela & Tenovuo, 1990; Craig, Powell & Cooper, 1981). Likewise, *in vitro* studies noted that using silver compounds to treat caries in permanent or primary teeth inhibits carious lesions' spread and progression and plaque accumulation (Oppermann & Johansen, 1980; Oppermann & Rölla, 1980; McDonald & Sheiham, 1994).

Recent bibliometric studies have demonstrated an increased interest in the use of SDF globally since 2014, with a peak from 2016 to the present; this can be attributed to the global acceptance of SDF as an adjunct agent to treat tooth sensitivity and arrest and prevent dental carious lesions (cavitated or not) (Jiang et al., 2021). However, the increase

in interest in using SDF from 2019 to the present can be attributed to the COVID-19 pandemic and the ensuing limitation of available dental care.

In 2014, the US Food and Drug Administration approved SDF for treating tooth sensitivity, and experienced dentists have used SDF for caries arrest (*U.S. Food & Drug Administration, 2017*), for which it was approved by the ADA (code D-1354) (*Horst, Ellenikiotis & Milgrom, 2016; Horst, Ellenikiotis & Milgrom, 2017*). In 2017, SDF was also approved by Health Canada for use in dental care (*Lamberghini, 2017; American Dental Association, 2017*), and in 2020, SDF was found to have fulfilled the United States Institute of Medicine and the World Health Organization criteria. By 2021, the British Association of Pediatric Dentistry supported using SDF in caries treatment (*Jiang et al., 2021*).

Dental caries continues to be of high concern globally reflecting a high burden on health institutes (*Ndagire et al., 2020; Kutesa et al., 2015*). The prevalence of caries lesions both enamel and dentine continue to increase among primary and permanent teeth. A study stated that the prevalence of white spot lesions (enamel caries) was as high as 31% among children and young adults (*Massignan et al., 2016*) and another study stated a high provenance of enamel caries lesions as high as 99% in Finnish adults (*Laajala et al., 2019*). Coronal caries starts with an initial sub-clinical enamel lesion with the start of mineral loss through bacterial acid-byproducts if no prevention regimen is applied caries will progress with clinical manifestations beginning with a white lesion, followed by minor cavitation, and later reaching dentin and definite cavitation. With the latest oral health institute recommendation, it is favorable to prevent the lesion in the earliest stages possible to limit tissue loss and the need for drilling and restorations (*Featherstone, 1999; Sakulratchata et al., 2024*).

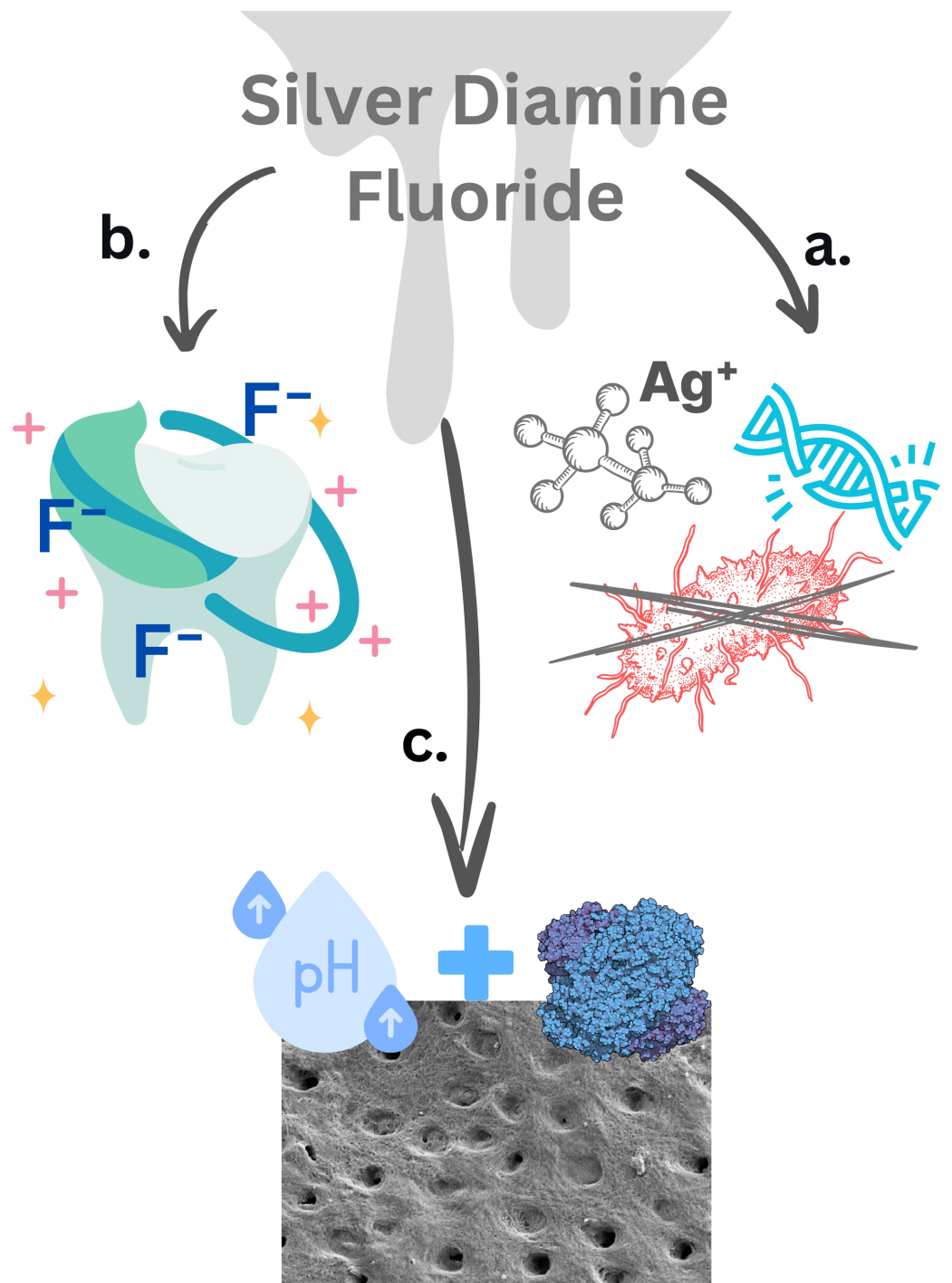
Silver diamine fluoride is a minimally invasive, safe, effective, and economical agent that prevents and arrests dental caries in primary and permanent teeth (*Rosenblatt, Stamford & Niederman, 2009*). SDF interacts with cariogenic bacteria and the tooth structure (*Fig. 1*). Different modes of action of the silver compounds with these bacteria have been proposed: silver interacting with DNA and sulfhydryl groups of proteins, DNA unwinding, cell wall synthesis, altering hydrogen bonding and inhibiting respiratory processes, and cell division. The interaction of silver with thiol groups is thought to occur through the following mechanism (*Rosenblatt, Stamford & Niederman, 2009; Liau et al., 1997*):



where A, amino acid; N, nucleic acid; SH, thymol group; Ag, silver; and X, anion.

Regarding the tooth structure, the initial interaction is through the formation of silver oxides, calcium nitrate, and silver phosphates, and, further to that, the reaction of sodium fluoride with calcium phosphate occurs to form fluorapatite and sodium hydroxide (*Rosenblatt, Stamford & Niederman, 2009*).

*Yu, Zhou & Zheng (2020)* discovered that SDF's antibacterial characteristics successfully inhibited cariogenic bacterial development and biofilm formation, mainly those of *S. mutans*. SDF can remineralize demineralized enamel and dentin, further arrest carious lesions, reduce mineral loss, and create a highly mineralized surface rich in calcium and phosphate. SDF also guards dentin collagen against deterioration by preventing collagenase formation. Furthermore, SDF can potentially offer a successful therapy for



**Figure 1** The effects of fluoride, silver nitrate, and silver diamine fluoride on bacteria and teeth. Mechanism of action of SDF: (A) silver ion actions: Ag ions bind to bacterial DNA preventing bacterial replication. Additionally, Ag ions attached to bacterial cell walls lead to cell damage and lysis. (B) Fluoride ion action: fluoride ions enhance the remineralization of the tooth enamel by forming fluorapatite, which is more resistant to acid attack than (continued on next page...)

Full-size DOI: 10.7717/peerj.17897/fig-1

**Figure 1 (...continued)**

hydroxyapatite. With calcium and phosphate ions in the saliva calcium fluoride-like deposits on the enamel and dentin act like fluoride reservoirs. (C) Protein coagulation and lesion stabilization: the high PH of SDF causes the proteins in the demineralized dentin to coagulate and denature these proteins precipitate and block open dentinal tubules, thus act as barriers to protect soft dentin and reduce sensitivity (Rosenblatt, Stamford & Niederman, 2009; Liao et al., 1997). Created using Canva (<https://www.canva.com>).

enamel carious lesions because it functions as a bactericidal agent, inhibits demineralization, and encourages remineralization (Yu, Zhou & Zheng, 2020).

Though there is an increase in the SDF literature with some focusing on its use with enamel caries, there are limited reviews summarizing the findings and suggesting guidelines to the use of SDF for enamel lesions given that the common standard use of SDF is with dentin and primary lesions. The primary objective of this review was to comprehensively assess the existing literature on the application of silver diamine fluoride (SDF) as a treatment modality for enamel caries. The intended audience for this literature review are dentists concerned with caries prevention and oral public health, restorative dentists, and pediatric dentists as well as researchers in cariology and caries management.

## SURVEY METHODOLOGY

The literature search was conducted in MEDLINE and PubMed for articles published in WoS and/or Scopus-indexed journals after the year 2018, and to ensure a thorough review, the following search strategies were employed:

- A. Electronic databases: Comprehensive searches were conducted using academic databases: PubMed, Scopus, Web of Science, MEDLINE, articles with relevance and significance and were used in this article review.
- B. Keywords: A combination of keywords—“silver diamine fluoride,” “enamel caries,” “treatment,” and “effectiveness”—was used to identify relevant articles.
- C. Inclusion criteria: Studies in English published in the last ten years were included. In vitro studies, clinical trials, reviews, and observational studies were targeted.
- D. Exclusion criteria: Studies with no enamel samples, those with insufficient data, case reports, and studies not directly related to the topic were excluded.

All collected articles were inserted into endnote to review the title and abstract of the publication and accordingly, duplicates were removed. After ensuring the relevance of the abstract, each publication was retrieved and inspected thoroughly. The initial search generated 285 articles. After eliminating duplicates, articles not in English or those with English translations, non-retrievable articles, and other unrelated articles, the number was reduced to 30. Table 1 summarizes the articles ultimately included. Table 1 summarizes the type of publications/study, year of publication, type of SDF, and if any other treatment was compared to SDF as well as the article conclusion.

This review used published data, so ethical approval was not required.

**Table 1** List of articles used for this review.

Ref.	Author	Year	Type of SDF used	Comparison	Study design	Sample size	Aging process	Duration of study	Conclusion
<b>Studies investigating enamel remineralization, mineral content, or hardness</b>									
51	<a href="#">Akyildiz &amp; Sönmez (2019)</a>	2019	Nano silver fluoride (experimental solution) Silver diamine fluoride	Sodium fluoride	<i>In vitro</i> human enamel blocks	180 divided into 4 groups	pH-cycling model	7 days	There were statistically significant differences among all groups. Microhardness: NaF>SDF>NSF>Control. Additional investigation is needed.
24	<a href="#">Abdelaziz et al. (2022)</a>	2022	Silver diamine fluoride 38% (Advantage Arrest™; Elevate Oral Care)	Number of SDF applications: 1 vs. 2	<i>In vitro</i> bovine enamel and dentin blocks	46 samples per group	None	12 weeks	SDF application showed significant changes in reflectivity, OP, and permeability in both sound and demineralized dentin.
49	<a href="#">Alcorn et al. (2022)</a>	2022	38% SDF (Advantage Arrest; Elevate Oral Care)	FV Prevident 5% NaF Varnish (Colgate), KF (Sigma–Aldrich), AgNO <sub>3</sub> (Sigma–Aldrich), and deionized water	<i>In vitro</i> bovine enamel blocks	180, 10 groups each with 18 samples	pH-cycling model	2 weeks	FV may be better suited than SDF for treating early, incipient, non-cavitated, white-spot, enamel carious lesions.
48	<a href="#">Hamdi et al. (2022)</a>	2022	38% silver diamine fluoride followed by potassium iodine (SDF-KI)	CPP-ACP (amorphous calcium phosphate-nanocomplexes), and TCS (tricalcium silicate paste)	<i>In vivo</i>	45 patients in the age range of 15–50 years (in total, 90 teeth)	<i>In vivo</i> study	24 months	Annual application of SDF-KI compared to twice-daily application of CPP-ACP or TCS showed a significant remineralization effect after 24 months ( $p < 0.001$ ). There was a significant difference between (SDF-KI and CPP-ACP) and (SDF-KI and TCS) at the different follow-up periods of 3, 6, 12, and 24 months ( $p < 0.001$ ).
52	<a href="#">Heukamp et al. (2022)</a>	2022	Riva Star (silver diamine fluoride)	Bifluorid 12 (NaF, CaF <sub>2</sub> ), Cervitec F (CHX, CPC, NH <sub>4</sub> F), and negative control	<i>In vitro</i> human enamel	50 human tooth samples	pH cycling	28 days	The fluorescence behavior of SDF varnish on smooth surfaces with artificial initial enamel lesions was significantly lower compared to Cervitec F varnish after short-term use (SDF showed the lowest fluorescence values).
15	<a href="#">Hiraishi et al. (2022)</a>	2022	38% SDF	–	<i>In vitro</i> bovine enamel and dentin blocks		None		Fluoride-substituted carbonate groups were detected in the SDF-treated enamel and dentin. In particular, the formation of FHAp indicated that SDF is effective in reducing the risk of tooth decay.
20	<a href="#">Jabin et al. (2021)</a>	2021	38% SDF	Acidulated phosphate fluoride and sodium fluoride	<i>In vitro</i> 40 caries-free primary human molars	10 samples per group (3 enamel blocks tested using SEM)	None	7 days	Topical application of a 38% SDF solution inhibited the demineralization of enamel.
32	<a href="#">Kale et al. (2022a)</a>	2022	Two SDF products: 38% SDF and FAgamin (FAgamin Silver Diamine Fluoride 38%)	None	<i>In vitro</i> human teeth	32 extracted primary molars divided into two groups ( $n = 16$ each: 8 tooth enamel, 8 tooth dentin)	Plaque bacterial model	30 days	FAgamin and SDF showed similar cariostatic and remineralization potential for dental caries.

