

Review article

Minimizing tooth discoloration caused by topical silver diamine fluoride application: A systematic review

Grace Y Xu^a, Iris X Yin^a, Irene S Zhao^{b,*}, Christie YK Lung^a, Edward CM Lo^a, Chun Hung Chu^{a,*}

^a Faculty of Dentistry, The University of Hong Kong, Hong Kong, PR China

^b School of Dentistry, Shenzhen University Health Science Center, Shenzhen, PR China

ARTICLE INFO

Keywords:

Silver diamine fluoride
Glass ionomer cement
Composite
Potassium iodide
Silver
Nanoparticles

ABSTRACT

Objective: The objective of this systematic review is to examine the methods used to minimize discoloration of the carious lesions after topical silver diamine fluoride (SDF) application.

Data/Sources: Two independent researchers conducted a search of English literature published up to 30th April 2024 in three databases (PubMed, Scopus, and Web of Science). They screened titles and abstracts, excluding conference proceedings, books, reviews and publications unrelated to SDF. They included only original research on methods to minimize SDF-induced discoloration. The publications lacking comparative color change data were excluded. Full texts of the included articles were then analyzed. The Cochrane guidelines for clinical trials and the guidelines for in-vitro studies on dental materials were used for the risk of bias assessment.

Results: The systematic review included 33 publications from 1,283 identified publications (26 laboratory studies and 7 clinical studies). Thirteen laboratory studies and five clinical studies were rated as having 'low risk'. Three main methods to minimize discoloration were identified: masking with restoration, using chemicals, and substituting silver with nano-silver. Nine studies used resin composite or glass ionomer cement to mask the SDF-induced discoloration. Twenty-nine studies used chemicals to reduce SDF-induced discoloration. These chemicals included precipitating agents like potassium iodide, oxidizing agents like hydrogen peroxide, and chelating agents like glutathione. Seven publications used chemicals (potassium iodide or glutathione) before restoration and six of them found improved masking effect. Four studies substituted silver ions with silver nanoparticles which did not discolor carious lesion.

Conclusions: Masking with restoration, using chemicals, and substituting silver ions with nano-silver particles have been reported to address the discoloring effects of SDF therapy. However, most are laboratory studies, and more clinical trials are needed to confirm their effectiveness in reducing SDF-induced discoloration.

Clinical significance: SDF effectively arrests caries, but it discolors carious lesions. This review summarizes the methods and their outcomes for reducing SDF-induced discoloration. This study is supported by the General Research Fund of Research Grant Council No. 17,100,222.

1. Introduction

Dental caries remains one of the most widespread chronic diseases worldwide, especially in socioeconomically disadvantaged populations [1]. Untreated dental caries imposes a significant burden, both in terms of human suffering and economic costs [2,3]. Severe tooth decay results in pain, infection, and tooth loss, which can negatively impact the quality of life [4]. The cost of treating dental caries can be substantial,

especially when left untreated, as it often requires more invasive procedures.

Invasive dental treatments can be painful and may harm healthy tooth structures, causing patients anxiety and stress. Conversely, non-invasive dental treatments preserve the natural tooth structure, offering a more conservative option for patients. Non-invasive treatments can also serve as preventive measures to reduce future dental caries risks [5]. Silver diamine fluoride (SDF) has gained popularity for arresting

* Corresponding author: 34 Hospital Road, Sai Ying Pun, Hong Kong, PR China.

** Corresponding author.

E-mail addresses: zhao110@szu.edu.cn (I.S. Zhao), chchu@hku.hk (C.H. Chu).

<https://doi.org/10.1016/j.jdent.2024.105353>

Received 28 July 2024; Received in revised form 5 September 2024; Accepted 9 September 2024

Available online 14 September 2024

0300-5712/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

dental caries and preventing further decay [6]. SDF has strong antibacterial and remineralization properties [7]. It is effective in treating dental caries in children and older adults, and patients who are intolerant of traditional procedures [8-10]. While generally safe and effective, SDF discolors permanently demineralized dental hard tissues, limiting their use to non-visible tooth surfaces [11]. The discoloration caused by SDF is more noticeable in areas weakened by caries, ranging from dark brown to black. This concern may affect dentists' recommendation of this treatment [11]. The formation of black stains may result from the decomposition of SDF, leading to the reduction of silver ions to metallic silver particles. Silver salts, including silver chloride, silver phosphate and silver oxide, are also responsible for the black staining of caries lesion [12]. Additionally, the photosensitivity of silver ions can cause dark staining during the light curing process in subsequent restoration stages [13].

Researchers are exploring various approaches to reduce the discoloring effects of SDF in caries management. We identified two systematic reviews on this topic. One review, which included five laboratory studies and one case report, evaluated the use of potassium iodide to reduce discoloration [14]. The other review, based on nine laboratory studies, concluded that the application of chemicals, particularly potassium iodide, following SDF treatment, helped reduce discoloration [15]. However, more recent studies have emerged that were not included in these earlier reviews. Therefore, the objective of this study is to systematically review methods developed to minimize the discoloration of carious lesions after topical SDF application.

2. Methods

This review was conducted and reported according to the Preferred Reporting Items for Systematic review and Meta-Analyses (PRISMA) 2020 checklist.

2.1. Search

Two independent researchers searched three databases (PubMed,

Scopus, and Web of Science) with the keywords (tooth decay OR dental caries OR caries OR carious lesions) AND silver AND (staining OR discoloration OR discolouration). The final search was carried out on April 30, 2024. The search was limited to English-language publications. Fig.1 presents the flowchart for the literature search process.

2.2. Study selection

This systematic review included original investigations on methods for minimizing staining after topical SDF application in caries management (Fig. 1). Researchers removed duplicates before screening titles and abstracts of the publications to identify potentially eligible publications. They excluded conference proceedings, book, review and other publications that are unrelated to SDF. The investigators obtained full texts of the remaining publications for review. They excluded publications not including the comparison of color change among different methods. They then performed a manual screening to choose suitable publications from the reference lists of the selected papers. They turned to discuss with the third researcher on the disagreements on including or excluding publications.

