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Does potassium iodide application following silver diamine fluoride reduce staining of tooth? A systematic review

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ABSTRACT

Objectives: To assess if using potassium iodide (KI) immediately after application of silver diamine fluoride (SDF) significantly reduces the staining of tooth structure.
Data source and selection: Four online databases (OVID, Scopus, PubMed and Google Scholar) were searched (June 2019). Additional studies were sought through grey literature search and hand searching the reference list of included articles. All studies that analysed the effect of KI on SDF staining of tooth structure with access to full text in English language were included.
Data synthesis: Of the six articles included in the review, five reported stain reduction in the teeth treated with application of KI to carious tooth structure following the application of SDF while one article reported no significant beneficial effect on reducing staining, when compared to SDF alone. Of the materials selected to restore SDF + KI treated teeth, resin-modified glass ionomer was found to produce the lightest results, followed by glass ionomer cement and composite resin. An *in vivo* case report also revealed some staining after six months, even with SDF + KI treatment.
Conclusions: Although some studies reported a positive effect, insufficient evidence exists supporting a tangible clinical benefit of SDF + KI treatment on the tooth staining, mainly due to methodical variations within the current literature.

Keywords: Caries, minimum intervention dentistry, potassium iodide, SDF + KI, silver diamine fluoride.

Abbreviations and acronyms: GIC = Glass Ionomer Cement; KI = Potassium Iodide; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RMGIC = Resin Modified Glass Ionomer Cement; SDF = Silver Diamine Fluoride.

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INTRODUCTION

Dental caries is considered a public health challenge and despite being largely preventable, remains one of the most prevalent chronic diseases affecting humans worldwide.[1,2] Characterized by the progressive demineralization and degradation of organic tooth structure, dental caries results from the dynamic interaction between dietary sugars and the acidic metabolic by-products of bacteria.[3] The extent of decay is heavily influenced by environmental factors such as the availability of dental care, socioeconomic groupings and attitudes towards oral hygiene and tooth loss.[4]

In Australia, socially, economically and geographically disadvantaged populations experience a higher burden of dental disease, when compared to the general population.[5] This is further exacerbated by a problem-orientated pattern of dental attendance, which can be due to a host of reasons including lack of perceived need for treatment, difficulty accessing dental services and financial constraints.[6] The lack of timely dental care results in limited treatment options, tooth loss and higher rates of Potentially Preventable Hospital Separations (PPHS).[7] In cases where the tooth can be repaired, current mainstream treatment follows an invasive procedure, whereby infected tooth structure is removed and then replaced with a restorative material.[8] As an alternative, topical application of silver diamine fluoride (SDF) adopts a modern conservative approach in managing dental caries specifically affecting high risk populations.[2,8–10]

As a dental therapeutic agent, silver diamine fluoride (SDF) was first approved for clinical use in Japan during the 1960s.[11] In 2015, the U.S. Food and Drug Administration (FDA) approved SDF as a dentine hypersensitivity agent and also recognized its off-label use for caries arrest and prevention.[3]

Silver ions in the SDF can inhibit and eliminate cariogenic bacteria by interfering with the structure and

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function of bacterial nucleic acids and proteins.[8,12] Furthermore, silver ions penetrate enamel up to a depth of 25 microns forming silver-protein conjugates that enhances resistance of carious dentine to acid and enzymatic breakdown.[3,13] Fluorides are known to promote remineralization through fluorapatite formation and topical application of SDF enhances local availability of fluoride ions by two to three fold when compared to other topical fluorides.[13,14] Additionally, carious lesions treated with SDF decrease in size and increase in mineral density and hardness.[15] Furthermore, the SDF-treated dentine maintains a reservoir of silver and fluoride and bacteria are unable to form biofilms on the treated surface.[14] Published clinical trials have also reported that annual application of 38% SDF is more effective in remineralizing carious lesions and preventing caries than a 3-monthly application of fluoride varnish.[16–18]