(continued on next page)

Table 1 (continued)

Ref.	Author	Year	Type of SDF used	Comparison	Study design	Sample size	Aging process	Duration of study	Conclusion
33	<a href="#">Kale et al. (2022b)</a>	2022	Two SDF products: Advantage Arrest, and e-SDF	None	<i>In vitro</i> human teeth	32 extracted primary molars divided into two groups ( $n = 16$ )	Thermo-cycling	30 days	Advantage arrest and e-SDF showed similar cariostatic and remineralization potential for dental caries. The plaque bacterial model used in this study is an efficient method to induce artificial carious lesions in teeth.
41	<a href="#">Lee et al. (2022)</a>	2022	38% SDF, and 38% SDF with potassium iodide	5% sodium fluoride varnish	<i>In vitro</i> bovine teeth	60 divided into 4 groups ( $n = 15$ )	None	24 h	SDF/KI was effective for dental enamel remineralization even with KI, which reduced discoloration.
47	<a href="#">Luk et al. (2021)</a>	2021	SDF and SDF following CO laser	Co laser and negative control	<i>In vitro</i> human enamel specimens	40 divided into 4 groups ( $n = 10$ )	pH cycling		Using the CO laser or SDF separately enhanced the resistance of enamel to cariogenic challenge. Moreover, there was an additional effect of the combined use of the CO laser and SDF for preventing enamel demineralization.
43	<a href="#">Mashhour, Allam &amp; Wassel (2023)</a>	2023	38% SDF	5% sodium fluoride (Clinpro white varnish), enhanced fluoride varnish treatment with calcium and phosphate (MI varnish), and negative control	<i>In vitro</i> human teeth	48 molars divided into 4 groups ( $n = 12$ )	pH cycling	24 h	In primary teeth, lesions treated with MI varnish displayed better resistance to demineralization compared to lesions treated with Clinpro white varnish and SDF.
50	<a href="#">Mohammadi &amp; Farahmand Far (2018)</a>	2018	38% SDF	Fluoride varnish and negative control	<i>In vitro</i> human teeth	45 caries-free deciduous canine teeth ( $n = 15$ )	pH cycling	24 h	SDF solution and fluoride varnish displayed similar effectiveness in preventing the demineralization of deciduous anterior teeth, and no significant difference was observed.
25	<a href="#">Phonghanyudh et al. (2022)</a>	2022	38% SDF	5% sodium fluoride	Clinical trial	960 active carious tooth surfaces in 137 children/group		18 months	The semi-annual application of 38% SDF and 5% NaF varnish had comparable effectiveness in arresting enamel caries in primary teeth.
28	<a href="#">Punhagui et al. (2021)</a>	2021	Two different concentrations of SDF: 30% (Soforide) and 38% (Cariestop) Two sub-groups of application time: 1 or 3 min	Two negative controls: sound enamel, demineralized enamel	<i>In vitro</i> blocks of deciduous tooth enamel	66 divided into 6 groups ( $n = 11$ )	pH cycling		The 1 min application time promoted enamel remineralization regardless of the SDF concentration (30% or 38%).
45	<a href="#">Punyanirum et al. (2018)</a>	2018	38% SDF in adjunct to fluoride toothpaste	Control group: fluoride toothpaste only	<i>In vitro</i> human premolars	18 artificial caries slabs	bacterial pH cycling	5 days	The adjunctive use of 38% SDF enhanced the remineralization of initial carious lesions based on mineral density, depth and remineralization percentage compared with the use of 1,000 ppm fluoride toothpaste alone. SDF might be used as an adjunct to fluoride toothpaste to remineralize incipient carious lesions on smooth tooth surfaces.

(continued on next page)

Table 1 (continued)

Ref.	Author	Year	Type of SDF used	Comparison	Study design	Sample size	Aging process	Duration of study	Conclusion
31	Romero & Lippert (2021)	2020	38% SDF	Deionized water	<i>In vitro</i> bovine dentin sections	48 divided into 4 groups ( $n = 12$ )	24 and 48 h demineralization	48 h	When applied to only demineralized teeth, in this chemical model, 38% SDF completely inhibited demineralization in adjacent untreated sound enamel. Demineralization prevention was observed to a lesser extent in adjacent pre-demineralized enamel but not in dentin.
46	Savas et al. (2015)		38% SDF	Distilled water, acidulated phosphate fluoride, ammonium Hexafluoro-silicate (AHF), ammonium hexa-fluoro-silicate + cetylpyridinium chloride (AHF+CPC), and 0.2% chlorhexidine (CHX)	<i>In vitro</i> saliva-coated enamel slabs	48		2 days	SDF showed the highest antibacterial activity; none of the other fluoride agents used in this study, or 0.2 CHX agent, showed an antibacterial effect comparable to that of SDF.
19	Xue et al. (2022)	2022	38% SDF	With or without 445 nm diode laser; deionized water control	<i>In vitro</i> human enamel	33 samples	pH cycling	7 days	Superior caries-preventive effect of a combined treatment of the diode laser and SDF. Because the diode laser and SDF are affordable and readily available, clinicians can provide this treatment to their patients for caries prevention.
16	Yu et al. (2018)	2018	38% SDF	5% NaF and deionized water	<i>In vitro</i> human teeth	48	pH cycling	48 h	The adjunctive application of SDF and NaF varnish had a similar remineralizing effect to that of SDF on enamel caries.
44	Zhao et al. (2018)	2021	38% SDF	Carbon dioxide laser (CO <sub>2</sub> ), and deionized water control	<i>In vitro</i> human teeth	34 ( $n = 24$ )	pH cycling	8 days	Adding SDF to laser significantly increased the preventive effect and antibacterial ability.
<b>Studies investigating the effect of SDF on bonding and adhesion</b>									
27	Markham et al. (2020)	2020	38% SDF (Advantage Arrest; Elevate Oral Care)		<i>In vitro</i> human enamel and dentin preparations	90 IBSS 20 FBS 20 SBS	Dynamic fatigue testing	Until failure	The results suggest that SDF application on enamel and dentin reduces the bond stability of universal adhesives in self-etching mode. Spot application of SDF is recommended.
21	Favaro et al. (2021)	2021	Nano silver fluoride (experimental solution), silver diamine fluoride (Cariestop Biodinâmica, Brazil)	Positive control: intact enamel (IE) Negative control: demineralized enamel (DE)	<i>In vitro</i> human enamel blocks	60 divided into 6 groups, each with 10 samples	pH-cycling model	24 h	Anti-caries agents did not have a negative effect on the $\mu$ -SBS of composite resin when it was used on IE or DE.

(continued on next page)

Table 1 (continued)

Ref.	Author	Year	Type of SDF used	Comparison	Study design	Sample size	Aging process	Duration of study	Conclusion
22	Pérez-Hernández et al. (2018)	2018	38% SDF followed by sealant	Negative control: no SDF	<i>In vitro</i> human enamel	120 human molars (without caries and caries grade 1)	Thermo-cycling	24 h	There was an improvement in the retention properties of a fissure sealant applied after treatment with silver diamine fluoride. The application of a fissure sealant to improve the esthetics of teeth treated with SDF is recommended.
38	Sorkhdini et al. (2021)	2021	SDF (38%), SDF followed by application of potassium iodide (SDF + KI)	Silver nitrate (silver control), potassium fluoride (fluoride control), and deionized water	<i>In vitro</i> human teeth	180 divided into 5 groups ( $n = 36$ )	pH-cycling model	7 days	SDF and SDF + KI appeared to be effective options in preventing primary coronal caries.
30	Tiba et al. (2022)	2022	38% SDF (Riva Star) followed by potassium iodide	5% sodium fluoride solution (Mark3) Restoration: glass ionomer cement GC Fuji II LC capsules, and Filtek Z250	<i>In vitro</i> human teeth	10	None	24 h	Mechanical and antimicrobial testing indicated Riva Star compared favorably with—and, in some cases, performed better in the laboratory than—a Mark3 NaF varnish.
<b>Studies investigating tooth structure staining and color with the use of SDF</b>									
41	Lee et al. (2022)	2022	38% SDF, and 38% SDF with potassium iodide	5% sodium fluoride varnish	<i>In vitro</i> bovine teeth	60 divided into 4 groups ( $n = 15$ )	None	24 h	SDF/KI was effective for dental enamel remineralization even with KI, which reduced discoloration.
39	Rafiee, Memarpour & Benam (2022)	2022	SDF-treated enamel followed by 8 h/day application of 10% CP; SDF + KI-treated enamel followed by 8 h/day application of 10% CP	None	<i>In vitro</i>	96 teeth divided into 4 groups ( $n = 24$ )	Thermo-cycling aging	2 weeks (2 groups); 3 weeks (the other 2 groups)	SDF application on demineralized primary tooth enamel completely recovered enamel microhardness. 10% carbamide peroxide effectively bleached SDF stain without causing a significant decrease in EMH values. Color improvement was more evident with the use of KI immediately after SDF application.
37	Sayed et al. (2018)	2018	SDF only (control), SDF followed by application of a potassium iodide solution, and SDF mixed with 20% GSH	After treatment	<i>In vitro</i> bovine teeth	120: 60 enamel, 60 dentin ( $n = 20$ )	Half the specimens were exposed to light and the remainder kept in the dark	2 weeks	The SDF + GSH group was effective in decreasing the color changes under both light and dark conditions. The SDF + KI group showed an insignificant color change over time.
40	Sorkhdini et al. (2021)	2021	38% SDF, and 38% SDF followed by potassium iodide (SDF+KI)	Silver nitrate (silver control), potassium fluoride (fluoride control), and deionized water	<i>In vitro</i> human teeth	180 divided into 5 groups ( $n = 36$ )	pH-cycling model	7 days	KI did not interfere with the remineralization effect of SDF.
38	Sorkhdini et al. (2020)	2020	38% SDF, and 38% SDF followed by potassium iodide	Silver nitrate (silver control), potassium fluoride (fluoride control), and deionized water	<i>In vitro</i> human enamel specimens	180 divided into 5 groups ( $n = 36$ )	None	3 days	KI application after SDF treatment appeared to reduce dark discoloration but impaired SDF's ability to prevent biofilm-mediated but not chemically induced demineralization.



## The rationale for considering using sdf on enamel

Several factors are considered when evaluating a caries prevention agent, including the agent's safety, method of action, and efficacy; all play a significant role in favoring one agent over another. SDF has been proven with acceptable scientific evidence to be efficient, cost-effective, and practical as an addition to routine or mass treatment, with a key benefit to its use being its ease of application. It has been approved and used to treat tooth sensitivity. Still, in addition to that application, the precipitation of silver compounds is believed to stop caries progression by enhancing remineralization and through a bactericidal effect.

SDF offers a non-surgical caries management alternative to traditional preventive and restorative dental treatment, particularly in at-risk populations with limited adaptive capacity. It has been proven to be effective in preventing and arresting dental caries in various populations, not only children with carious lesions but also medically compromised patients, elderly adults, and residents living in nursing homes. Additionally, SDF has been found to impact oral health-related quality of life and has the potential to address the epidemic of untreated decay in young children ([Jiang et al., 2021](#)). Furthermore, SDF has been used to control caries in large populations in various countries and has been suggested to become a key element of oral health promotion programs for children and medically compromised patients to meet the WHO Millennium Goals ([Horst, Ellenikiotis & Milgrom, 2016](#); [Horst, Ellenikiotis & Milgrom, 2017](#)).