2.3. Data extraction

Two researchers collected information on the publications, including the authors, publication years, methods used to reduce staining, study designs, sample sizes, color assessment methods, and main findings.

2.4. Risk of bias

Two researchers independently evaluated the potential bias in each study using criteria adapted from guidelines for in-vitro studies on dental materials [16]. Fifteen parameters were considered across all reviewed in-vitro publications. Studies reporting fewer than ten parameters were categorized as having a high risk of bias, while those reporting ten or more parameters were classified as having a low risk. The risk of bias in the clinical studies was assessed independently by the

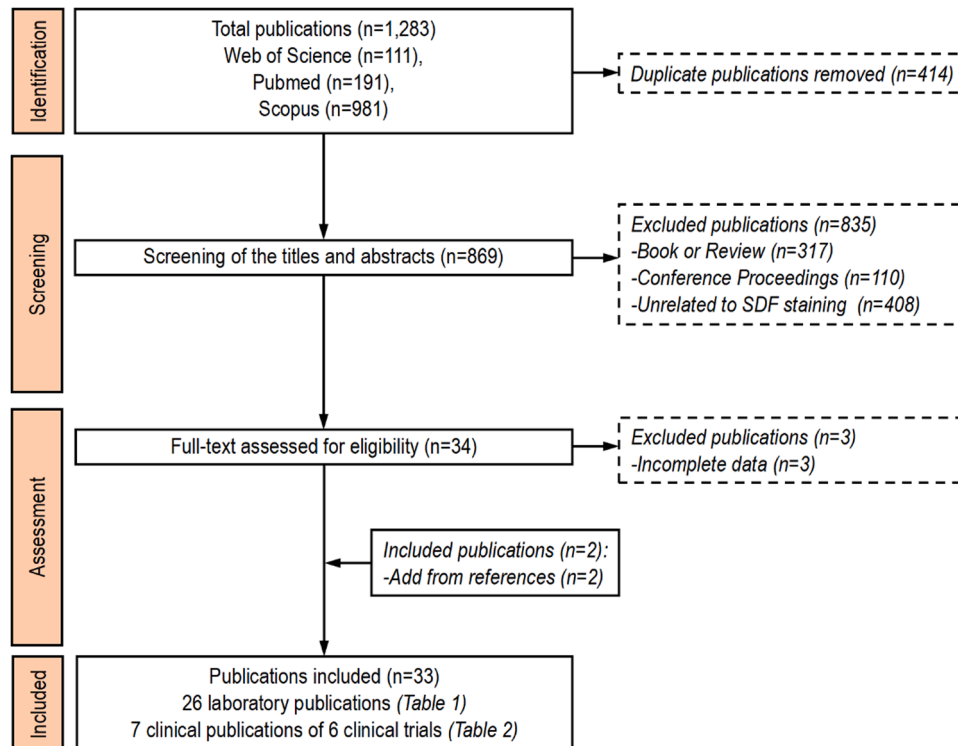


Fig. 1. Flowchart of conducting systematic review.

same two researchers using the Cochrane risk-of-bias tool for randomized trials, evaluating each study across five domains, which are a) sequence generation, b) allocation concealment, c) blinding, d) incomplete outcome data, and e) selective reporting. Each domain was assessed at two levels: 'yes' or 'unclear'. If less than three domains were rated as 'yes,' the study was classified as having a high risk.

3. Results

The initial search identified 1283 publications (191 publications in Pubmed, 981 publications in Scopus, 111 publications in Web of Science). After removing 414 duplicate publications, the researchers screened the titles and abstracts of the remaining 869 publications. They then removed 835 publications which were review ($n = 235$), book chapters ($n = 82$), conference proceedings ($n = 110$), or publications unrelated to SDF ($n = 408$). The full text of the remaining publications were retrieved for assessment. The researchers identified and added two publications from the references of the remaining publications. They excluded three publications which reported incomplete data. Finally, thirty-three articles were selected for analysis. Twenty-six publications (26/33, 78 %) were laboratory studies, and seven publications (7/33, 21 %) were clinical studies.

The methods employed in the laboratory studies can be categorized into three main approaches: (1) masking using resin composite or glass ionomer cement restorations, (2) applying chemicals such as potassium iodide to precipitate silver ions, and (3) substituting silver ions with silver nanoparticles. Table 1 presents the methods used to mitigate SDF discoloration in 26 laboratory studies.

Dentists show interest on the availability of masking the SDF discoloration with the restorative materials. The masking effect of discoloring lesions can be achieved using two main types of tooth-colored restorative materials. These two types of restorative materials are resin composite and glass ionomer cement and their derivatives, such as resin-modified glass ionomer cement, and zirconia-reinforced glass ionomer cement [17–25]. Following the application of SDF on the prepared cavity, researchers placed the tooth-colored restoration immediately or at a subsequent visit after one to two weeks [17,18]. Studies investigated whether the presence of potassium iodide enhances the esthetic appearance after restoration. One study found out that the use of potassium iodide after application of SDF prevents staining under resin composite restorations after sixty days [20]. Another study verified that the potassium iodide-treated group exhibited discoloration upon aging when subjected to a suntest aging device for 24 h in water at 37 °C [21]. Only one study concluded that there was no significant difference in staining between groups with or without the use of potassium iodide [22]. However, in the clinical setting, the masking effect may raise additional concerns, especially regarding the stability of color change and the questionable bonding strength [17].