Clinically, there are a multitude of benefits associated with the application of SDF in clinical management of caries. One such benefit is its cost-effectiveness wherein small volumes (2.5μL) of SDF can be used to treat up to five teeth.[8] Another major advantage is the simple application protocol that can enable utilization of dental auxiliaries for its application and consequently, increase access to treatment.[8,13] Given these factors, SDF is a safe and effective therapeutic material that can be used in 'at risk' and difficult to treat populations, with the exception of individuals with silver allergy.[2,8,12,16,19,20]

Although effectiveness and applicability of SDF are vastly supported, there are barriers to its adoption into everyday practice. Adverse effects associated with SDF use includes nausea (due to its taste) and more so the gingival irritation that has been often considered to be a major limitation for its clinical application that necessitates additional steps to protect gingival tissues.[8,12] However, pronounced and permanent black staining of dental tissues has been the most common and significant adverse effect reported with SDF.[2,8,10,12] Specifically, SDF-related black staining in aesthetic regions of the dentition is of particular concern for patients and parents.[9,21] To alleviate this effect and increase patient acceptance, application of saturated solution of potassium iodide (KI) immediately after SDF has been suggested.[22,23] It is postulated that KI prevents staining through the precipitation of excess silver ions as white silver iodide.[8] Although there are some reports on the clinical application of SDF + KI combination, there have been no systematic reviews carried out to assess the effectiveness and extent of staining reduction achieved when SDF is followed by application of KI.

The main objective of this systematic review was to analyse and critically appraise current scientific literature to determine if the application of KI immediately following SDF on carious and non-carious tooth structure has a significant and positive effect on reduction of SDF-induced staining.

MATERIALS AND METHODS

This systematic review was performed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),[24] and the PICO framework to address the following clinical question "Does the use of Potassium Iodide have a significant impact on the aesthetics of teeth after the use of SDF, in comparison to SDF alone?" Where (*P* = population) is the teeth; (*I* = intervention) is the use of Potassium Iodide after SDF; (*O* = outcome) is better aesthetics and (*C* = comparison) is SDF alone. This review protocol is registered with PROSPERO with a registration number: CRD42018089715.[25]

Information sources and search strategy

Scopus, Ovid, PubMed and Google Scholar databases were searched using different combinations of MeSH terms to retrieve the articles (Table 1). Only articles published up to and including the June 3, 2019 were included, with no location restriction. EndNote (Clarivate Analytics, EndNote X8.2, 2018) was used to store and sort articles. After duplicates were removed, articles were selected based on title, abstract and full article following the PRISMA guidelines.[24] To ensure literature saturation, reference lists of included studies were also hand-searched for eligible studies. Open grey literature sources such as SIGLE database were also searched to identify studies not indexed in the databases listed above.

Table 1. Databases searched, and corresponding MeSH terms used

Database	Keywords (MeSH) term and text word search
Scopus	TITKE_ABS ("Silver diamine fluoride" OR sdf OR "silver fluoride" OR "silver diamine fluoride/potassium iodide" OR "Diamine silver fluoride" OR saforide OR advantage OR arrest OR cariesop OR bioride OR fluoroplatv OR diamine) AND TITLE-ABS ("potassium iodide" OR "silver bullet" OR thyrosafe OR thyroshield)
Ovid	("Silver diamine fluoride" OR "SDF" OR "silver fluoride" OR "Silver Diamine fluoride" OR "silver Bullet" OR "riva star") AND ("potassium iodide")
Medline/PubMed	("Silver diamine fluoride" OR sdf OR "silver fluoride" OR "silver diamine fluoride/ potassium iodide" OR "Diamine silver fluoride" OR saforide OR advantage OR arrest OR cariesop OR bioride OR fluoroplatv OR diamine) AND ("potassium iodide" OR "silver bullet" OR thyrosafe OR thyroshield)
Google Scholar	"silver diamine" must include "potassium iodide")

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Study selection process

Studies were eligible for inclusion if they satisfied the following criteria:

(1) Type of Studies: All original research articles, irrespective of study design prospective, retrospective and randomized controlled clinical trials on patients with caries or *in vitro* studies
(2) Type of Participants: Teeth, treated with KI after SDF.
(3) Outcome measure: Qualitatively or quantitatively addressed the effects of the SDF alone or in combination with KI on aesthetics (staining) of tooth structure.