[Hiraishi et al. \(2022\)](#) showed that SDF has a stronger reactivity with dentin than with enamel. These researchers discovered fluorhydroxyapatite (FHAp) precipitations in both enamel and dentin, showing that SDF efficiently increases the enamel and dentin resistance to acid attacks and lowers the risk of caries progression. In addition,  $\text{CaF}_2$  and fluoride-substituted carbonate compounds were found in both enamel and dentin ([Hiraishi et al., 2022](#)). According to [Yu et al. \(2018\)](#) SDF exhibits more potent remineralizing effects than sodium fluoride (NaF) alone. The high fluoride concentration in SDF promotes enamel remineralization, while its alkaline nature aids in remineralization, neutralizes bacterial acids, and inhibits dentin collagenases. The silver in SDF adds to its ability to prevent enamel caries; it can integrate into hydroxyapatite crystals, resulting in silver-containing hydroxyapatite, which lowers bacterial adherence and tissue cytotoxicity against cariogenic bacteria ([Yu et al., 2018](#)).

The formation of structurally stable fluorhydroxyapatite after SDF application indicates its effectiveness in reducing the risk of tooth decay. FHAp forms a strong ionic bond with fluoride ions and contributes to caries prevention, according to [Hiraishi et al. \(2022\)](#) Other fluoride compounds, such as  $\text{CaF}_2$  and fluoride-substituted carbonate, are also detected, acting as fluoride reservoirs in the oral cavity and gradually releasing fluoride ions that inhibit carious lesion development. SDF, alone or combined with sodium fluoride varnish, has a remineralizing effect on enamel caries, attributed to the high fluoride concentration (448,000 ppm) in SDF and the formation of silver-containing hydroxyapatite ([Hiraishi et al., 2022](#)).

[Zhao et al. \(2018\)](#) highlighted the antibacterial properties of SDF against cariogenic bacteria, its ability to remineralize demineralized enamel, and its protective effect on dentin collagen. By inhibiting the growth of cariogenic bacteria, reducing mineral loss, and

promoting remineralization, SDF offers a non-invasive, simple, and low-cost approach to arresting dental caries (Zhao *et al.*, 2018). Furthermore, Xue *et al.* (2022) demonstrated that the combination of diode laser treatment and SDF application effectively prevented enamel demineralization. Hence, Xue *et al.* (2022) proposed that the combined use of a diode laser and SDF could offer an improved preventive effect against caries compared to the use of SDF only. Moreover, Jabin *et al.* (2021) demonstrated that when applied topically, SDF promotes remineralization and protects against demineralization, making it a viable approach for enamel remineralization and caries prevention.

Other investigators have justified the rationale of using SDF on enamel lesions before sealant or adhesive restoration application for a dual effect, as they believe SDF improves adhesion and bond strength. In the event of debonding or adhesive failure, the exposed enamel surface will be more resistant to caries due to the presence of silver compounds. Favaro *et al.* (2021) put forward the rationale for using SDF on enamel lesions, utilizing its anti-caries actions and ability to react with tooth mineral hydroxyapatite and form calcium fluoride and silver phosphate. This contributes to preventing and remineralizing carious lesions. Favaro *et al.* (2021) also suggested that SDF treatment can improve bond strength values, potentially enhancing the retention of resin composite restorations on decayed teeth. Pérez-Hernández *et al.* (2018) meanwhile, suggested that pre-treating the enamel with SDF improves the retention properties of the sealant, potentially enhancing its clinical performance and providing a minimally invasive treatment option for caries prevention.

### Clinical concerns about using SDF

Initial enamel carious lesions are superficial lesions. However, sometimes, they are located on surfaces that affect the patient's smile, esthetics, and appearance. The smile and esthetics significantly impact patients' appreciation of the treatment provided, confidence, and quality of life (Baiju *et al.*, 2017). SDF deposition reduces optical penetration in enamel and dentin, indicating the presence of silver metal, according to Abdelaziz *et al.* (2022). Additionally, SDF application reduces reflectivity and subsurface reflectivity in enamel, suggesting the formation of a surface barrier and hindered optical penetration (Abdelaziz *et al.*, 2022). Thermal imaging showed alterations in permeability, as indicated by changes in  $\Delta Q$  (temperature integrated over time), indicating deeper penetration of silver particles. The study also discussed the formation of silver compounds, contributing to greyish staining observed after SDF treatment. However, thermal imaging and optical coherence tomography (OCT) indicated that lesions ceased activity after SDF application (Abdelaziz *et al.*, 2022).

According to Favaro *et al.* (2021) and Zhao *et al.* (2018), there is evidence of dark staining on the tooth surface when using silver diamine fluoride and silver nanoparticle (SNP) anti-caries agents, compromising esthetics. With SDF therapy, carious lesions frequently become blackened or stained; according to Phonghanyudh *et al.* (2022) the alteration in esthetic and teeth staining may affect how satisfied the patients and guardians are, especially in the case of children. However, in Phonghanyudh *et al.* (2022), there were no appreciable changes between the 38% SDF and 5% NaF varnish groups at 18 months, and parental satisfaction with the look of their children's teeth remained constant; this might encourage

the use of SDF as the discoloration might be comparable to other preventive agents/varnish in 18 months.

Clinically, there is a concern regarding gingival irritation and reaction when the tissues encounter SDF during application. Based on the recommended SDF use protocol, gingiva should be protected using a rubber dam or petroleum jelly (Yan *et al.*, 2022).

Another consideration is whether SDF may significantly weaken the adhesive bond to enamel by reducing bond strength, a concern raised by Markham *et al.* (2020). In their study, enamel staining confirmed the presence of silver, and reduced bond stability, by about one-third, which was attributed to surface alteration, the alkaline pH of SDF, and potential interference with adhesive etching. Markham *et al.* (2020) recommended avoiding using 38% SDF on the entire bonding surface, but they proposed that spot application to a caries-affected tooth structure may still be beneficial.

In what follows, each of the concerns mentioned here is discussed in detail.

### SDF and composite bond strength

When choosing SDF to treat initial enamel carious lesions, the main purpose is to prevent caries progression. In some cases, further preventive measures are required, such as sealing the fissure to render it a non-retentive fissure. In other cases, further restoration, such as glass ionomer or resin composite restoration, is required either to restore tooth structure loss or improve esthetics and mask dark staining. Concerns have been raised regarding the presence of silver compounds and whether those will affect the ability to bond to the tooth structure and further jeopardize the bonding of adhesives or glass ionomers to the treated tooth structure.

Favaro *et al.* (2021) conducted an *in vitro* investigation to determine the effect of silver nanoparticles (SNPs) and SDF on the bonding strength of composite resin to intact and demineralized enamel after subjecting the samples to pH-cycling aging. The study found that using these anti-caries agents did not negatively affect the bond strength on intact or demineralized enamel. However, demineralized enamel treated with the agents showed lower bond strength than intact enamel treated with SDF or SNP. Nevertheless, the bond strength values surpassed the required thresholds for composite resin retention. SNPs were favored due to their esthetic advantages and lack of tooth staining. However, the researchers highlighted the need for further *in situ* and clinical studies to validate these findings in the oral cavity (Favaro *et al.*, 2021).

To determine the effect of SDF on the adhesion and microleakage of pit and fissure sealants on tooth enamel, Pérez-Hernández *et al.* (2018) carried out an *in vitro* investigation. They found that pre-application of SDF improved sealant retention, with 100% of SDF-treated samples retaining the sealant compared to only 81.6% without SDF. Although there were no significant differences in the adhesion test, the SDF group exhibited slightly higher attachment values. Microleakage was also reduced in the SDF group. The researchers emphasized the importance of strong adhesion and complete sealant retention to prevent microleakage, recommending the use of resin-based sealants for optimal outcomes. The strengths of the study were that the researchers addressed contamination concerns by cleaning the tooth surfaces and assessing the effect of oral temperature changes on

microleakage. However, the study was limited by the subjective nature of the adhesive remaining index (ARI) evaluation and the absence of significant differences in ARI scores between the groups (*Pérez-Hernández et al., 2018*).

*Markham et al. (2020)* inspected how 38% silver diamine fluoride affected the bond stability of universal adhesives to enamel and dentin in self-etching mode. The researchers used shear bond strength (SBS) and fatigue bond strength (FBS) tests to assess bond stability. This study's results contradict the previous, they stated SDF treatment before bonding to both enamel and dentin surfaces considerably reduced the bond durability of universal adhesives. The study's methodology was well-designed, with dynamic stress evaluation methodologies and the mold-enclosed approach for bonding testing. These strategies offered helpful information on bond stability. Although *Markham et al. (2020)* found a detrimental effect of SDF treatment on the bond durability of universal adhesives, the study's limitations must be considered; The study results, highlight the need for more research and understanding of the impact of SDF treatment on bonding. However, the lack of thorough examination of existing studies on SDF application and bonding limits the context and comprehensibility of the findings (*Markham et al., 2020*). Furthermore, according to the clinical outcomes, the researchers advised against applying 38% SDF to the whole bonding surface of a prepared cavity, while remarking that spot treatment on caries-affected dentin may still be beneficial. However, it was noted that changes to the SDF application strategy are needed over time to improve its combination with restorative materials while keeping its benefits, but a limitation of their work was that the researchers did not investigate the long-term effects of SDF therapy on bond durability.

*Camacho et al. (2018)* investigated how pre-treatment with SDF affected the bonding strength of orthodontic brackets on non-carious permanent molar teeth. The control group received only phosphoric acid to etch, while the experimental group received SDF therapy between bracket bonding and phosphoric acid to etch. The researchers discovered no appreciable variation in the shear bond strengths between the two groups. However, the SDF group had more adhesive left on the enamel surface, and there was a significant difference in the bond failure characteristics. Meanwhile, no silver staining was found. These results led *Camacho et al. (2018)* to hypothesize that pre-treatment with SDF has no adverse effects on *in vitro* bond strength. These results indicate that the use of SDF can be beneficial if it is planned for use as a preventive measure to avoid caries initiation and white spot formation around the brackets, which is found to be a challenge when treating teenagers. However, we must highlight that this study investigated intact enamel and not carious enamel, as discussed already for other studies discussed earlier.

*Tiba et al. (2022)* compared the shear bond strengths of two dental restorative materials, Filtek Z250 and GC Fuji I, I LC, when combined with two fluoride treatments, Riva Star (SDR) and Mark3 NaF. According to the data, the Filtek Z250 and Riva S combination had a 16% greater SBS than Filtek Z250 with Mark3 NaF. According to the researchers, Riva Star enhances enamel and dentinal hardness and lowers oral biofilm production. These data indicate that SDF may be a promising therapeutic option for military dentistry applications, given its suitability for mass application and for scenarios where there are limited resources and time. However, more research is required to replicate the findings in

a clinical context and compare the effectiveness of Riva Star with various other restorative materials (Tiba et al., 2022).

Most of the reviewed articles stated that the SDF did not have a negative effect on the adhesive bond strength of the treated tooth structure, except Markham et al. (2020). All discussed studies were *in vitro*, where specimens were subjected to a pH-cycling aging process and tested within 24 h to 7 days. Only Markham et al. (2020) subjected the samples to dynamic fatigue until failure. In this area of the field, further investigation is required to state that SDF has no adverse effect confidently, and its spot application can be recommended when needed.

### SDF and carious tooth enamel structures

Cariou tooth structures refer to tissue that has been affected by dental caries, a bacterial infection that causes demineralization and destruction of the tooth's hard tissues, such as enamel and dentin. If left untreated, caries can progress, leading to the formation of cavities. SDF has recently been recommended as a non-invasive treatment option for carious lesions, especially in children or individuals who may have difficulty undergoing traditional dental treatments. The application of SDF can arrest the progression of caries. It is beneficial when the affected tooth structure is minimal, and the decay has not progressed to a point where more extensive restorative measures are necessary.

Abdelaziz et al. (2022) utilized thermal imaging and optical coherence tomography to examine the effects of SDF on carious lesions. Their study highlighted the benefits of OCT and thermal imaging for the non-invasive monitoring of structural changes. The results showed notable changes in enamel and dentin after SDF application, suggesting silver deposition. Microscopy confirmed the presence of silver and fluoride on the surface and penetration into both sound enamel and lesion areas. However, limitations included the *in vitro* nature of the study, the lack of a control group, and the focus on structural changes rather than remineralization. Furthermore, the study did not address SDF treatment's potential adverse effects or long-term implications (Abdelaziz et al., 2022).