The use of additional chemicals is considered as another viable alternative for minimizing staining. One potential agent is potassium iodide, which can react with free silver ions to generate a creamy white precipitate of silver iodide. An immediate reduction of staining was observed in six studies after the application of potassium iodide [26–31]. Three studies investigated the durability of color change for up to fourteen days [27,29,30]. One study investigated the impact of various concentrations of potassium iodide on color change, revealing a dose-dependent effect on immediate discoloration reduction [27]. But this disparity diminished after one week. However, a laboratory study reported a persistent color enhancement after the application of potassium iodide on the seventh day [30]. But it has been discovered that in clinical setting the color improvement with potassium iodide is only temporary, and the darkening of tooth surfaces proceeds [32]. Another chemical used to solve the staining problem is chelating agent, such as glutathione, to stabilize silver ions [33]. Glutathione shows a strong affinity for adsorption onto metal surfaces, forming a coating and controlling the release rate. As a result, glutathione-modified SDF solutions

had a reduced potential for tooth staining [33–35]. Bleaching treatments offer another quick and affordable option for aesthetic management. The at-home bleaching protocol utilizing carbamide peroxide with longer application time has shown significant efficacy in reducing the staining caused by 38 % SDF [36]. To minimize susceptibility of further demineralization, it is recommended to add fluoride or other remineralization agents after bleaching. It has been found that the application of fluoridated carbamide peroxide can effectively bleach the staining caused by 38 % SDF treatment on primary anterior teeth [37].

Silver nanoparticles are another alternative since they cause no staining for no oxides production when exposed to oxygen in the medium [38]. Among the four articles substituting silver with silver nanoparticles as intervention groups [39–43], two studies selected 38 % SDF as the positive control for comparison [39,42]. Another two studies used 30 % SDF or 12 % SDF as positive control [40,43]. Staining effects were investigated using dentin blocks in three studies, with only one study examining enamel [40]. The longest follow-up period in these studies did not exceed one month [39,40]. Both objective and subjective color evaluation techniques were employed. Three studies used a spectrophotometer [39,42,43]. Two studies relied on photographic images for direct color change observation [40,42] while one of the studies further compared the color parameters including intensity of color or L^* , C^* and h^* to reach an objective conclusion [42]. These four studies concluded that the inclusion of silver nanoparticles into fluoride solutions did not lead to significant tooth discoloration.

Table 2 summarizes the 7 publications on 6 randomized clinical trials. Among these clinical publications, two studies are split-mouth randomized clinical trials, and five are parallel-design randomized clinical trials. Two studies used permanent molars as study subjects and other five focused on primary teeth. All studies compared the color change of SDF followed by potassium iodide. Additionally, one study compared the masking effect of resin-modified GIC [44]. Another trial included two additional groups: silver fluoride solution and silver fluoride followed by potassium iodide [45,46]. Color change is assessed and compared using subjective (color ranking) or objective approaches (ΔE and mean gray values). The follow-up timepoint is different among studies, with the longest being 30 months. Although potassium iodide significantly decreased discoloration immediately, it did not have long-term effectiveness in preventing staining and may have compromised arresting efficacy. Table 2 lists the study design including study subjects, intervention groups (with SDF) and color assessment measures, and main results of the identified clinical trials. Two publications had the same study design but different endpoints [45,46].

Table 3 shows the risk of bias assessment of seven randomized controlled clinical trials. Five publications presented with a medium risk. While two publications had a high risk of bias because of no proper randomization at the teeth level as well as no blinding. For the laboratory studies, half of the publications (13/26, 50 %) presented low risk and (Table 4).

4. Discussion

While the discoloring effect of SDF on carious teeth is a concern, the benefits of SDF in preventing and treating caries are well-established [47]. According to our findings, there are three strategies for reducing the staining of SDF: employing SDF in combination with chemical agents, substituting with silver nanoparticles, and masking with restorations. The most commonly used chemical agent is potassium iodide. While the combined application of potassium iodide can temporarily mitigate the impact of silver ion staining, its long-term effectiveness remains uncertain. Silver nanoparticles exhibit superior efficacy compared to other methods in eliminating staining. The utilization of resin composites and other materials to mask stains is therapeutically viable; however, it limits the use of SDF in clinical caries control scenarios such as outreach services.

Registering a systematic review protocol before conducting the

Table 1

The three methods to reduce silver diamine fluoride (SDF) discoloration in 26 laboratory studies.