Studies were excluded if they did not include use of KI with SDF, did not evaluate staining of teeth as an outcome and those that were inaccessible as full text, not in English language, literature reviews or conference abstract(s) or opinion papers.

The PRISMA flow chart (Fig. 1) illustrates the selection process followed during this review. For screening and assessment of inclusion criteria, titles and abstracts were independently screened by four assessors (JB, SM, JVG, TP). Disagreements were resolved by discussion moderated by one of the two independent assessors (AR, DS). Full-text articles of the eligible studies were obtained and evaluated to confirm the eligibility for inclusion into this review.

Quality assessment of included studies

Full text articles were collated and data were extracted using a custom designed spreadsheet (Table 2 and 3). Three assessors (SM, JB, AR) independently assessed risk of bias and level of evidence for each of the studies included. Disagreements were resolved by discussion moderated by other independent assessor (DS). Oxford centre for evidence-based medicine's scale was utilized to assess the levels of evidence provided by each of the included studies.[26] Furthermore, Modified CONSORT checklist items for reporting *in vitro* studies on dental materials[27,28] was utilized (Table 4) to assess the quality and risk of bias of included studies, excluding one article that was a case report.[29]

Data collection and data synthesis

Data were extracted and collated into a spreadsheet by three authors independently (JB, AR, SM) using custom designed data extraction forms. Extracted data

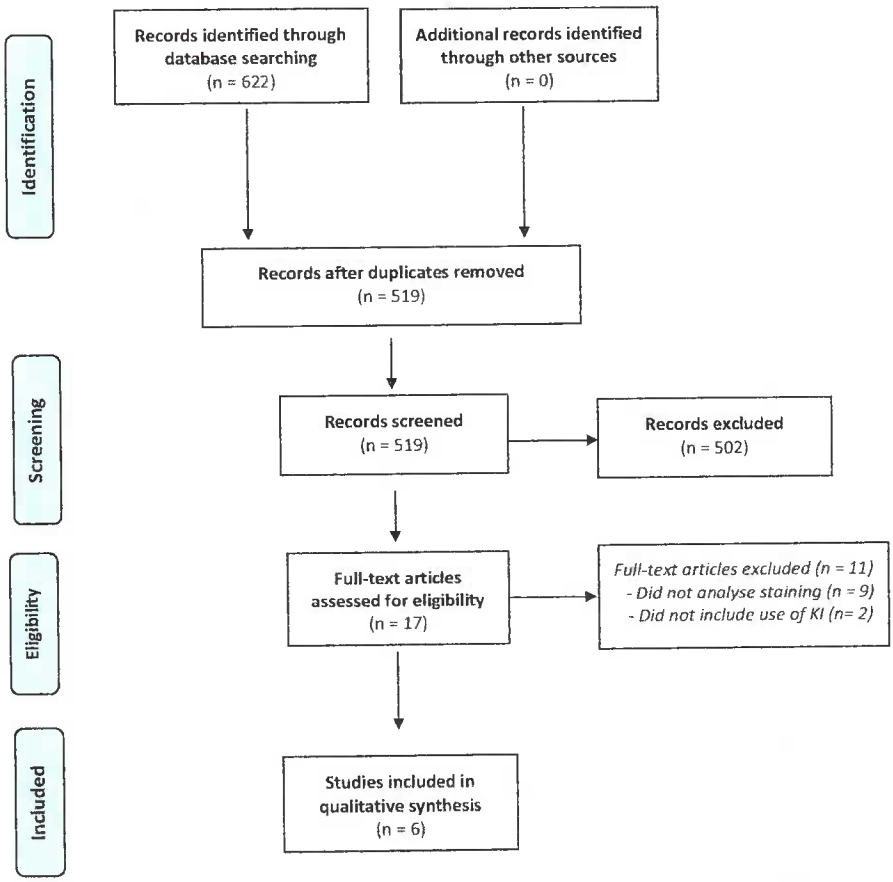

Fig. 1 Flowchart of the systematic review according to preferred reporting items for systematic reviews and meta analyses guidelines.[24]

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Table 2. General characteristics of the included studies and level of evidence, based on Oxford Centre for evidence-based medicine – levels of evidence[26]