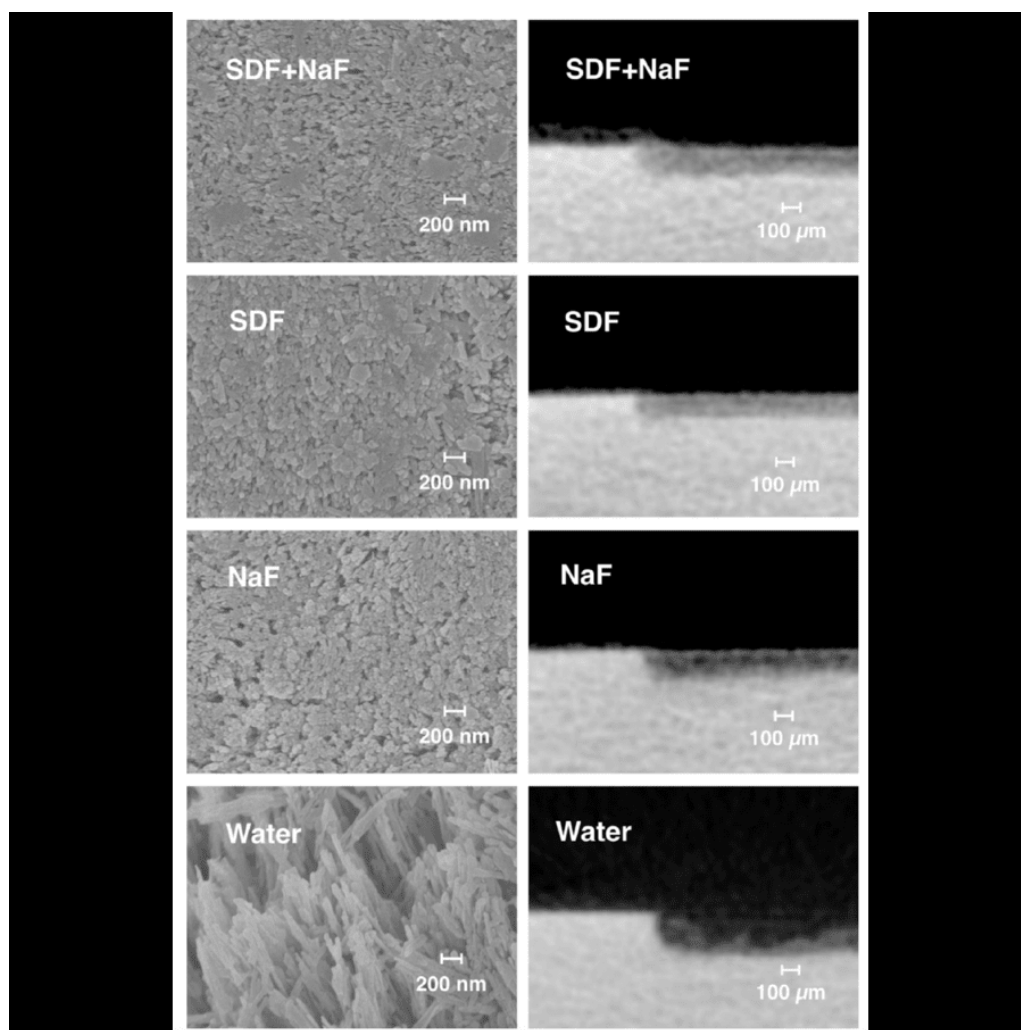
Jabin et al. (2021) tested the efficacy of sodium fluoride, acidulated phosphate fluoride (APF), and SDF in stopping primary tooth enamel from demineralizing. Their findings showed that enamel treated with SDF exhibited inhibition of demineralization. The study utilized SEM, Fourier transform infrared spectroscopy (FTIR), and X-ray diffraction (XRD) analysis to assess enamel characteristics. The results revealed smooth enamel surfaces with grooves and microporosities in all groups. Hydroxyapatite and carbonate apatite were identified as the main crystalline phases, with a higher concentration of type B carbonate. The study emphasizes the potential of SDF as a caries-preventing agent but underscores the need for further clinical trials to validate the findings, particularly in primary tooth enamel (Jabin et al., 2021).

Bovine enamel and dentin treated with silver diamine fluoride were studied by Hiraishi et al. (2022) using solid-state magic angle spinning–nuclear magnetic resonance (MAS NMR) spectroscopy to inspect the generation of fluoride compounds. In the  $^{19}\text{F}$  MAS NMR spectra, the study found fluorhydroxyapatite and other fluoride compounds, demonstrating SDF's efficacy in lowering caries incidence. In contrast to enamel, SEM scans revealed the

presence of more sediments and particles in dentin. According to [Hiraishi et al. \(2022\)](#) the structural variations in the crystals and the existence of lattice vacancies in the dentin were responsible for the distinct fluoride formation profiles between enamel and dentin. However, the study's findings on bovine teeth may not directly apply to human teeth, and further research is needed to evaluate the clinical effectiveness of SDF in preventing enamel carious lesions and validate the identified fluoride compounds ([Hiraishi et al., 2022](#)).

[Punhagui et al. \(2021\)](#) explored how varied treatment periods and concentrations of silver diamine fluoride affected the remineralization of deciduous tooth enamel. The authors used microhardness tests, pH cycling, and micro-CT analysis to assess the remineralization and porosity of enamel samples treated with SDF. According to their results, there was no significant difference in enamel remineralization based on surface and cross-sectional microhardness, independent of SDF application duration or concentration. Regardless of SDF concentration, the 1-minute application duration was observed to improve enamel remineralization. The micro-CT data showed that 30% SDF for 3 min resulted in fewer pores, indicating higher mineralization. Yet, while the study offers valuable information about the effect of SDF on enamel remineralization, it has numerous drawbacks—for instance, [Punhagui et al. \(2021\)](#) employed deciduous enamel, which varies from permanent enamel, limiting the findings' generalizability. Furthermore, the study was performed *in vitro*, which excluded *in vivo* variables such as salivary enzyme assaults and pH variations, which might impact the efficiency of enamel remineralization. In addition, the researchers did not directly evaluate fluoride and silver ion concentrations, critical determinants of SDF effectiveness ([Punhagui et al., 2021](#)).

In another study, [Yu et al. \(2018\)](#) sought to determine the remineralizing effects of supplementary applications of 5% sodium fluoride varnish and 38% silver diamine fluoride solution on simulated enamel carious lesions. The surface morphology, fluoride content, lesion depth, crystal characteristics, and precipitates were evaluated using a variety of techniques, including scanning electron microscopy (SEM), energy-dispersive spectroscopy (EDS), micro-computed tomography, transmission electron microscopy (TEM), and X-ray photoelectron spectroscopy (XPS). According to [Yu et al. \(2018\)](#) the adjunctive application of SDF and NaF varnish exhibited a remineralizing impact on enamel caries comparable to that of SDF alone. As opposed to utilizing SDF alone, the results demonstrated that adding NaF did not lessen lesion depths ([Figs. 2 and 3](#)) ([Yu et al., 2018](#)). In the SDF-treated specimens, silver nanoparticles formed silver chloride and were incorporated into hydroxyapatite crystals. It was proposed that silver's presence in SDF aided in the progression of caries arrest by lowering bacterial adherence and serving as an antibacterial agent. However, [Yu et al. \(2018\)](#) employed chemical models and artificial enamel carious lesions, which might not accurately reflect the clinical environment in real life. One risk is underestimating the function of silver due to the absence of a biological component in the chemical system. The SDF + NaF and SDF groups had equal fluoride absorption rates, showing that the extra fluoride from NaF did not enhance the amount of fluoride on the specimen surface. Additionally, [Yu et al. \(2018\)](#) pointed out that the specimens in the SDF group received less fluoride than those in the NaF



**Figure 2** Scanning electron micrographs of the enamel surface morphology. Representative scanning electron micrographs of the enamel surface morphology (images in the left column) and typical images of micro-computed tomography images (images in the right column) of the enamel caries lesions of the four treatment groups. SDF—silver diamine fluoride; NaF—sodium fluoride. Image credit: *Yu et al. (2018)*, ©Elsevier.

Full-size DOI: [10.7717/peerj.17897/fig-2](https://doi.org/10.7717/peerj.17897/fig-2)

group. The fluoride concentration and the short contact duration may have impacted the remineralization results (*Yu et al., 2018*).

The mechanisms of action of SDF for preventing and treating enamel carious lesions were thoroughly reviewed by *Zhao et al. (2018)*. According to the researchers, SDF has antibacterial qualities and can stop the growth of microorganisms that cause caries, notably *S. mutans*. Additionally, it prevents the development of cariogenic biofilms on teeth. SDF encourages the remineralization of demineralized enamel and dentin by preventing mineral loss and creating a highly mineralized surface rich in calcium and phosphate on carious lesions whose progression has been stopped. Additionally, SDF prevents collagenases from breaking down dentin collagen. However, quantitative analysis was complicated for

*Zhao et al. (2018)* because of the studies' methodological inconsistencies, which included differences in techniques and results evaluation amongst the included research data.

*Romero & Lippert (2021)* assessed the effectiveness of 38% SDF in preventing and treating enamel carious lesions. The effects of SDF on nearby untreated sound and pre-demineralized enamel and dentin were evaluated using a single-section model for digital transverse microradiography (TMR-D). According to the findings, SDF prevented demineralization in nearby sound enamel that had not been treated and, to a lesser extent, in enamel that had already undergone demineralization. SDF did not stop demineralization in dentin, although it did reduce the severity compared to the control group. *Romero & Lippert (2021)* recommended more research should be conducted so that we can better comprehend the processes and long-term effects of SDF in caries prevention, including clinical trials and comparisons with other fluoride treatments.

Using a bacterial plaque model, *Kale et al. (2022a)* examined the cariostatic and remineralizing effects of two commercial SDF preparations on enamel and dentinal caries: Advantage Arrest and e-SDF. The study employed confocal laser scanning microscopy (CLSM) and energy-dispersive X-ray spectroscopy–scanning electron microscopy (EDX-SEM) to assess the samples. Silver (Ag) and fluoride (F) concentrations in enamel and dentinal carious lesions were higher in both SDF preparations after treatment compared to before treatment. Under SEM, there was demineralization with exposed collagen. Both SDF formulations had equal remineralization capacities and decreased the depths of the lesions. According to *Kale et al. (2022a)* and *Kale et al. (2022b)*, Advantage Arrest and e-SDF have equivalent cariostatic and remineralization abilities for dental caries, and the bacterial model employed was efficient in producing fake carious lesions.

Using a pH-cycling model, Romo et al. investigated the effects of several commercially available SDF products on the development of non-cavitated enamel carious lesions in primary teeth. The findings revealed that all tested SDF products reduced the depths of carious lesions compared to the control group. Higher concentrations of SDF showed a trend toward a more significant reduction, although statistical differences were not observed for some concentrations. According to the researchers, the mechanism of action of SDF is that it includes the development of mineral deposits on the enamel surface, such as fluorapatite and calcium-fluoride-like compounds, which stop mineral loss and dental caries from progressing. *Romão et al. (2020)* stressed SDF's potential as a therapy for non-cavitated enamel carious lesions, especially in clinical settings with few resources or situations involving low patient compliance. Future research should confirm these results, explore various SDF concentrations using validated models, and examine how SDF affects oral biofilms (*Romão et al., 2020*).

*Surendranath, Krishnappa & Srinath (2022)* posited that SDF is a non-invasive, painless, and cost-effective treatment for preventing caries, especially in primary dentition and young children. In vivo and *in vitro* investigations, systematic reviews, and case reports were among the studies included in their review. The results revealed that SDF is a beneficial technique for treating caries in primary dentition, but its effectiveness in permanent molars needs to be improved and requires additional research. Even though the black staining created by SDF was highlighted as a potential downside, it was noted that parents/patients prefer SDF



because it is painless and safe. Furthermore, SDF has acceptable bonding strength with composites, which helps to disguise the black stains (*Surendranath, Krishnappa & Srinath, 2022*).

*Zaffarano et al. (2022)* discovered considerable diversity in SDF administration techniques, which may impact research results. Despite this variation, the researchers proposed that SDF is effective at halting caries development, especially when given biannually. The study emphasized the importance of uniform treatment techniques and conducting more research on SDF effectiveness in posterior primary teeth. The DMFT index's usage as an assessment tool was also criticized, with the ICDAS II index suggested to provide more accurate information. Furthermore, the presented data indicated the potential advantages of SDF therapy in primary molars, particularly in uncooperative children who may have difficulty with typical surgical methods (*Zaffarano et al., 2022*).

Based on the discussed articles, it seems that SDF can offer an effective tool in managing enamel caries. However, the use of SDF is a topic of ongoing research, and its application may vary depending on the specific clinical situation and the dentist's judgment. In particular, SDF is a beneficial anti-cariogenic agent when the use scenario requires mass application, treatment of non-cooperative or non-compliant patients, or patients without access to regular dental care.

### **SDF and tooth structure staining**

As mentioned earlier, treating enamel lesions sometimes involves anterior teeth, which play a significant role in a patient's appearance and smile, and SDF is well-known for its staining effect. In this regard, a reasonable amount of research and literature has addressed different techniques or treatments to reduce SDF's resultant staining and improve patient response.

*Sayed et al. (2018)* investigated the influence of glutathione (GSH) on enamel and dentin discoloration after applying a 38% silver diamine fluoride solution. The study divided bovine tooth specimens into three groups: SDF alone (control), SDF followed by application of a potassium iodide solution (KI), and SDF combined with 20% GSH. A spectrophotometer was used to assess color changes at different time intervals, and SEM/energy-dispersive X-ray spectroscopy analysis was performed on treated enamel and dentin. According to the findings, GSH significantly reduced color changes following SDF treatment, primarily on enamel and, to a lesser extent, on dentin. A similar effect was observed with the KI group, which had insignificant color changes over the examined time intervals. The study's highlights were the systematic methodology, the use of a spectrophotometer for reliable color measurement, and SEM/EDS analysis for comprehensive evaluation of enamel and dentin (*Sayed et al., 2018*). However, the study used bovine teeth, and some argue that bovine teeth differ slightly from human teeth. In addition, including GSH as a viable remedy for reducing color changes in SDF-treated teeth led to valuable insights into how we can enhance esthetic outcomes, but the study focused mainly on color changes and ignored other significant elements, such as the effect of GSH on SDF's bactericidal or remineralization characteristics. Furthermore, the difficulty in dissolving GSH in SDF limited the researchers' ability to investigate greater concentrations,

raising issues regarding the ideal GSH concentration for maximum effectiveness. Further studies on more accessible techniques for increasing the GSH concentration in SDF solutions are required (*Sayed et al., 2018*).