Authors, Year	Comparison groups	Tooth tissue	Assessment	Discoloring minimizing effect
1 Masking with resin composite (RC) or glass ionomer cement restoration (GIC) (8 studies)				
Alsagob et al. 2022	1) SDF 2) SDF + RC or GIC	Human carious teeth	Spectrophotometry	RC and GIC masked the SDF discoloration.
Hamdy et al. 2021	1) SDF 2) SDF + KI 3) SDF + RC or GIC	Human carious teeth	Spectrophotometry	KI reduced SDF discoloration. RC and GIC masked SDF discoloration.
Frohlich et al. 2021	1) SDF 2) SDF + RC 3) SDF + KI 4) SDF + KI + RC	Sound bovine teeth	Spectrophotometry	RC masked SDF discoloration. KI reduced SDF discoloration. KI + RC reduced more discoloration.
Kamble et al. 2021	1) SDF + GIC 2) SDF + KI + GIC 3) SDF + Glutathione + GIC	Human carious teeth	Spectrophotometry	KI and Glutathione reduced SDF discoloration under GIC restoration.
Raafat et al. 2022	1) SDF + GIC 2) SDF + KI + GIC	Human sound teeth	Spectrophotometry	KI reduced more SDF discoloration under GIC restoration.
Vennela et al. 2021	1) SDF + RC or GIC 2) SDF + KI + RC or GIC	Human carious teeth	Digital imaging	KI reduced more SDF discoloration under RC or GIC restoration.
Zhao et al. 2017	1) SDF + GIC 2) SDF + KI + GIC	Human sound teeth	Spectrophotometry	KI reduced more SDF discoloration under GIC restoration.
Miller et al. 2016	1) SDF + GIC 2) SDF + KI + GIC	Human carious teeth	Visual assessment	KI didn't reduce more SDF discoloration under GIC restoration.
2 Using chemicals reduce discoloration induced by SDF (14 studies)				
Thurston et al. 2024	1) SDF 2) SDF + KI	Human sound teeth	Colorimetry	KI reduced SDF discoloration.
Camatta et al. 2023	1) SDF 2) SDF + KI	Human sound dentin blocks	Spectrophotometry	KI reduced SDF discoloration.
Samaddar et al. 2023	1) SDF 2) SDF + KI	Human sound dentin blocks	Digital camera	KI reduced SDF-discoloration.
Detsomboonrat et al. 2022	1) SDF 2) SDF + KI	Human carious teeth	Digital imaging	KI reduced SDF-discoloration
Lee et al. 2022	1) SDF 2) SDF + KI	Bovine sound enamel blocks	Digital imaging	KI reduced SDF discoloration.
Luong et al. 2022	1) SDF 2) SDF + KI	Human sound dentin blocks	Colorimetry	KI reduced SDF discoloration.
Zhao et al. 2019	1) SDF 2) SDF + KI	Human sound dentin blocks	Spectrophotometry	KI reduced SDF discoloration.
Patel et al. 2018	1) SDF 2) SDF + KI	Human carious teeth	Digital imaging	KI reduced SDF discoloration.
Sayed et al. 2018	1) SDF 2) SDF + KI 3) SDF + Glutathione	Bovine sound dentin and enamel blocks	Spectrophotometry	KI reduced SDF discoloration. Glutathione is more effective than KI in reducing discoloration.
Asghar et al. 2022	1) SDF 2) SDF + Glutathione 3) SDF + Carboxymethyl chitosan 4) SDF + Gallic acid 5) SDF + Tannic acid	Bovine sound dentin blocks	Spectrophotometry	Tannic acid, glutathione, chitosan and gallic acid reduced SDF discoloration. Discoloring minimizing effect: Gp5 > Gp2 > Gp3 > Gp4
Islam et al. 2023	1) SDF 2) SDF + Ascorbic acid 3) SDF + Alpha lipoic acid	Bovine sound teeth	Colorimetry	Alpha lipoic acid but not ascorbic acid reduced SDF discoloration.
Al-Angari et al. 2019	1) SDF 2) SDF + Carbamide peroxide 3) SDF + Hydrogen peroxide	Human sound dentin blocks	Spectrophotometry	Carbamide peroxide and hydrogen peroxide reduced SDF discoloration.
Rafiee et al. 2022	1) SDF + Carbamide peroxide 2) SDF + KI + Carbamide peroxide	Human sound enamel blocks	Spectrophotometry	The combination of KI with Carbamide peroxide reduced more discoloration.
Rodrigues et al. 2024	1) SDF + Garlic extract 2) SDF + Bentonite 3) SDF + Hydrogen peroxide	Human sound dentin blocks	Spectrophotometry	Only hydrogen peroxide reduced SDF discoloration
3 Replacing silver ions with nano silver particles (4 studies)				
Favaro et al. 2022	1) SDF 2) Nano silver in silver fluoride	Human sound enamel blocks	Digital imaging	Nano silver in silver fluoride (but not SDF) had no discoloring effect.
Espíndola et al. 2020	1) SDF 2) Nano silver fluoride, 3) SDF + KI	Human sound dentin blocks	Spectrophotometry and Digital imaging	Nano silver fluoride (but not SDF) had no discoloring effect. KI reduced SDF discoloration.
Zhao et al. 2020	1) SDF 2) Nano silver in sodium fluoride	Human sound dentin blocks	Spectrophotometry	Nano silver in sodium fluoride (but not SDF) had no discoloring effect.
Yin et al. 2020	1) SDF 2) Nano silver in sodium fluoride	Human sound dentin blocks	Spectrophotometry	Nano silver in sodium fluoride (but not SDF) had no discoloring effect.

Table 2
Summary of the 7 publications on 6 randomized clinical trials.

Authors, Year	Study design				Discoloring effect
	Period	Sample size	Assessment	Intervention	
Li et al. 2016	30 months	157 carious lesions	Visual assessment	Gp1:SDF Gp2:SDF + KI	Gp1 = Gp2
Turton et al. 2020*	6 months	4606 tooth surfaces	Visual assessment	Gp1:SDF Gp2:SDF + KI	Gp1 > Gp2
Turton et al. 2021*	12 months	4606 tooth surfaces	Visual assessment	Gp1:SDF Gp2:SDF + KI	Gp1 > Gp2
Aly et al. 2022	12 months	30 teeth	Spectrophotometry	Gp1:SDF Gp2:SDF + KI	Gp1 = Gp2
Karuna et al. 2023	6 months	60 teeth	Digital imaging	Gp1:SDF Gp2:SDF + KI Gp3:SDF + Glutathione	Gp1 > Gp2 > Gp3
Baraka et al. 2022	12 months	108 teeth	Visual assessment	Gp1:SDF + GIC + RC Gp2:SDF + KI + GIC + RC	Gp1 > Gp2
Patel et al. 2024	6 months	100 tooth surfaces	Digital imaging	Gp1:SDF + KI	No (SDF) as control group

* Same clinical trial; SDF: silver diamine fluoride, KI: Potassium iodide, GIC: Glass ionomer cement, RC: Resin composite.

Table 3
Risk of bias assessment of the seven clinical studies.

Authors, Year	Checklist items					Risk of bias
	Sequence generation	Allocation concealment	Blinding	Addressing missing data	No selective reporting	
Li et al. 2016	O	O	O	O	O	Low
Aly et al. 2022		O	O	O	O	Low
Baraka et al. 2022	O		O	O	O	Low
Karuna et al. 2023	O	O	O		O	Low
Patel et al. 2024	O			O	O	Low
Turton et al. 2021				O	O	High
Turton et al. 2020				O	O	High

Table 4
Risk of bias assessment of the 26 laboratory studies (adapted from Faggion CM Jr., 2012).