Author, year	Location	Funding source	Study design	Measuring scale/device used	Initial recording	Further Follow-up (days) Post-intervention	Evidence level [27]
Miller *et al.*[22]	USA	Not specified	Randomized, Controlled, single blind post-test only	Subjective 0–5 scale by reviewers	30 days after intervention	No further follow-up	3b
Nguyen *et al.*[8]	USA	Unclear	Controlled, pre-post test	Photographs and Nix™ Pro Colour sensor (ΔE & ΔL)	Immediately after intervention	28 days	3b
Zhao *et al.*[30]	Hong Kong	Research Grant Council	Randomized controlled pre-post test	Dental spectrophotometer	Prior to intervention and Immediately after intervention	T1 = directly after intervention T7 = 7 days after intervention T14 = 14 days after intervention of bacteria	3b
Patel *et al.*[32]	Australia	Not specified	Controlled pre and post test	Photographs analysed using ImageJ Software	Prior to intervention & Immediately after intervention	1, 2, 3, 4, 5, 10, 15, 30, 45, 60, 90, 120 minutes 3, 4, 5, 6, 12, 24, 48, 72, 120, 168 hours	3b
Zhao *et al.*[31]	Hong Kong	Hong Kong University	Controlled pre and port test	Colorimeter (CIELAB system)	1-day post intervention	No further follow-up	2b
Garg *et al.*[29]	USA	Not specified	Case report (*in vivo*)	Photographs – visual analysis	Pre-intervention & Immediately Post-intervention	6 months	4

included study design, number of participants or number of teeth, details of intervention, treatment outcomes, instrument or methodology used for assessing outcomes, initial findings, follow-up period, funding source, location of the study and final outcome. Final data to be included were agreed upon by all the authors and any differences were resolved by further discussion. The extracted data were checked for accuracy by two authors (DS, TP).

RESULTS

Study characteristics

Details of the study selection process are outlined in Figure 1. The initial search returned 622 articles from the above databases. After duplicates were removed and remaining articles were screened based on title and then by abstract that resulted in 17 articles that underwent full text analysis, to assess their suitability based on the inclusion criteria. Six articles were included for final review and rest (11 articles) did not meet the inclusion criteria (Table 5). The details of included studies are outlined in Table 2 and Table 3.

Quality assessment of included studies

Most of the assessed *in vitro* studies (4/5) included in the review were deemed to have a good quality and with low[22,30,31] or unclear risk of bias[32], as determined by Modified CONSORT checklist (Table 6). However, one of the papers was not included in the quality assessment scoring due to its focus on a single clinical case.[29]

Staining: immediate and during follow-up

All of the included articles examined the change in colour of the tooth and SDF either after a specific period of time[22] or over multiple time points after placement.[8,30] However, significant inter-study variations existed in the sampling or cavity preparation protocol as some studies used (pre-existing) carious teeth[22,29] while others used a cavity or slices prepared on an intact tooth[30,31] or a combination of both[8,32] as the test sample (Table 3). Miller *et al.*[22] used extracted teeth with existing caries in their study and reported no difference in staining intensity between the intervention and control groups after 30 days. On the contrary, Nguyen *et al.*[8] reported minimal to no staining in teeth treated with SDF + KI over the follow-up period of four weeks. Zhao *et al.*[30] used box-shaped cavity prepared on intact premolars and reported that treatment with SDF + KI produced significantly less staining compared to SDF alone, at all follow-up time points and staining increased slightly over this period

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Table 3. Data extracted from the included articles and their major findings