Conversely, shortly following SDF therapy, the application of KI dramatically decreased SDF-induced discoloration. The formation of photosensitive silver iodide (AgI) through the reaction of the iodine released by KI with the remaining unreacted silver, which can transform into metallic silver and iodine following light exposure, may explain why KI can prevent silver staining altogether after demineralization (*Sorkhdini et al., 2020*).

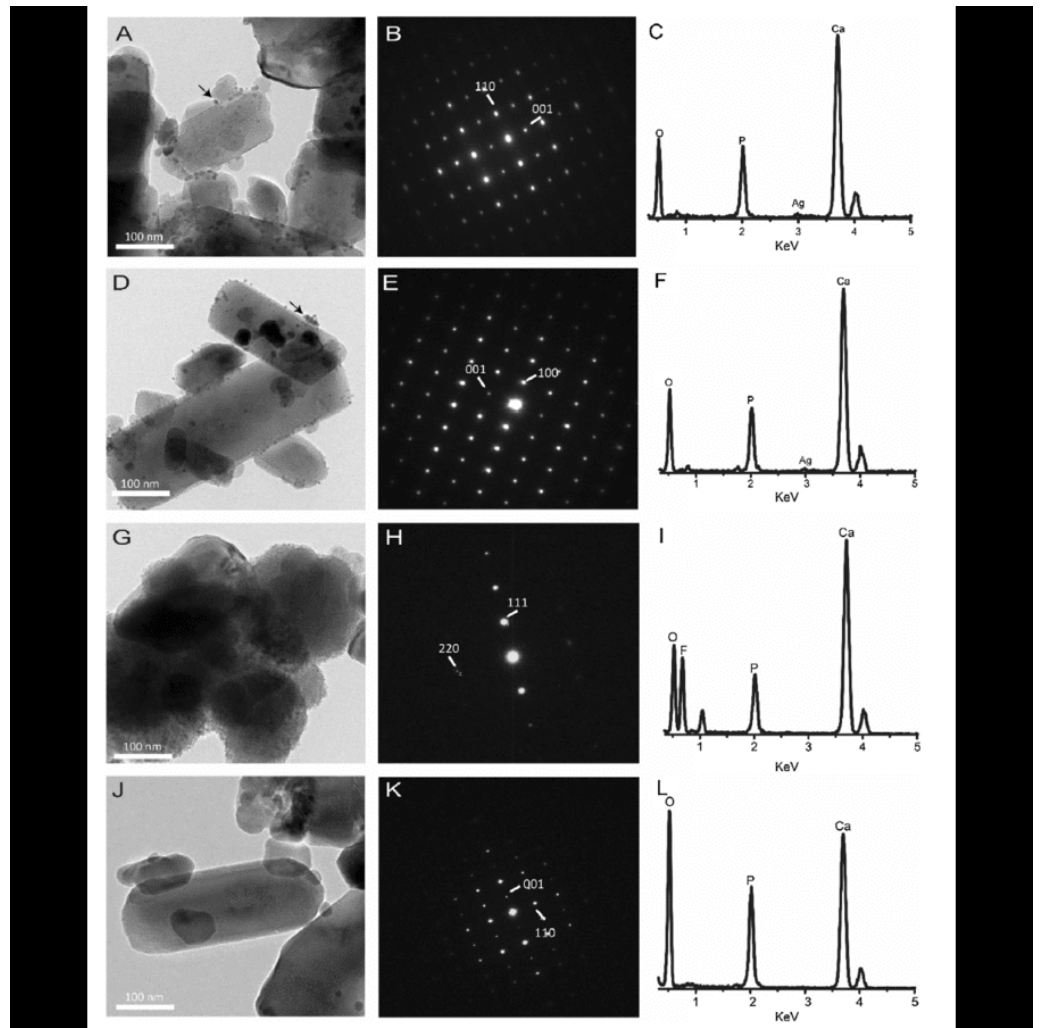
In their study, *Rafiee, Memarpour & Benam (2022)* addressed the need for a remedy to the problem of tooth discoloration by using potassium iodide. The study team discovered that applying SDF to primary tooth enamel that had undergone demineralization fully recovered the enamel microhardness (EMH) values. The SDF-treated samples had hardness comparable to sound enamel, indicating that remineralization had been effective (*Rafiee, Memarpour & Benam, 2022*). Similar results were found by *Sorkhdini et al. (2021)*, who added that no significant difference was detected regarding hardness when using SDF, SDF+KI, or potassium fluoride (KF).

After using a 38% silver diamine fluoride solution, *Sayed et al. (2018)* investigated how combining SDF with biomolecule glutathione reduced enamel and dentin discoloration. According to the spectrophotometric data, the SDF group showed the greatest color change under both light-exposed and dark circumstances. In contrast, the SDF + GSH group showed significantly decreased color changes under both conditions, suggesting an improved esthetic compared to the SDF group (*Sayed et al., 2018*).

*Lee et al. (2022)* discovered that the administration of SDF/KI did not result in notable discoloration when compared to saline control and NaF groups. The lack of prominent discoloration showed that KI addition reduced tooth surface discoloration. The researchers proposed that silver iodide removes the excess silver ions and thereby helps lessen the resultant discoloration. From the extant research, we can surmise that clinical experiments and *in vitro* studies have shown KI works well in reducing SDF-induced discoloration and adult root cavities; however, it still has a chance of causing some tooth discoloration. The progression of caries may influence the amount of discoloration, based on whether it has simply impacted the enamel or reached the dentin (*Figs. 4 and 5*) (*Lee et al., 2022*).

The effectiveness of SDF in preventing and curing enamel carious lesions was studied by *Haiat et al. (2021)*. The antibacterial effect of an SDF/potassium iodide combination on cariogenic microorganisms and the potential of KI to decrease tooth discoloration associated with SDF treatment were the subjects of a systematic study. Twelve data points were included in the evaluation, all showing SDF/KI to have promising antibacterial effects against cariogenic microorganisms. However, there were conflicting data on the impact of SDF/KI on tooth color. According to *Haiat et al. (2021)* combining SDF with KI may reduce the chance of staining. However, additional well-planned clinical trials are required to provide solid data and overcome methodological shortcomings (*Haiat et al., 2021*).

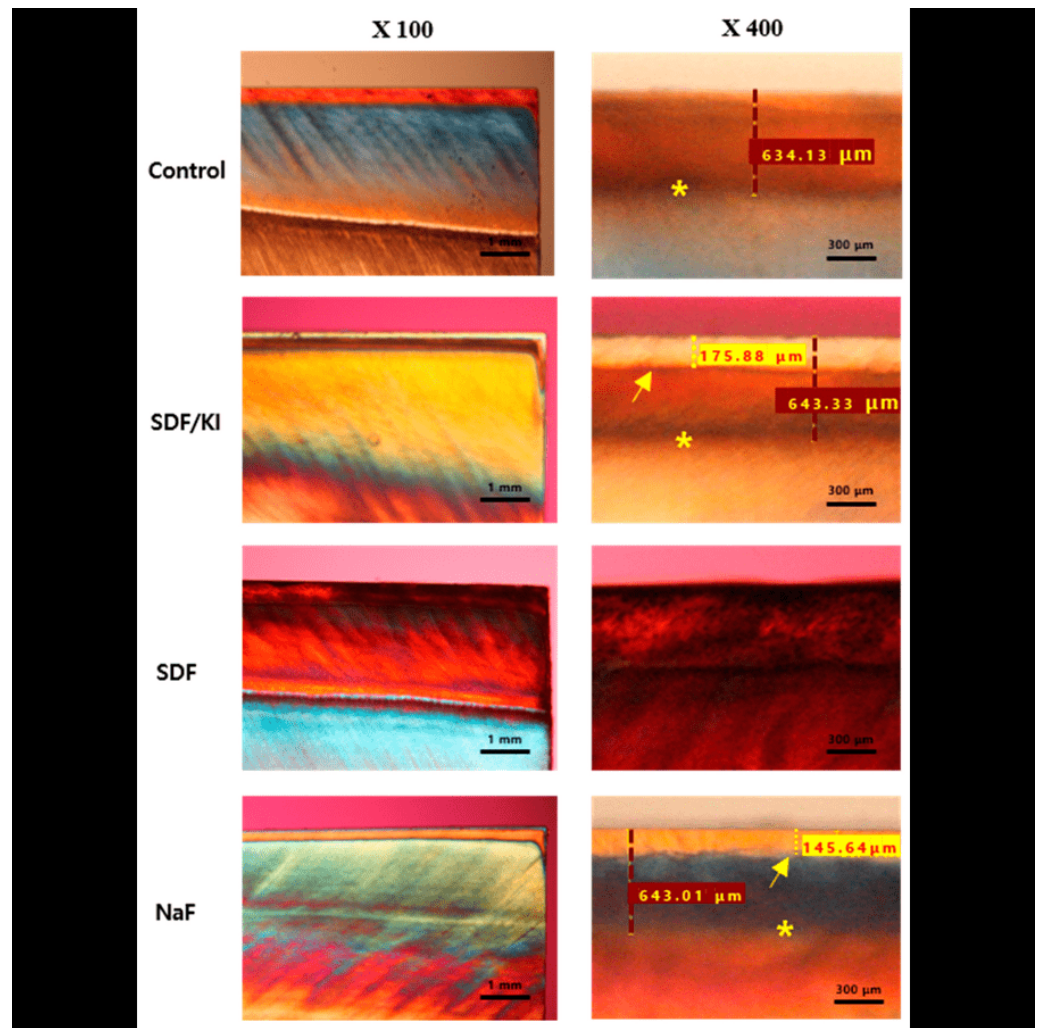
The effects of applying fluoridated carbamide peroxide (CP) with or without potassium iodide on enamel surfaces treated with silver diamine fluoride in primary teeth were examined by *Rafiee, Memarpour & Benam (2022)*. The study focused on



**Figure 3** Transmission electron microscopy data of experimental groups. SDF + NaF group: (A) morphology, (B) SAED pattern, (C) EDS spectra. SDF group (D) morphology, (E) SAED pattern, (F) EDS spectra. NaF group (G) morphology, (H) SAED pattern, (I) EDS spectra. Water group (J) morphology, (K) SAED pattern, (L) EDS spectra. EDS—energy-dispersive X-ray spectroscopy; F—fluoride; O—oxygen; P—phosphorus; Ag—silver. SAED—selected-area electron diffraction; SDF—silver diamine fluoride; NaF—sodium fluoride. Image credit: *Yu et al. (2018)*, ©Elsevier.

Full-size DOI: [10.7717/peerj.17897/fig-3](https://doi.org/10.7717/peerj.17897/fig-3)

enamel microhardness, surface topography, and color changes. Enamel penetration and mineral content were not evaluated, limiting the understanding that could be gained of the mechanisms involved. Furthermore, the study lacked a control group and did not consider long-term stability or potential adverse effects. Despite these limitations, *Rafiee, Memarpour & Benam (2022)* provided valuable insights into using SDF and fluoridated CP for enamel caries prevention and treatment. SDF application effectively restored enamel microhardness, while fluoridated CP improved color changes caused by SDF. Further research is needed to address the study's limitations and provide a more comprehensive understanding of these interventions (*Markham et al., 2020*).