Authors, Year	Checklist items															Total score	Risk of Bias
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15		
Hamdy et al. 2021	O	O	O	O	O	O	O	O	O		O	O	O	O	O	14	Low
Favaro et al. 2022	O	O	O	O	O	O	O				O	O	O	O	O	12	Low
Frohlich et al. 2021	O	O	O	O	O	O				O	O	O	O	O		11	Low
Rafiee et al. 2022	O	O	O	O	O		O				O	O	O	O	O	11	Low
Camatta et al. 2023	O	O	O	O	O	O					O	O	O	O	O	11	Low
Thurston Nash et al., 2024	O	O	O	O	O	O	O				O	O	O	O		11	Low
Miller et al. 2016	O	O	O	O	O	O				O	O	O	O			10	Low
Al-Angari et al. 2019	O	O	O	O	O	O					O	O	O	O		10	Low
Detsomboonrat et al. 2022	O	O	O	O	O	O					O	O	O	O		10	Low
Lee et al. 2022	O	O	O	O	O	O					O	O	O	O		10	Low
Asghar et al. 2022	O	O	O	O	O						O	O	O	O	O	10	Low
Raafat, et al. (2022)	O	O	O	O	O	O	O				O	O	O			10	Low
Rodrigues et al. 2024	O	O	O	O	O						O	O	O	O	O	10	Low
Zhao et al. 2017	O	O	O	O	O						O	O	O	O		9	High
Sayed et al. 2018	O	O	O	O	O						O	O	O	O		9	High
Zhao et al. 2019	O	O	O	O	O						O	O	O	O		9	High
Espíndola-Castro et al. 2020	O	O	O	O	O	O					O	O		O		9	High
Yin et al. 2020	O	O	O	O	O						O	O	O	O		9	High
Zhao et al. 2020	O	O	O	O	O	O					O	O		O		9	High
Vennela et al. 2021	O	O	O	O	O						O	O	O	O		9	High
Luong et al. 2022	O	O	O	O	O						O	O	O	O		9	High
Patel et al. 2018	O	O	O	O	O						O	O	O			8	High
Alsagob et al. 2022	O	O	O	O	O						O	O		O		8	High
Samaddar et al. 2023	O	O	O	O	O						O	O	O			8	High
Islam et al. 2023	O	O	O	O	O						O	O	O			8	High
Kamble et al. 2021	O	O	O	O	O	O					O					7	High

Checklist items:
1. Abstract, 2. Introduction-Background, 3. Introduction-Objectives, 4. Methods-Intervention, 5. Methods-Measures of outcomes,.
6. Methods-Sample size, 7. Methods-Sequence generation, 8. Methods-Allocation concealment, 9. Methods-Implementation,.
10. Methods-Blinding, 11. Methods-Statistical analysis, 12. Results-Outcomes, 13. Discussion-Limitations, 14. Disclosure of funding, 15. Open access protocol.

review helps prevent duplication, reduce bias, and enhance reproducibility. It also enables peer review and feedback, which can improve the review's quality. A limitation of this review is that we did not register our protocol. It may reduce the visibility and impact of our findings.

This review conducted a literature search using Web of Science, PubMed, and Scopus. Web of Science was chosen for its prominence in academic references [48]. PubMed was chosen for its frequent updates and coverage of early online articles in medicine and biomedical sciences. Scopus was chosen for its broad journal range beyond medical field [49]. This review did not perform searches in non-English databases, particularly Chinese and Japanese databases. This is a limitation because SDF has been reported in Japanese since the 1970s and in Chinese since the 1980s [50]. We conducted an exhaustive review of non-English publications on SDF published by March 2016 [50,51]. Both reviews included literature searches in Chinese literature via the China National Knowledge Infrastructure (CNKI), Japanese papers in Ichushi-web, and Spanish and Portuguese publications in Biblioteca Virtual en Salud España (BVSE) and Biblioteca Virtual em Saúde (BVS). We could not identify publications reporting methods to minimize SDF-induced discoloration. On the contrary, we found that there is a custom of dyeing the teeth black (Ohaguro). This custom has been around since prehistoric times in Japan, Vietnam, and other parts of Southeast Asia [52]. Thus, discoloration of teeth is probably more acceptable in Asian cultures than in Western cultures.

This review also did not include gray literature to provide a more comprehensive view of the available strategies for minimizing SDF-induced discoloration. Gray literature, however, is not typically standardized in the same way as academic literature. It can be difficult to locate and access, and often lacks full methodological detail. More importantly, the research quality and reliability of gray literature are not always guaranteed. There is a risk of publication bias, as studies with significant or positive results are more likely to be published. While gray literature can help mitigate this bias, it can also introduce other biases if not carefully assessed and controlled. Hence, we decided not to include gray literature in this review.

A review in 2020 included only five laboratory studies and one case report [14], whereas another review in 2023 identified nine laboratory studies [15]. We have identified 33 publications in this review, which is more comprehensive than the two reviews. Our comprehensive search identified three main strategies. In the chemical strategies, we found that not only potassium iodide but also oxidizing agents and chelating agents were used to minimize discoloration. Additionally, we incorporated clinical trials which in general provide higher level of evidence than laboratory studies.

SDF is a solution composed of silver fluoride and ammonia, which is one of the most commonly used silver compounds for caries management. It works by inhibiting the growth of bacteria and promoting the remineralization of the tooth [51]. It can be used as a non-invasive treatment for arresting caries, particularly in children as well as elderly who may not be able to tolerate traditional dental procedures [10,53]. SDF has been shown to be as effective as sodium fluoride in preventing in primary upper anterior teeth [54]. The staining effect is less noticeable on the posterior teeth and is more acceptable for severe caries [55]. The staining of arrested carious lesions is correlated with higher concentrations of silver ions [56]. However, 38 % SDF demonstrates superior efficacy in arresting active caries in primary teeth compared to 12 % SDF [57]. Consequently, it is imperative to explore alternatives for minimizing staining.

The objective of our review was to examine the various methods used to minimize discoloration after SDF application. We have identified several methods for reducing the staining of SDF. The heterogeneity among the included studies does not allow us to determine which method is superior. The variations in reporting the effectiveness of these methods, assessment techniques and timepoints made it difficult to perform a meta-analysis. The specimens used in these studies were either primary teeth or permanent teeth, depending on the specific

research objectives. Among the included laboratory studies, five experiments utilized bovine teeth while twenty-one studies employed human teeth. Although bovine teeth share certain similarities with human teeth in terms of radiopacity and dentin surface roughness, the enamel of bovine teeth demineralizes at a faster rate and has a different chemical composition [28,33]. All laboratory publications have observed the immediate color change following the application of the corresponding solution or restoration. Several studies have investigated the alteration in color over a longer period, with study timepoints ranging from one minute to sixty days [20,27,29,30,39-41,58]. The study timepoints for the clinical trials included in our study vary from one month to thirty months.