Author, year	Sample type	Sample size and grouping	Restorations	Measured outcome	Reported findings
Miller *et al.*[22]	Extracted Teeth with existing caries	Total: 20 • SDF + KI: 10 • SDF Control: 10	GIC restoration with SDF or SDF/KI	Intensity of staining	• No significant difference between the groups
Nguyen *et al.*[8]	Extracted Teeth with existing caries, Caries-free, Class I restoration	Total: 45 • SDF + KI: 20 • SDF control: 20 • Negative control: 5	No restoration, GIC, RMGIC, or composite restoration with either SDF, SDF/KI, or neither	Change in colour (ΔE), change in lightness (ΔL)	• SDF + KI groups showed minimal to no staining • SDF intervention groups darkened
Zhao *et al.*[30]	Intact extracted premolars teeth in which box shaped cavity were prepped at CEJ	Total: 30 • SDF + KI: 10 • SDF control: 10 • Negative control: 10	GIC restoration with either SDF, SDF/KI or neither	Change in colour (ΔE), *Supplementary measures:* • cariogenic biofilm challenge • outer lesion depth assessment • structural evaluation of dentine	• SDF had a decrease in lightness and a perceptible colour change from T1, but SDF + KI had less colour change than SDF • Drop in lightness in SDF + KI group from T7 to T14 with perceptible difference in colour at T14 • SDF + KI is slightly less effective at inhibiting secondary decay
Patel *et al.*[32]	Extracted (a) Carious primary molars teeth (b) Intact premolars	Total: 35 • SDF + KI: 10 • Control (SDF): 10 • Other groups (a) SDF (38% or 12%): 10 (5 each) (b) Crown and Root: 5	Treated with SDF and KI, 38% or 12% SDF, SDF applied to crown and root surface	Mean Grey Values/Change in Grey Value over time	• SDF + KI: No noticeable staining observed following KI application • SDF: clinically noticeable stain, largest change after 5 mins. • No significant difference in the staining between 38% and 12% SDF • SDF staining more pronounced in pits, fissures, and grooves in enamel. Cementum stains more readily
Zhao *et al.*[31]	Decalcified Dentine slices prepared form extracted sound third molars	Total: 60 • SDF + KI: 20 • SDF Control: 20 • Negative control: 20	Treated with SDF alone or SDF + KI, then restored with GIC	Change in colour (ΔE), change in lightness (ΔL)	• SDF and KI showed statistically significant higher ΔL values • SDF + KI did produce a visually perceptible colour change which was deemed 'non-adverse,' and was significantly less than SDF alone
Garg *et al.*[29]	Single patient treated on five teeth	Total: 5 SDF + KI + RMGIC restoration	SDF + KI + RMGIC restoration of 5 anterior teeth	Presence of dark discolouration	• Overall staining was greatly reduced. No grey discolouration at placement of restoration • Visually perceptible darkening (greying) of restoration noted at 6 month compared to immediately after restoration

Table 4. Modified CONSORT checklist of items for reporting *in vitro* studies of dental Materials[27,28]

Item	Domain
1	Abstract: Structured summary of trial design, methods, results and conclusions
Introduction	
2	Scientific background and explanation of rationale with specific objectives and/or hypotheses
Methods	
3	Intervention: The intervention for each group, including how and when it was administered, with sufficient detail to enable replication
4	Outcomes: Completely defined, pre-specified primary and secondary measures of outcome, including how and when they were assessed
5	Sample size: How sample size was determined
6	Randomization: Method used to generate the random allocation sequence
7	Allocation: Mechanism used to implement the random allocation sequence, describing any steps taken to conceal the sequence until intervention was assigned
8	Implementation: Who generated the random allocation sequence, who enrolled teeth, and who assigned teeth to intervention
9	Blinding: If done, who was blinded after assignment to intervention and how
10	Statistics: Statistical methods used to compare groups for primary and secondary outcomes
Results	
11	For each primary and secondary outcome, results for each group, and the estimated size of the effect and its precision
Discussion	
12	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
Other information	
13	Sources of funding and other support role of funders
14	Where the full trial protocol can be accessed, if available

of 14 days in the latter group. With SDF + KI treatment, staining was not noticeable from baseline to day 7; but the staining increased to a perceptible level between day 7 and day 14.[30] Notably, when the difference between SDF and SDF + KI staining immediately after restoration was analysed, significant and perceptible staining was reported with the use of SDF alone when the tooth was subsequently restored with GIC, while the addition of the KI step led to elimination of perceptible staining.[30] Furthermore, the results were also found to be statistically significant.[30] A similar trend was also observed by Patel *et al.*[32] wherein carious primary molars were utilized and followed up for a maximum of seven days. This study employed the SDF + KI on the carious teeth alone and intact teeth were utilized to evaluate effect of different SDF concentration and its site specific (crown vs. root) staining intensity. The secondary outcomes reported in this study confirmed that both high (38%) and lower concentration (12%) of SDF produced similar degree of staining and that the cementum and enamel defects stained readily.[32] Another study utilized dentine slices (decalcified, prepared from extracted sound third molars) treated with SDF + KI showed better aesthetic outcome (minimal but non-adverse colour change) in comparison to SDF alone (adverse colour change).[31] A single case report (the only *in vivo* paper included in this review) found that the application of KI following SDF significantly reduced the staining immediately after placement of restoration. However, some amount of greying was noted at 6 months follow-up.[29]