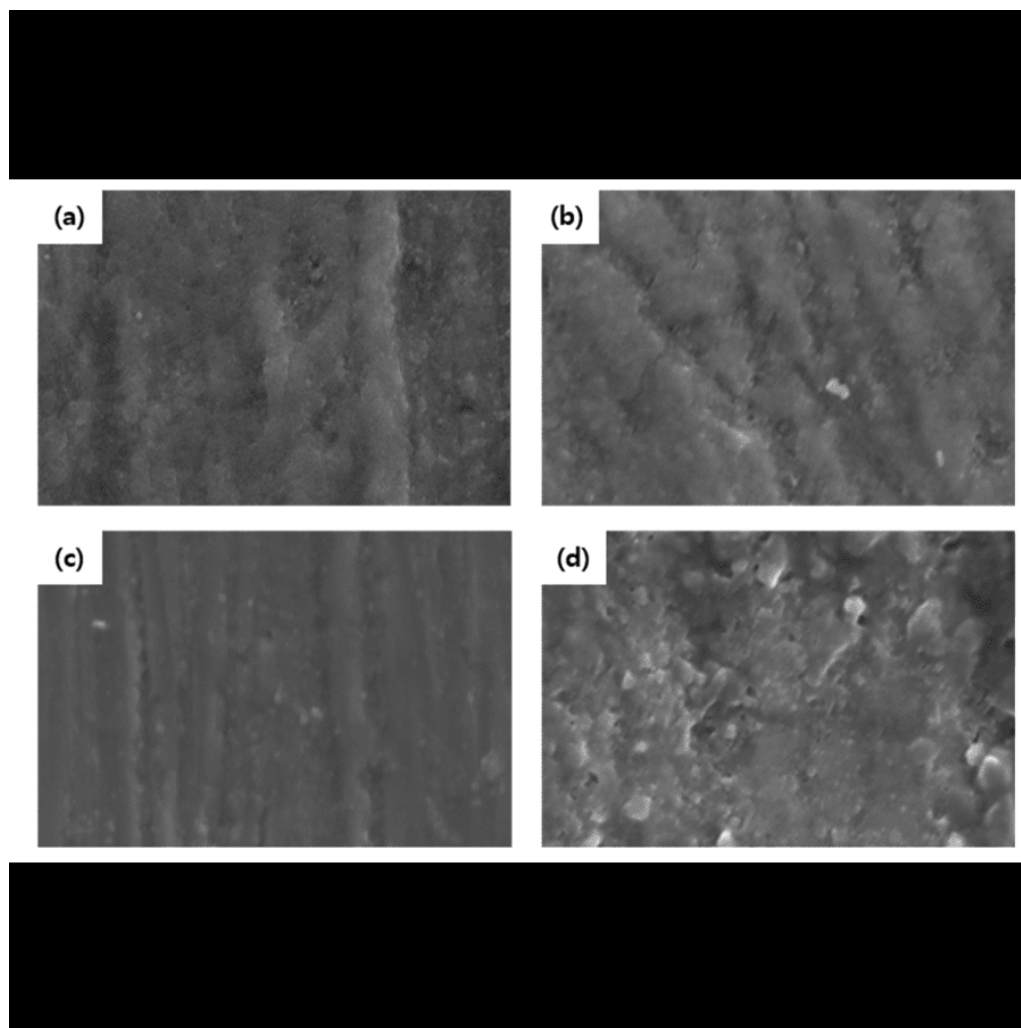
**Figure 4** Polarization light micrograph images of post-demineralization and remineralization. Representative polarization light micrograph images of post-demineralization and remineralization at magnifications of 100 X and 400 X \*: Margin of demineralization; arrow: margin of remineralization; red dashed line: the depth of demineralization; yellow dashed line: the depth of remineralization. The border of the SDF group could not be measured due to discoloration. Image credit: *Lee et al. (2022)*.

Full-size  DOI: [10.7717/peerj.17897/fig-4](https://doi.org/10.7717/peerj.17897/fig-4)

Based on the reviewed articles, using KI or GSH has been proven to reduce staining caused by SDF. Theoretically, removing the excess silver to reduce staining will reduce silver's effect on bonding and acid attack resistance; however, further clinical investigation is needed to explore the long-term impacts of adding KI or GSH to SDF on color stability, the antibacterial effect, and adhesive bonds.

### SDF and other preventive agents

Over the years, many caries-preventive agents have been introduced and utilized. Therefore, when recommending SDF as an anti-caries agent, it is logical to compare it with established, reliable, available preventive agents.



**Figure 5** Scanning electron micrographs of enamel surfaces. Scanning electron micrographs of enamel surfaces after remineralization. (A) Control group; (B) SDF/KI; (C) SDF; (D) NaF (magnification: 8000 X). Image credit: *Lee et al. (2022)*.

Full-size  DOI: [10.7717/peerj.17897/fig-5](https://doi.org/10.7717/peerj.17897/fig-5)

*Mashhour, Allam & Wassel (2023)* compared the efficiency of three topical treatments in preventing demineralization of white spot lesions (WSLs) in the enamel of primary teeth: Clinpro™ White varnish containing 5% sodium fluoride and functionalized tricalcium phosphate, MI varnish containing 5% NaF and casein phosphopeptide–amorphous calcium phosphate (CPP–ACP), and 38% silver diamine fluoride. All three treatments successfully remineralized demineralized enamel according to the authors. However, MI varnish and Clinpro white varnish were superior to SDF regarding calcium (Ca) and phosphate (P) contents and lesion depth. As such, *Mashhour, Allam & Wassel (2023)* offered insightful comparative information on the effectiveness of these three therapies for enamel demineralization. Nevertheless, some restrictions to their study must be considered (*Mashhour, Allam & Wassel, 2023*). First, the research was performed in a

laboratory setting, which may not have accurately reflected the oral cavity's dynamic and intricate biological processes. Because of this, care must be used when extending the results to clinical situations. Additionally, the antimicrobial properties of the treatments studied—which play a crucial role in the clinical remineralization of carious lesions—were not considered. To better simulate the oral environment, [Mashhour, Allam & Wassel \(2023\)](#) called for more studies incorporating the presence of microorganisms. Despite these drawbacks, [Mashhour, Allam & Wassel \(2023\)](#) noted the possible advantages of Clinpro white varnish and MI varnish in improving enamel remineralization and acid resistance. Additionally, they implied that SDF can be advantageous for patients who are uncooperative or have low finances. However, clinical studies are required to confirm the results of this *in vitro* research ([Mashhour, Allam & Wassel, 2023](#)).

[Zhao et al. \(2021\)](#) meanwhile, examined the use of a 9.3 mm carbon dioxide (CO<sub>2</sub>) laser combined with SDF on enamel to evaluate demineralization prevention and cariogenic bacterium inhibition. They found that the CO<sub>2</sub> laser alone could prevent demineralization, reduce bacterial adhesion, and disrupt biofilm formation on enamel. The adjunctive use of SDF further enhanced these effects. Various techniques were employed to assess the outcomes, including pH cycling, SEM with EDS, and CFU and CLSM evaluations. The study demonstrated that the combined use of the CO<sub>2</sub> laser and SDF showed promising results in preventing demineralization and inhibiting bacteria. The laser treatment improved enamel resistance through changes in hydrophobicity and crystallographic alterations. SDF contributed to preventing demineralization and inhibiting biofilm formation by disorganizing and disaggregating the biofilm and inhibiting its metabolism and growth. The findings provide insights into the potential of using a CO<sub>2</sub> laser and SDF to improve enamel health and caries prevention ([Zhao et al., 2021](#)).

In research comparing the efficiency of 38% SDF and 5% sodium fluoride varnish in halting enamel caries in young children, [Phonghanyudh et al. \(2022\)](#) found that when administered semi-annually over 18 months to children aged 1–3 years with active carious surfaces, both therapies were equally effective in halting enamel caries in primary teeth. The study filled a gap in the literature by studying the use of 38% SDF in high-caries-risk toddlers in non-fluoridated settings. The study's strengths included its low dropout rate, adequate sample size, and reliable examinations. However, limitations included the absence of a negative control group, reliance on visual inspection alone for caries assessment, and potential bias introduced by SDF staining. Furthermore, the findings applied to high-risk children in outreach settings, and further research is needed to explore the effectiveness of SDF in different populations ([Phonghanyudh et al., 2022](#)).

Using both biofilm and chemical models, [Sorkhdini et al. \(2020\)](#) investigated the efficiency of silver diamine fluoride and its components, silver (Ag<sup>+</sup>) and fluoride (F<sup>-</sup>), in preventing enamel demineralization. The study design was noteworthy, with appropriate controls and two models used to evaluate SDF's action. It is also worth noting the addition of potassium iodide as a post-SDF application therapy to reduce staining caused by SDF. In all models, [Sorkhdini et al. \(2020\)](#) showed that SDF and SDF + KI were superior to silver nitrate (AgNO<sub>3</sub>) and deionized water (DIW) in preventing carious lesion development. In the biofilm model, however, SDF + KI was much less efficient in

preventing demineralization than SDF alone. [Sorkhdini et al. \(2020\)](#) hypothesized that KI may reduce the bioavailability of silver ions or increase organic acid generation by bacteria, impairing the silver antibacterial activity. Nonetheless, it is critical to emphasize the study's limitations, such as the absence of remineralization intervals and longitudinal studies of SDF's capacity to prevent caries. Furthermore, the study concentrated on immediate impacts rather than long-term effectiveness. Future studies utilizing clinical models and monitoring lactic acid generation will extend our knowledge of SDF's potential ([Mashhour, Allam & Wassel, 2023](#)).

[Xue et al. \(2022\)](#) investigated the effects of a 445 nm diode laser (L) and silver diamine fluoride (F) in terms of preventing enamel demineralization and suppressing cariogenic bacteria. They employed scanning electron microscopy, nano-hardness testing, micro-computed tomography, and biofilm evaluation to determine the efficiency of the treatments. Compared to other groups, the combination therapy of diode laser and silver diamine fluoride had a more significant caries-preventative effect. The utilization of different assessment methodologies by [Xue et al. \(2022\)](#) allowed for a complete investigation of the therapies' impact on enamel. The SEM scans showed that the enamel treated with the diode laser and silver diamine fluoride had a smooth surface, indicating that the enamel was protected. Furthermore, nano-hardness measures and lesion depths supported the findings of decreased demineralization in the combined therapy group. The biofilm analysis also demonstrated that the combination therapy significantly reduced bacterial adhesion and growth ([Xue et al., 2022](#)).

However, [Xue et al. \(2022\)](#) employed enamel slices sectioned into blocks, which may not have adequately depicted the intricacy of regular teeth and caries progression. Furthermore, the sample size (33) could have been more extensive, which may have impacted the findings' generalizability. Moreover, [Xue et al. \(2022\)](#) concentrated on the laboratory environment, and the practical application of combination therapy requires additional research mimicking the oral environment. Also, the mechanism behind the interaction between the diode laser and silver diamine fluoride remains unknown, according to [Xue et al. \(2022\)](#). More research is necessary to determine how the therapies reduce enamel demineralization and bacterial development. The possible esthetic concerns connected with employing the diode laser and silver diamine fluoride, such as black staining and decreased silver ion penetration depth, impact the willingness of dentists to use either treatment ([Xue et al., 2022](#)).

[Lee et al. \(2022\)](#) explored the remineralization of enamel carious lesions using 38% silver diamine fluoride and potassium iodide. The effects of SDF/KI varnish were compared with those of 38% SDF and 5% sodium fluoride varnish. Colorimetric analysis, Vickers microhardness tests, and microscopic exams were used to evaluate the remineralization capability of bovine incisors that had been demineralized for 120 h. According to Lee et al., SDF/KI did not induce substantial discoloration compared to the control and NaF groups, suggesting that adding KI minimized color alterations. According to polarized light microscopy (PLM) and scanning electron microscopy investigations, SDF/KI had the highest mean microhardness and the best remineralization capacity. Despite its limitations, the study emphasized the benefits of SDF as a productive, efficient, and

cost-effective therapy option, and showed that adding KI alleviates the cosmetic problem of tooth discoloration caused by SDF usage. The findings added to the expanding body of evidence that supports the use of SDF as an alternate agent for caries prevention and enhancement (*Lee et al., 2022*).

The efficacy of 38% SDF as a supplement to fluoride toothpaste in remineralizing enamel carious lesions was investigated by *Punyanirun et al. (2018)*. Artificial caries enamel slabs were used in the study and submitted to pH cycling and micro-CT analysis. The findings demonstrated that, compared to the control group, the SDF group displayed considerably better mineral density, depth of remineralization, and remineralization %. According to the study's findings, using SDF and fluoride toothpaste improves the remineralization of early carious lesions. However, further clinical investigations are necessary, particularly in high-caries-risk patients, to validate these findings and assess the inhibition of lesion progression (*Punyanirun et al., 2018*).

*Savas et al. (2015)* assessed the efficiency of several antibacterial treatments, including silver diamine fluoride, to prevent and treat enamel carious lesions. The research used a biofilm model with *S. mutans*, the most potent cariogenic microorganism. The results indicated that SDF had the highest antibacterial activity compared to other fluoride agents and chlorhexidine. *Savas et al. (2015)* suggested that SDF effectively reduces viable microorganisms in the biofilm and demonstrates potential as an anti-caries agent. However, they also highlighted that the antibacterial effect of fluoride alone is lower than the synergistic effect of fluoride and silver ions present in SDF. Additionally, the study showed a correlation between plaque pH and viable microorganism count, implying the antibacterial impact of remineralization agents (*Savas et al., 2015*).

*Luk et al. (2021)* meanwhile, investigated the potential of carbon dioxide (CO<sub>2</sub>) laser irradiation followed by the application of SDF to enamel to prevent caries. Human enamel samples were divided into four groups for the study: SDF-treated, CO<sub>2</sub>-treated, CO<sub>2</sub>-treated then SDF-treated, and controlled untreated. The outcomes demonstrated that Group 3's CO<sub>2</sub> laser and SDF combination produced the lowest lesion depth and maximum microhardness compared to the other groups. Group 4 had the deepest lesions and the lowest microhardness since it received no treatment. According to *Luk et al. (2021)* combining SDF with CO<sub>2</sub> laser increases enamel's resistance to cariogenic challenge and prevents enamel demineralization.