Four publications utilize visual grading scales to rank the staining [22,44-46]. Digital cameras record fundamental image information and provide a more intuitive contrast among different intervention groups. However, either naked eyes or photographic records are subjective and is influenced by various factors including environmental lighting and eye fatigue. Nineteen laboratory publications included in our study (19/26, 73 %) used spectrophotometer or colorimeter as the evaluation tool. The collected information, regardless of the approach used, must be translated into comparable data. The quantified value for the color change test includes parameters such as CIE L*a*b* system, chroma, hue for spectrophotometer and colorimeter measurements; mean gray value, intensity of color, and RGB values for digital camera analysis. The L* values represent the color gradients ranging from white to black, while the a* values represent the gradient from green to red, and the b* values indicate the gradient from blue to yellow. The quantitative interpretation of color changes (ΔE) was utilized for verifying the alteration of stained lesions over time. The reported clinical perceptibility threshold ranges from 1 to 6.8 [59,60].

The laboratory studies included in our study have confirmed that the use of potassium iodide following SDF improved aesthetic outcomes immediately [26-31,33,61,62]. However, it should be noted that over time, significant discoloration was observed during subsequent follow-up visits due to the formation of silver iodide [32,63]. This photosensitive material can undergo dissociation into silver and iodine upon exposure to light. In addition to poorer color stability, the inclusion of potassium iodide may result in a reduced caries arrest rate compared to groups solely treated with silver compounds [46]. The reduction of free silver ions may impair the anti-caries effect of SDF [25]. The guidelines proposed by the American Academy of Pediatric Dentistry suggest that the restoration of arrested cavitated caries lesions by SDF to enhance aesthetic outcomes. [64]. The combination of potassium iodide and restoration materials showed enhanced masking effects compared to restoration materials alone. [23-25,44]. More well-designed clinical trials are imperative in order to determine the optimal approach for minimizing staining.

Silver nanoparticles have gained attention due to their unique physical and chemical properties [65]. These particles possess a high surface area-to-volume ratio and exhibit significant antimicrobial efficacy. Unlike ionic silver, their small size and optoelectronic properties allows them to apply on demineralized dentine without visible discoloration [42,43]. SDF contains both silver ions and fluoride. It causes staining due to the formation of silver oxide or other silver compounds. However, a combination of silver nanoparticles and fluoride solution offers a promising alternative. This approach combines the antimicrobial properties of silver nanoparticles and the remineralizing effects of fluoride. By using silver nanoparticles instead of ionic silver, the extent of oxidation and subsequent staining can be reduced. Some researchers have raised concerns about the use of nano silver products due to their toxicity to human cells and potential for bioaccumulation [66,67]. Further research and comprehensive evaluations are needed to confirm their safe use in dental treatments.

Other factors including the concentration, application frequency, and amount of SDF can affect discoloration intensity. A laboratory study comparing the staining effect of 38 % and 12 % SDF on carious primary

molars found no significant difference [30]. Conversely, a clinical study reported that black stains appeared about three times more frequently in the 38 % SDF group than in the 12 % SDF group [55]. The same clinical trial also demonstrated that semi-annual application of SDF resulted in a 1.7 times higher chance of discoloration compared to annual application of the same concentration [54]. Lower concentration and less frequent application of SDF may reduce staining intensity on arrested carious lesions. However, it is noteworthy that 12 % SDF reduced the caries-arresting efficacy by nearly half compared to 38 % SDF in primary teeth. The mean amount of 38 % SDF applied to three teeth was reported to be 7.6 mg [68]. The amount of SDF solution delivered varies depending on the brand and size of the micro-applicators [69]. No studies have compared the discoloration effects of different amounts of SDF application. While lower concentrations and reduced frequency of SDF application may minimize staining intensity, they also significantly diminish caries-arresting efficacy. Further research is needed to explore the impact of varying amounts of SDF on discoloration and to optimize the balance between aesthetic outcomes and clinical effectiveness.

5. Conclusion

SDF provides a non-invasive, effective option for treating and preventing dental caries, especially in vulnerable populations. Our research identifies three main strategies to reduce staining from SDF: adding chemical agents, substituting with silver nanoparticles, and applying masking techniques with resin composite or glass ionomer cement restoration. Both dentists and patients should weigh the disadvantages and advantages of each approach to make informed choices based on specific needs and preferences. Additional clinical researches are essential to fully realize the benefits of SDF in caries management.

Funding support

This study is supported by the General Research Fund of Research Grant Council (No. 17,100,222).