Effect of restorative materials

A range of restorative materials have been used to restore cavitated teeth following SDF treatment (alone or with KI). When SDF alone was used, restorative materials that required light curing (RMGIC and Composite resin) showed greyish discolouration immediately after placement, but the subsequent colour change was minimal over the follow-up period of 28 days.[8] Self-cure GIC developed marginal staining within hours, but no further colour change was reported. In addition, carious tooth structure treated with SDF darkened within hours, while non-carious teeth developed dark stains in the pits and fissures over an unstated time. Only Nguyen *et al.* compared different white restorative materials and their subsequent impacts on lightness of tooth structure.[8] Mean lightness values of teeth treated with SDF alone were less than those treated with SDF + KI regardless of the restorative material or lack thereof used. Of teeth treated with SDF + KI, non-carious teeth did not develop staining and had the highest mean lightness value. Teeth restored with RMGIC were the next lightest in colour, followed by GIC, Composite resin and finally unrestored carious teeth.

DISCUSSION

An abundance of scientific literature supports the safety and efficacy of SDF as treatment for dentin hypersensitivity and is widely accepted as a caries arresting agent.[2,3,8–11,13,16,18] However, significant aesthetic barriers preclude its widespread acceptance by adults since there has been a paradigm shift in expectations from advanced dental care focussing highly on aesthetic outcomes.[8,21,33] We were able to identify and critically appraise six publications that evaluated the use of SDF + KI and reported findings in regard to discolouration, with variable levels of evidence and differing results. Miller *et al.*[22] reported no difference in the staining intensity between SDF and SDF + KI, while Zhao *et al.*[30], Patel *et al.*[32] and Zhao *et al.*[31] found a statistically significant decrease in staining intensity, and Garg *et al.*[29] described a reduction in staining with SDF + KI at placement.

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Table 5. Summary of papers excluded and reasons for exclusion, after accessing full text

Author, year	Country	Objectives of the study	Reason of exclusion
Bersezio *et al.*, 2015	Brazil	To evaluate the influence of time of application of SDF on the hydraulic conductance	Did not analyse aesthetics
Hamama *et al.*, 2015	Australia	To evaluate the antimicrobial effect of SDF/KI (Riva Star) on the viability of intratubular bacteria	Did not analyse aesthetics
Knight *et al.*, 2006	Australia	To compare the bond strengths of auto cure GIC to dentine surfaces treated with SDF and KI and without treatment	Did not analyse aesthetics
Knight *et al.*, 2007	Australia	To compare the differences between normal and demineralized dentine pretreated with SDF and KI after an *in vitro* challenge by *Streptococcus mutans*	Did not analyse aesthetics
Knight *et al.*, 2006	Australia	To determine if a prior application of SDF and KI to demineralised dentine affected the uptake of strontium and fluoride from a GIC cement	Did not analyse aesthetics
Knight *et al.*, 2005	Australia	To develop an *in vitro* model that would provide an indication of the permeability of demineralised dentine *to streptococcus mutans* after treatment of the dentine with SDF followed by KI	Did not analyse aesthetics
Knight *et al.*, 2009	Australia	To measure whether a topical application of SDF followed by KI on partially demineralised dentin affected the formation of *streptococcus mutans* biofilm	Did not analyse aesthetics
Koizumi *et al.*, 2006	Japan	To determine whether Riva Star influenced bond strengths to an etch-and-rinse and all-in-one resin-based adhesive and a resin-modified GIC	Did not analyse aesthetics
Selvaraj *et al.*, 2016	India	To compare the micro-shear bond strengths of bonding systems to dentin pre-treated with SDF + KI and nano-leakage at the resin-dentin interface	Did not analyse aesthetics
Nelson *et al.*, 2016	USA	To investigate practice, teaching and perceived barriers to the use of SDF and other caries control agents in U.S. pediatric dentistry residency programs	Did not use KI
Sayed *et al.*, 2018	Japan	Evaluation of discoloration of sound/demineralized root dentin with silver diamine fluoride *in-vitro*	Did not use KI