*Hamdi et al. (2022)* examined the remineralization effects of casein phosphopeptide amorphous calcium phosphate, silver diamine with fluoride potassium iodide (SDF-KI), and tricalcium silicate paste (TCS) on early enamel lesions. There were three therapy groups for the 45 patients with early enamel lesions: SDF-KI, CPP-ACP, and TCS. The study discovered that after 24 months, both twice-daily treatment with CPP-ACP and TCS paste and a yearly application of SDF-KI significantly remineralized early enamel lesions. At various follow-up intervals, there were sizable differences between SDF-KI and CPP-ACP, as well as between SDF-KI and TCS. CPP-ACP and TCS, however, did not significantly vary from one another (*Hamdi et al., 2022*).

In their study, *Alcorn et al. (2022)* sought to assess the effects of SDF therapy on the surface microhardness of early enamel carious lesions. Bovine enamel samples with carious



lesions were split into several treatment groups and put through pH cycling. The research discovered that SDF considerably outperformed deionized water (DI), silver nitrate, and 5% sodium fluoride varnish (FV) in terms of remineralization immediately after pH cycling. In comparison to FV, delayed cycling groups had increased remineralization. SDF showed reduced surface softening following a second demineralization test compared to AgNO<sub>3</sub>, DI, potassium fluoride, and FV. Based on the results, [Alcorn et al. \(2022\)](#) speculated that FV may be more effective than SDF for treating early enamel carious lesions.

[Mohammadi & Farahmand Far \(2018\)](#) compared the effects of SDF solution and fluoridated varnish on the primary tooth enamel's resistance to demineralization. Three groups of enamel samples—control (distilled and deionized water), fluoride varnish (V), and SDF solution—were created from caries-free deciduous canine teeth. Surface microhardness (SMH) was assessed before and after the pH cycling and treatment of the samples. Although the difference between SDF and the other groups was not statistically significant, the study discovered that SDF led to the greatest resistance to mineral loss. According to [Mohammadi & Farahmand Far \(2018\)](#) fluoride varnish and SDF solution are equally efficient at preventing the demineralization of deciduous front teeth.

[Akyildiz & Sönmez \(2019\)](#) used an *in vitro* remineralization model to assess the remineralization impact of an experimental nano-silver fluoride (NSF) formulation compared to sodium fluoride varnish and SDF. Artificial lesions resembling caries were formed on enamel samples, and the remineralization agents were then administered. The samples were subjected to pH cycling, and their microhardness and surface morphology were evaluated. The demineralized enamel specimens responded to all remineralization treatments by rehardening statistically significantly more than the other samples. However, NSF was less successful in remineralizing artificial enamel carious lesions than sodium fluoride varnish and SDF. Before suggesting NSF as a substitute for regular fluoride treatments, [Akyildiz & Sönmez \(2019\)](#) recommended that more research be performed.

[Heukamp et al. \(2022\)](#) measured fluorescence behavior using human teeth samples and quantitative light-induced fluorescence (QLF). After 28 days, SDF exhibited a statistically significant decreased fluorescence value compared to Cervitec F and Bifluorid 12 varnishes. SDF showed promise in preventing demineralization and may offer a viable treatment option for reversible early carious lesions. However, the authors highlighted limitations to their methodology, such as the absence of cariogenic bacteria and biofilm in the demineralization solution and the cosmetic disadvantage of yellow discoloration associated with SDF. Despite these limitations, the data demonstrated SDF's therapeutic importance in preventing demineralization development, particularly in individuals with fixed orthodontic appliances or poor dental hygiene. More research is required to overcome the reported limitations and investigate long-term consequences ([Heukamp et al., 2022](#)).

In sum, the majority of the articles mentioned above indicate that SDF exhibits a superior ability for remineralization, specifically in increasing enamel hardness compared to defective enamel when compared with other preventive agents. However, [Alcorn et al. \(2022\)](#) and [Heukamp et al. \(2022\)](#) deviated from this trend; both teams utilized bovine teeth in their studies and conducted investigations over two weeks, yielding different results from similar studies that employed human teeth and longer durations. This divergence in

outcomes may thus be attributed to the study duration and/or variations in the histology or structure between bovine and human teeth.

In a noteworthy *in vivo* study by [Hamdi et al. \(2022\)](#), conducted over 24 months, it was concluded that annual application of SDF-KI, when compared to twice-daily application of CPP-APC or TCS, exhibited a significant remineralization effect. These findings position SDF as a more convenient and cost-effective option.

## LIMITATIONS

While the article highlighted several positive aspects and benefits of using SDF to prevent and treat enamel caries lesions, it is essential to consider the limitations of this article:

- Lack of long-term clinical trials: the discussed studies showed promising results when using SDF in short-term caries arrest and remineralization, long-term clinical trials are essential to fully understand the SDF action durability and effect of caries recurrence.
- Adverse reaction and side effects: although SDF is well tolerated initially, long-term clinical studies can help assess potential risks and side effects when using SDF, especially with diverse patient populations.
- Scope of effectiveness: the scope of effectiveness of SDF can vary based on the targeted population, and understanding its limitations for certain populations is crucial for informed clinical decision-making.
- Most of the published articles investigated the SDF under controlled laboratory environments with no regard to the oral environment changes and biofilm variation among the different populations. The same applies for the testing protocols; the studies are not in harmony with choosing the aging process or methods in testing enamel hardness or remineralization.

## CONCLUSION

Overall, the reviewed literature showed that silver diamine fluoride may be beneficial in preventing and treating enamel carious lesions. SDF possesses antibacterial characteristics, preventing bacterial growth and biofilm formation while encouraging demineralized enamel and remineralization. In addition, there is not enough evidence to ensure that SDF can damage composite resin restorations or sealants bonding to enamel. Concerns about tooth staining caused by SDF therapy have been expressed, and it has been shown that adding potassium iodide or glutathione may help decrease discoloration. The dental community had accepted the use of SDF for treating teeth sensitivity as well as treating cavitated and non-cavitated carious lesions. Although there is an increased interest in using SDF for caries treatment and prevention, it is important to recognize that the SDF is not approved for this use by the regulatory agencies.

Bibliometric studies exposed an increased interest globally in SDF since 2014, reaching a peak from 2016 to the present. The rush to use the SDF from 2019 onward can be attributed to the COVID-19 pandemic, the pandemic limited access to dental care leading to increasing reliance on alternative treatments like SDF.

Despite its limitations, the extant research shows that SDF has potential as a therapy for enamel caries prevention and remineralization and as an adjuvant to other dental treatments. Some showed superior results when using SDF compared to other preventive agents and other studies suggested the use of SDF in conjunction with other preventive agents. The factors that might influence the publicity of SDF are the ease of use and the required number of applications, while other agents require daily, or quarterly use SDF can be applied once to twice yearly. In limited cases such as deep retentive fissures, further preventive sealant might be indicated, in other cases when the patients require orthodontic treatment the effect of SDF on adhesive bonding should be considered.

Future studies should explain the specific processes through which SDF interacts with other therapies and investigate its potential in broader therapeutic applications. Dental professionals may leverage SDF's benefits to enhance oral health outcomes by addressing uncertainties, answering outstanding questions, and improving SDF's application methods.

### **Prospective developments**

Based on this study limitations and further future investigating opportunities exist, such as the following:

- Long-term clinical trials to assess SDF effectiveness, durability, and any possible side effects. Population diversity as well as acceptance and other factors like age and lesion depth should be considered.
- Developing a standardized protocol for SDF application for various dental uses and concerns. The protocol should include application technique, duration, recall and expected outcome.
- Educating and raising awareness among dental professionals, patients as well and caregivers about the SDF uses, benefits, and limitations.

## **ACKNOWLEDGEMENTS**

I would like to thank Dr. Abdul Samad Khan Muhammad, Dr. Khalifa Al Khalifa, and Dr. Moataz Elgezawi for guiding me through the writing and submission process. All doctors consented to the acknowledgment.

## **ADDITIONAL INFORMATION AND DECLARATIONS**

### **Funding**

The author received no funding for this work.

### **Competing Interests**

The author declares they have no competing interests.

### **Author Contributions**

- Rasha N. AlSheikh conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.

## Data Availability

The following information was supplied regarding data availability:

This is a literature review and did not generate raw data.

## REFERENCES

- Abdelaziz M, Yang V, Chang NN, Darling C, Fried W, Seto J, Fried D. 2022. Monitoring silver diamine fluoride application with optical coherence tomography and thermal imaging: an *in vitro* proof of concept study. *Lasers in Surgery and Medicine* 54:790–803 DOI 10.1002/lsm.23528.
- Akyildiz M, Sönmez IS. 2019. Comparison of remineralising potential of nano silver fluoride, silver diamine fluoride and sodium fluoride varnish on artificial caries: an *in vitro* study. *Oral Health & Preventive Dentistry* 17:469–477 DOI 10.3290/j.ohpd.a42739.
- Alcorn A, Al Dehailan L, Cook NB, Tang Q, Lippert F. 2022. Longitudinal *in vitro* effects of silver diamine fluoride on early enamel caries lesions. *Operative Dentistry* 47:309–319 DOI 10.2341/20-237-L.
- American Dental Association. 2017. *CDT 2017 Dental Procedures Codes*. Chicago: American Dental Association Publishing.
- Baiju RM, Peter E, Varghese NO, Sivaram R. 2017. Oral health and quality of life: current concepts. *Journal of Clinical and Diagnostic Research* 11:ZE21–ZE26 DOI 10.7860/JCDR/2017/25866.10110.
- Camacho KJ, English JD, Jacob HB, Harris LM, Kasper FK, Bussa HI, Quock RL. 2018. Silver diamine fluoride and bond strength to enamel *in vitro*: a pilot study. *American Journal of Dentistry* 31:317–319.
- Craig GG, Powell KR, Cooper MH. 1981. Caries progression in primary molars: 24-month results from a minimal treatment programme. *Community Dentistry and Oral Epidemiology* 9:260–265 DOI 10.1111/j.1600-0528.1981.tb00342.x.
- Favaro JC, De Mello Peixoto YCT, Geha O, Dias FA, Guiraldo RD, Lopes MB, Berger SB. 2021. Can silver diamine fluoride or silver nanoparticle-based anticaries agents to affect enamel bond strength? *Restorative Dentistry & Endodontics* 46:1–8.
- Featherstone JD. 1999. Prevention and reversal of dental caries: role of low level fluoride. *Community Dentistry and Oral Epidemiology* 27:31–40 DOI 10.1111/j.1600-0528.1999.tb01989.x.
- Haiat A, Ngo HC, Samaranayake LP, Fakhruddin KS. 2021. The effect of the combined use of silver diamine fluoride and potassium iodide in disrupting the plaque biofilm microbiome and alleviating tooth discoloration: a systematic review. *PLOS ONE* 16:e0252734 DOI 10.1371/journal.pone.0252734.
- Hamdi K, Hamama HH, Motawea A, Fawzy A, Mahmoud SH. 2022. Long-term evaluation of early-enamel lesions treated with novel experimental tricalcium silicate paste: a 2-year randomized clinical trial. *Journal of Esthetic and Restorative Dentistry* 34:1113–1121 DOI 10.1111/jerd.12941.

- Heukamp J, Korbmacher-Steiner H, Schmidt S, Neumann CM, Bottenberg P, Jablonski-Momeni A. 2022.** Remineralisation capability of silver diamine fluoride in artificial enamel lesions on smooth surfaces using quantitative light-induced fluorescence measurements *in-vitro*. *Scientific Reports* **12**:8498 DOI [10.1038/s41598-022-12498-6](https://doi.org/10.1038/s41598-022-12498-6).
- Hiraishi N, Sayed M, Hill R, Shimada Y. 2022.** Solid-state NMR spectroscopy measurement of fluoride reaction by bovine enamel and dentin treated with silver diamine fluoride. *Dental Materials* **38**:769–777 DOI [10.1016/j.dental.2022.04.017](https://doi.org/10.1016/j.dental.2022.04.017).
- Horst JA, Ellenikiotis H, Milgrom PL. 2016.** UCSF protocol for caries arrest using silver diamine fluoride: rationale, indications and consent. *Journal of the California Dental Association* **44**:16–28.
- Horst JA, Ellenikiotis H, Milgrom PM. 2017.** UCSF protocol for caries arrest using silver diamine fluoride: rationale, indications and consent. *Pennsylvania dental journal* **84**(14):16–26.
- Jabin Z, Nasim I, Vishnu Priya V, Agarwal N. 2021.** Quantitative analysis and effect of SDF, APF, NaF on demineralized human primary enamel using SEM, XRD, and FTIR. *International Journal of Clinical Pediatric Dentistry* **14**:537–541 DOI [10.5005/jp-journals-10005-1988](https://doi.org/10.5005/jp-journals-10005-1988).
- Jiang CM, Duangthip D, Chan AKY, Tamrakar M, Lo ECM, Chu CH. 2021.** Global research interest regarding silver diamine fluoride in dentistry: a bibliometric analysis. *Journal of Dentistry* **113**:103778 DOI [10.1016/j.jdent.2021.103778](https://doi.org/10.1016/j.jdent.2021.103778).
- Kale YJ, Misal S, Dadpe M, Dahake PT, Kendre SB, Jain M. 2022a.** Comparative evaluation of cariostatic and remineralizing potential of two commercial silver diamine fluoride preparations using confocal laser microscopy and EDX-SEM spectroscopy: an. *International Journal of Clinical Pediatric Dentistry* **15**:442–449 DOI [10.5005/jp-journals-10005-2423](https://doi.org/10.5005/jp-journals-10005-2423).
- Kale YJ, Misal S, Dadpe MV, Dahake PT, Kendre SB, Jain M. 2022b.** Comparison of cariostatic and remineralizing potential of two commercial silver diamine fluoride preparations using confocal laser microscopy and EDX-SEM spectroscopy: an. *International Journal of Clinical Pediatric Dentistry* **15**:643–651 DOI [10.5005/jp-journals-10005-2454](https://doi.org/10.5005/jp-journals-10005-2454).
- Kutesa A, Kasangaki A, Nkamba M, Muwazi L, Okullo I, Rwenyonyi CM. 2015.** Prevalence and factors associated with dental caries among children and adults in selected districts in Uganda. *African Health Sciences* **15**:1302–1307 DOI [10.4314/ahs.v15i4.33](https://doi.org/10.4314/ahs.v15i4.33).
- Laajala A, Pesonen P, Anttonen V, Laitala ML. 2019.** Association of enamel caries lesions with oral hygiene and DMFT among adults. *Caries Research* **53**:475–481 DOI [10.1159/000497358](https://doi.org/10.1159/000497358).
- Lamberghini F. 2017.** Silver diamine fluoride: a new way to treat caries in Canada. *CDA Essentials* **4**:21–22.
- Lee KE, Erdenebulgan M, Kang CM, Jung HI, Song JS. 2022.** Effect of silver diamine fluoride and potassium iodide solution on enamel remineralization and discoloration in artificial caries. *Materials* **15**(13):4523 DOI [10.3390/ma15134523](https://doi.org/10.3390/ma15134523).