CRediT authorship contribution statement

Grace Y Xu: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Iris X Yin:** Writing – original draft, Formal analysis, Data curation. **Irene S Zhao:** Writing – review & editing. **Christie YK Lung:** Writing – review & editing. **Edward CM Lo:** Writing – review & editing. **Chun Hung Chu:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they do not have known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- P.Y.F. Wen, et al., Global Burden and Inequality of Dental Caries, 1990 to 2019, *J. Dent. Res.* 101 (4) (2022) 392–399.
- A.J. Righolt, et al., Global-, regional-, and country-level economic impacts of dental diseases in 2015, *J. Dent. Res.* 97 (5) (2018) 501–507.
- L. Kastenbom, et al., Costs and health-related quality of life in relation to caries, *BMC Oral Health* 19 (1) (2019) 187.
- C.A. Ribeiro Junior, et al., The role of dental pain and psychosocial factors on the relationship between dental caries and oral health-related quality of life in children, *BMC Oral Health* 22 (1) (2022) 340.
- J.M. White, W.S. Eakle, Rationale and treatment approach in minimally invasive dentistry, *J. Am. Dent. Assoc.* 131 (2000) 13S–19S. Suppl.
- D. Duangthip, et al., Managing early childhood caries with atraumatic restorative treatment and topical silver and fluoride agents, *Int. J. Environ. Res. Public Health* 14 (10) (2017).
- J.J. Peng, et al., Silver compounds used in dentistry for caries management: a review, *J. Dent.* 40 (7) (2012) 531–541.
- S. Mabangkhu, et al., A randomized clinical trial to arrest dentin caries in young children using silver diamine fluoride, *J. Dent.* 99 (2020) 103375.
- A.K.Y. Chan, et al., Clinical evidence for professionally applied fluoride therapy to prevent and arrest dental caries in older adults: a systematic review, *J. Dent.* 125 (2022) 104273.
- S.S. Gao, et al., Arresting early childhood caries using silver and fluoride products – a randomised trial, *J. Dent.* 103 (2020) 103522.
- H.H. Chai, et al., Knowledge, practices and attitudes towards silver diamine fluoride therapy among dentists in japan: a mixed methods study, *Int. J. Environ. Res. Public Health* 19 (14) (2022).
- M.L. Mei, et al., Arresting dentine caries with silver diamine fluoride: what's behind it? *J. Dent. Res.* 97 (7) (2018) 751–758.
- C.N. Vinh N, F. Joel, P. Carolyn, Potassium Iodide, The solution to silver diamine fluoride discoloration? *Adv. Dent. Oral Health* 5 (1) (2017) 001–006.
- A. Roberts, et al., Does potassium iodide application following silver diamine fluoride reduce staining of tooth? A systematic review, *Aust. Dent. J.* 65 (2) (2020) 109–117.
- M. Asghar, et al., Approaches to minimize tooth staining associated with silver diamine fluoride: a systematic review, *J. Esthet. Restor. Dent.* 35 (2) (2023) 322–332.
- F.C.M. Jr, Guidelines for reporting pre-clinical in vitro studies on dental materials, *J. Evid. Based. Dent. Pract* 12 (4) (2012) 182–189.
- M.M. Aldosari, F.S. Al-Sehaibany, The Effect of Loading Time on Color Stability of Various Restorative Materials Bonded to Silver Diamine Fluoride-Treated Demineralized Dentin, *Clin. Cosmet. Invest.* 14 (2022) 123–130.
- E. Alsagob, et al., Silver diamine fluoride with delayed restoration reduces tooth discoloration, *Saudi J. Biol. Sci.* 29 (3) (2022) 1434–1438.
- A.C. Ferreira, et al., Remineralization of caries-affected dentin and color stability of teeth restored after treatment with silver diamine fluoride and bioactive glass-ceramic, *Clin. Oral Invest.* 26 (7) (2022) 4805–4816.
- T.T. Fröhlich, et al., Evaluation of the use of potassium iodide application on stained demineralized dentin under resin composite following silver diamine fluoride application, *Pediatr. Dent.* 43 (1) (2021) 57–61.
- D. Hamdy, et al., Laboratory evaluation of the potential masking of color changes produced by silver diamine fluoride in primary molars, *BMC Oral Health* 21 (1) (2021).
- M.B. Miller, et al., Silver diamine fluoride, potassium iodide, and esthetic perception: an in vitro pilot study, *Am. J. Dent.* 29 (5) (2016) 248–250.
- R. Raafat, et al., Evaluation of the masking effect of different glass ionomer restorations following silver diamine fluoride and potassium iodide application: an in vitro study, *European J. Gen. Dent.* 11 (3) (2022) 195–200.
- E. Vennela, et al., Comparison of staining potential of silver diamine fluoride versus silver diamine fluoride and potassium iodide under tooth-colored restorations: an in vitro study, *J. Indian Soc. Pedodontics Prev. Dent.* 39 (1) (2021) 47–52.
- I.S. Zhao, et al., Effect of silver diamine fluoride and potassium iodide treatment on secondary caries prevention and tooth discoloration in cervical glass ionomer cement restoration, *Int. J. Mol. Sci.* 18 (2) (2017).
- I.B. Camatta, et al., Influence of salivary acquired pellicle on colour changes and minerals content of dentine after application of silver diamine fluoride followed by potassium iodide, *Eur. Arch. Paediatr. Dent.* (2023).
- P. Detsomboonrat, et al., Optimal concentration of potassium iodide to reduce the black staining of silver diamine fluoride, *J. Dent. Sci.* 17 (1) (2022) 300–307.
- K.E. Lee, et al., Effect of silver diamine fluoride and potassium iodide solution on enamel remineralization and discoloration in artificial caries, *Mater* 15 (13) (2022).
- M. Luong, et al., Dentin discoloration and pulpal ion concentrations following silver diamine fluoride and potassium iodide treatment, *Oper. Dent.* 47 (6) (2022) 640–647.
- J. Patel, et al., Evaluation of the staining potential of silver diamine fluoride: in vitro, *Int. J. Paediatr. Dent.* 28 (5) (2018) 514–522.
- I.S. Zhao, et al., Effect of silver diamine fluoride and potassium iodide on shear bond strength of glass ionomer cements to caries-affected dentine, *Int. Dent. J.* 69 (5) (2019) 341–347.
- R. Li, et al., Randomized clinical trial on arresting dental root caries through silver diamine fluoride applications in community-dwelling elders, *J. Dent.* 51 (2016) 15–20.
- M. Sayed, et al., Effect of glutathione bio-molecule on tooth discoloration associated with silver diamine fluoride, *Int. J. Mol. Sci.* 19 (5) (2018).
- M. Asghar, et al., Incorporation of green capping agents to reduce silver-mediated dentine staining, *Caries Res* 56 (3) (2022) 149–160.
- A.N. Kamble, et al., Comparative evaluation of effect of potassium iodide and glutathione on tooth discoloration after application of 38% silver diamine fluoride in primary molars: an in vitro study, *Int. J. Clin. Pediatr. Dent.* 14 (6) (2021) 752–756.
- S.S. Al-Angari, et al., Dental bleaching efficacy and impact on demineralization susceptibility of simulated stained-remineralized caries lesions, *J. Dent.* 81 (2019) 59–63.
- A. Rafiee, et al., 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 (1) (2022).
- A. Almuqrin, et al., Amelioration strategies for silver diamine fluoride: moving from black to white, *Antibiotics* (Basel) 12 (2) (2023).
- L.F. Espíndola-Castro, et al., Dentin staining caused by nano-silver fluoride: a comparative study, *Oper. Dent.* 45 (4) (2020) 435–441.