- Liau SY, Read DC, Pugh WJ, Furr JR, Russell A.D. 1997.** Interaction of silver nitrate with readily identifiable groups: relationship to the antibacterial action of silver ions. *Letters in Applied Microbiology* 25:279–283 DOI 10.1046/j.1472-765x.1997.00219.x.
- Luk K, Niu JY, Gutknecht N, Zhao IS, Chu CH. 2021.** Preventing enamel caries using carbon dioxide laser and silver diamine fluoride. *Photobiomodulation, Photomedicine, and Laser Surgery* 39:8 DOI 10.1089/photob.2020.4894.
- Markham MD, Tsujimoto A, Barkmeier WW, Jurado CA, Fischer NG, Watanabe H, Baruth AG, Latta MA, Garcia-Godoy F. 2020.** Influence of 38% silver diamine fluoride application on bond stability to enamel and dentin using universal adhesives in self-etch mode. *European Journal of Oral Sciences* 128:354–360 DOI 10.1111/eos.12701.
- Mashhour A, Allam G, Wassel M. 2023.** Comparative evaluation of prevention of demineralization of artificial enamel caries treated with two fluoride varnishes and 38% SDF in primary teeth: an in vitro study. *BMC Oral Health* 23:110 DOI 10.1186/s12903-023-02799-1.
- Massignan C, Ximenes M, da Silva Pereira C, Dias L, Bolan M, Cardoso M. 2016.** Prevalence of enamel defects and association with dental caries in preschool children. *European Archives of Paediatric Dentistry* 17:461–466 DOI 10.1007/s40368-016-0254-8.
- McDonald SP, Sheiham A. 1994.** A clinical comparison of non-traumatic methods of treating dental caries. *International Dental Journal* 44:465–470.
- Mohammadi N, Farahmand Far MH. 2018.** Effect of fluoridated varnish and silver diamine fluoride on enamel demineralization resistance in primary dentition. *Journal of Indian Society of Pedodontics and Preventive Dentistry* 36:257–261 DOI 10.4103/JISPPD.JISPPD\_4\_18.
- Ndagire B, Kutesa A, Ssenyonga R, Kiiza HM, Nakanjako D, Rwenyonyi CM. 2020.** Prevalence, severity and factors associated with dental caries among school adolescents in Uganda: a cross-sectional study. *Brazilian Dental Journal* 31:171–178 DOI 10.1590/0103-6440202002841.
- Oppermann RV, Johansen JR. 1980.** Effect of fluoride and non-fluoride salts of copper, silver and tin on the acidogenicity of dental plaque in vivo. *Scandinavian Journal of Dental Research* 88:476–480 DOI 10.1111/j.1600-0722.1980.tb01257.x.
- Oppermann RV, Rölla G. 1980.** Effect of some polyvalent cations on the acidogenicity of dental plaque in vivo. *Caries Research* 14:422–427 DOI 10.1159/000260485.
- Ostela I, Tenovuo J. 1990.** Antibacterial activity of dental gels containing combinations of amine fluoride, stannous fluoride, and chlorhexidine against cariogenic bacteria. *Scandinavian Journal of Dental Research* 98:1–7 DOI 10.1111/j.1600-0722.1990.tb00933.x.
- Pérez-Hernández J, Aguilar-Díaz FC, Venegas-Lancón RD, Gayosso CAÁ, Villanueva-Vilchis MC, de la Fuente-Hernández J. 2018.** Effect of silver diamine fluoride on adhesion and microleakage of a pit and fissure sealant to tooth enamel: *in vitro* trial. *European Archives of Paediatric Dentistry* 19:411–416 DOI 10.1007/s40368-018-0374-4.
- Phonghanyudh A, Duangthip D, Mabangkhru S, Jirattanasopha V. 2022.** Is silver diamine fluoride effective in arresting enamel caries? a randomized clinical trial.

- International Journal of Environmental Research and Public Health* **19**(15):8992  
DOI [10.3390/ijerph19158992](https://doi.org/10.3390/ijerph19158992).
- Punhagui MF, Jussiani EI, Andrello AC, Favaro JC, Guiraldo RD, Lopes MB, Berger SB. 2021.** Effect of application time and concentration of silver diamine fluoride on the enamel remineralization. *Journal of Clinical and Experimental Dentistry* **13**:e653–e658 DOI [10.4317/jced.58318](https://doi.org/10.4317/jced.58318).
- Punyanirun K, Yospi boonwong T, Kunapinun T, Thanyasrisung P, Trairatvorakul C. 2018.** Silver diamine fluoride remineralized artificial incipient caries in permanent teeth after bacterial pH-cycling in-vitro. *Journal of Dentistry* **69**:55–59 DOI [10.1016/j.jdent.2017.09.005](https://doi.org/10.1016/j.jdent.2017.09.005).
- Rafiee A, Memarpour M, Benam H. 2022.** Evaluation of bleaching agent effects on color and microhardness change of silver diamine fluoride-treated demineralized primary tooth enamel: an in vitro study. *BMC Oral Health* **22**:347 DOI [10.1186/s12903-022-02371-3](https://doi.org/10.1186/s12903-022-02371-3).
- Romão DA, Fernández CE, De Melo Santos L. 2020.** Commercial silver diamine fluoride (SDF) products on caries lesion progression in primary enamel: an *in vitro* study. *Oral Health & Preventive Dentistry* **18**:1025–1029 DOI [10.3290/j.ohpd.b871057](https://doi.org/10.3290/j.ohpd.b871057).
- Romero MJRH, Lippert F. 2021.** Indirect caries-preventive effect of silver diamine fluoride on adjacent dental substrate: a single-section demineralization study. *European Journal of Oral Sciences* **129**:e12751 DOI [10.1111/eos.12751](https://doi.org/10.1111/eos.12751).
- Rosenblatt A, Stamford TC, Niederman R. 2009.** Silver diamine fluoride: a caries silver-fluoride bullet. *Journal of Dental Research* **88**:116–125 DOI [10.1177/0022034508329406](https://doi.org/10.1177/0022034508329406).
- Sakulratchata R, Saelow D, Banyat S, Wongto S, Sapppracha A, Kriangkrai R, Norchai P, Tohna S. 2024.** Progression of proximal caries in primary molars using the radiographic ICDAS: a retrospective cohort study. *European Archives of Paediatric Dentistry* **25**:327–334 DOI [10.1007/s40368-024-00886-7](https://doi.org/10.1007/s40368-024-00886-7).
- Savas S, Kucukyilmaz E, Celik EU, Ates M. 2015.** Effects of different antibacterial agents on enamel in a biofilm caries model. *Journal of Oral Science* **57**:367–372 DOI [10.2334/josnusd.57.367](https://doi.org/10.2334/josnusd.57.367).
- Sayed M, Matsui N, Hiraishi N, Nikaido T, Burrow MF, Tagami J. 2018.** Effect of glutathione bio-molecule on tooth discoloration associated with silver diamine fluoride. *International Journal of Molecular Sciences* **19**(5):1322 DOI [10.3390/ijms19051322](https://doi.org/10.3390/ijms19051322).
- Sorkhdini P, Crystal YO, Tang Q, Lippert F. 2021.** The effect of silver diamine fluoride in preventing in vitro primary coronal caries under pH-cycling conditions. *Archives of Oral Biology* **121**:104950 DOI [10.1016/j.archoralbio.2020.104950](https://doi.org/10.1016/j.archoralbio.2020.104950).
- Sorkhdini P, Gregory RL, Crystal YO, Tang Q, Lippert F. 2020.** Effectiveness of in vitro primary coronal caries prevention with silver diamine fluoride—Chemical vs biofilm models. *Journal of Dentistry* **99**:103418 DOI [10.1016/j.jdent.2020.103418](https://doi.org/10.1016/j.jdent.2020.103418).
- Surendranath P, Krishnappa S, Srinath S. 2022.** Silver diamine fluoride in preventing caries: a review of current trends. *International Journal of Clinical Pediatric Dentistry* **15**:S247–S251 DOI [10.5005/jp-journals-10005-2167](https://doi.org/10.5005/jp-journals-10005-2167).

- Thibodeau EA, Handelman SL, Marquis RE. 1978.** Inhibition and killing of oral bacteria by silver ions generated with low intensity direct current. *Journal of Dental Research* 57:922–926 DOI [10.1177/00220345780570091901](https://doi.org/10.1177/00220345780570091901).
- Tiba AA, Tiba A, Horvath F, Huh EY, Ford AA, Arens DK, Sarwar TA, Hwang YY. 2022.** Effects of a two-step silver diamine fluoride varnish on shear bond strength of restorations, dentin and enamel hardness, and biofilm formation. *Military Medicine* 189(3–4):592–597 DOI [10.1093/milmed/usac216](https://doi.org/10.1093/milmed/usac216).
- U.S. Food & Drug Administration. 2017.** Diammine silver fluoride dental hypersensitivity varnish. Available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K102973> (accessed on 28 February 2017).
- Xue VW, Yin IX, Niu JY, Lo ECM, Chu CH, Zhao IS. 2022.** Effects of a 445 nm diode laser and silver diamine fluoride in preventing enamel demineralisation and inhibiting cariogenic bacteria. *Journal of Dentistry* 126:104309 DOI [10.1016/j.jdent.2022.104309](https://doi.org/10.1016/j.jdent.2022.104309).
- Yan IG, Zheng FM, Gao SS, Duangthip D, Lo ECM, Chu CH. 2022.** A review of the protocol of SDF therapy for arresting caries. *International Dental Journal* 72:579–588 DOI [10.1016/j.identj.2022.06.006](https://doi.org/10.1016/j.identj.2022.06.006).
- Yu OY, Mei ML, Zhao IS, Li QL, Lo EC, Chu CH. 2018.** Remineralisation of enamel with silver diamine fluoride and sodium fluoride. *Dental Materials* 34:e344–e352 DOI [10.1016/j.dental.2018.10.007](https://doi.org/10.1016/j.dental.2018.10.007).
- Yu Y, Zhou X, Zheng LW. 2020.** Advanced research on root canal therapy for primary teeth. *Hua Xi Kou Qiang Yi Xue Za Zhi* 38:205–210 DOI [10.7518/hxkq.2020.02.016](https://doi.org/10.7518/hxkq.2020.02.016).
- Zaffarano L, Salerno C, Campus G, Cirio S, Balian A, Karanxha L, Cagetti MG. 2022.** Silver Diamine Fluoride (SDF) efficacy in arresting cavitated caries lesions in primary molars: a systematic review and metanalysis. *International Journal of Environmental Research and Public Health* 19(19):12917 DOI [10.3390/ijerph191912917](https://doi.org/10.3390/ijerph191912917).
- Zhao IS, Gao SS, Hiraishi N, Burrow MF, Duangthip D, Mei ML, Lo EC, Chu CH. 2018.** Mechanisms of silver diamine fluoride on arresting caries: a literature review. *International Dental Journal* 68:67–76 DOI [10.1111/idj.12320](https://doi.org/10.1111/idj.12320).
- Zhao IS, Xue VW, Yin IX, Niu JY, Lo ECM, Chu CH. 2021.** Use of a novel 9.3- $\mu$ m carbon dioxide laser and silver diamine fluoride: prevention of enamel demineralisation and inhibition of cariogenic bacteria. *Dental Materials* 37:940–948 DOI [10.1016/j.dental.2021.02.017H](https://doi.org/10.1016/j.dental.2021.02.017H).