- [40] J.C. Favaro, et al., Anticaries agent based on silver nanoparticles and fluoride: characterization and biological and remineralizing effects-an in vitro study, *Int. J. Dent.* 2022 (2022) 11.
- [41] K. Shitomi, et al., Human dentin coated with silver nanoclusters exhibits antibacterial activity against streptococcus mutans, *Nano Biomed* 11 (1) (2019) 21–28.
- [42] I.X. Yin, et al., Synthesis and characterization of fluoridated silver nanoparticles and their potential as a non-staining anti-caries agent, *Int. J. Nanomedicine* 15 (2020) 3207–3215.
- [43] I.S. Zhao, et al., Remineralising dentine caries using sodium fluoride with silver nanoparticles: an in vitro study, *Int. J. Nanomedicine* 15 (2020) 2829–2839.
- [44] M. Baraka, et al., Twelve-month randomized controlled trial of 38% silver diamine fluoride with or without potassium iodide in indirect pulp capping of young permanent molars, *J. Am. Dent. Assoc.* 153 (12) (2022) 1121–1133. e1.
- [45] B. Turton, et al., Caries arrest and lesion appearance using two different silver fluoride therapies with and without potassium iodide: 6-month results, *Heliyon* 6 (7) (2020).
- [46] B. Turton, et al., Caries arrest and lesion appearance using two different silver fluoride therapies on primary teeth with and without potassium iodide: 12-month results, *Clin. Exp. Dent. Res.* 7 (4) (2021) 609–619.
- [47] F.M. Zheng, et al., Silver diamine fluoride therapy for dental care, *Jpn. Dent. Sci. Rev.* 58 (2022) 249–257.
- [48] M.E. Falagas, et al., Comparison of PubMed, scopus, web of science, and google scholar: strengths and weaknesses, *FASEB J* 22 (2) (2008) 338–342.
- [49] I.G. Yan, et al., A review of the protocol of sdf therapy for arresting caries, *Int. Dent. J.* 72 (5) (2022) 579–588.
- [50] S.S. Gao, et al., Clinical trials of silver diamine fluoride in arresting caries among children: a systematic review, *JDR Clin. Trans. Res.* 1 (3) (2016) 201–210.
- [51] I.S. Zhao, et al., Mechanisms of silver diamine fluoride on arresting caries: a literature review, *Int. Dent. J.* 68 (2) (2018) 67–76.
- [52] A. Venugopal, A. Marya, Return of the ohaguro, *Br. Dent. J.* 231 (2) (2021) 69.
- [53] W. Zhang, et al., Silver diamine fluoride and education to prevent and arrest root caries among community-dwelling elders, *Caries Res* 47 (4) (2013) 284–290.
- [54] F.M. Zheng, et al., Caries prevention using silver diamine fluoride: a 12-month clinical trial, *Int. Dent. J.* 73 (5) (2023) 667–673.
- [55] H.H. Chai, et al., Parental perspectives on the use of silver diamine fluoride therapy to arrest early childhood caries in kindergarten outreach dental services: a qualitative study, *J. Dent.* 125 (2022) 104250.
- [56] D. Duangthip, et al., Adverse effects of silver diamine fluoride treatment among preschool children, *J. Dent. Res.* 97 (4) (2018) 395–401.
- [57] M.H.T. Fung, et al., Randomized clinical trial of 12% and 38% silver diamine fluoride treatment, *J. Dent. Res.* 97 (2) (2018) 171–178.
- [58] J.F. Hernández-Sierra, et al., In vitro determination of the chromatic effect of a silver nanoparticles solution linked to the gantrez S-97 copolymer on tooth enamel, *J. Clin. Pediatr. Dent.* 35 (1) (2010) 65–68.
- [59] W.M. Johnston, E.C. Kao, Assessment of appearance match by visual observation and clinical colorimetry, *J. Dent. Res.* 68 (5) (1989) 819–822.
- [60] A. Besinis, et al., Inhibition of biofilm formation and antibacterial properties of a silver nano-coating on human dentine, *Nanotoxicology* 8 (7) (2014) 745–754.
- [61] K. Samaddar, et al., A quantitative evaluation of the effects of potassium iodide on the clinical properties of silver diamine fluoride, *Gen. Dent.* 71 (6) (2023) 68–72.
- [62] W. Thurston Nash, et al., Potassium Iodide's Effect on Silver Diammine Fluoride Staining Properties as Measured Through Objective Color Analysis Using CIELAB, *Pediatr. Dent.* 46 (1) (2024) 52–57.
- [63] M.M. Aly, Y.M. Yousry, Potential discolouration of silver diamine fluoride versus silver diamine fluoride/potassium iodide in primary teeth: a randomised clinical study, *Brit. Dent. J.* 6 (2022) 1–6.
- [64] Y.O. Crystal, et al., Use of silver diamine fluoride for dental caries management in children and adolescents, including those with special health care needs, *Pediatr. Dent.* 39 (5) (2017) 135–145.
- [65] S.H. Lee, B.H. Jun, Silver nanoparticles: synthesis and application for nanomedicine, *Int. J. Mol. Sci.* 20 (4) (2019) 865.
- [66] M. Noga, et al., Toxicological aspects, safety assessment, and green toxicology of silver nanoparticles (AgNPs)-critical review: state of the art, *Int. J. Mol. Sci.* 24 (6) (2023) 5133.
- [67] E. Rezvani, et al., Adverse effects of nanosilver on human health and the environment, *Acta Biomater* 94 (2019) 145–159.
- [68] E. Vasquez, et al., Short term serum pharmacokinetics of diammine silver fluoride after oral application, *BMC Oral Health* 12 (2012) 60.
- [69] I.G. Yan, et al., Fluoride delivered via a topical application of 38% SDF and 5% NaF, *Int. Dent. J.* 72 (6) (2022) 773–778.