Table 6. Quality assessment of *in-vitro* studies according to the items of the modified CONSORT checklist[27,28]

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Summary assessment
Miller *et al.*[22]	+	+	+	+	?	?	–	–	+	+	?	+	+	–	Low
Nguyen *et al.*[8]	+	+	+	+	?	–	–	–	–	–	?	?	?	–	High
Zhao *et al.*[30]	+	+	+	+	?	?	–	–	–	+	+	+	+	–	Low
Patel *et al.*[32]	+	+	+	+	?	–	–	–	–	–	+	+	–	–	unclear
Zhao *et al.*[31]	+	+	+	+	?	–	–	–	–	+	+	+	+	–	Low

Key: (+) = low risk of bias, (?) = unclear risk of bias, (–) = high risk of bias.

However, staining was reported to increase from day 7 to day 14[30] that was visually perceptible, grey discolouration noted even after 6 months.[29] On the contrary, Nguyen *et al.*[8] found no or minimal colour change in SDF + KI treated teeth over the 28 days, while SDF treated teeth had perceptible darkening with all restorative materials within hours.

The majority of the studies included for analysis were *in vitro* studies, which limits the extrapolation of their results to the oral environment. Variations in findings between the included studies might be attributed to the differences in study design, sample type and preparation or changes in exposure parameters (e.g., artificial saliva) that the samples were subjected to. Although artificial saliva was used to immerse samples in an attempt to replicate the complex dynamic nature of the oral environment in two studies, acid demineralization protocol utilized reduces its similarity to complex dentine-caries microstructure.[30,31] On the contrary, Nguyen *et al.* did not utilize artificial saliva but had substantial clinical relevance with the range of restorative materials used, being the only study to compare composite, RMGIC and GIC restorations.[8] Zhao *et al.* introduced bacteria into their artificial saliva solution at day seven (T7) after which a perceptible increase in colour was observed.[30] Therefore, the increase in colour might have been influenced by this change in environment rather than the intervention itself, in comparison to Zhao *et al.*[31] where the solution was kept constant. In another study, Miller *et al.*[22] did not record the baseline staining (due to caries) and failed to eliminate stained carious tooth structure prior to intervention rendering it difficult to determine if the post treatment staining intensity observed is due to intervention or from the pre-existing caries. Patel *et al.* mitigated this (non-removal of stained tooth structure) by comparing changes over time, between intervention groups.[32]

A range of sample preparation strategies were reported across the *in vitro* studies included in this review. Four studies treated samples (teeth) prior to intervention using autoclave,[22,30] soaking in 3% sodium hypochlorite[8] or storage in 1% thymol solution.[31] These processes might alter dentine structure and thus interact differently, as compared to non-treated dentine. Patel *et al.* did not perform pre-treatment

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of teeth prior to intervention, however, no statistical analysis was reported in this study.[32] The only *in vivo* paper (case report) included in this review also had the longest follow-up period of six months, implying greatest clinical relevance.[29] However, this paper was assigned lowest level of evidence as it was a non-comparative case report lacking controls or quantitative assessment of staining.[29]

Another domain that could significantly contribute towards the variation between studies is the methodology of recording outcome. Staining was measured using either a visual six-point scale,[22] spectrophotometer,[8,30] colorimeter[31] or digitally calculated lightness values.[32] Miller *et al.*[22] assumed calibration of their examiners by using dental students but carried out no formal calibration or inter-operator reliability testing, thus potentially compromising the validity of their results. Other *in vitro* studies utilized pre-calibrated electronic methods to measure changes in colour or lightness before and after intervention or over time,[8,30–32] while Garg *et al.*[29] relied on subjective visual assessment of photographs.

Sample sizes across the studies included in the review were limited and there was numerical bias towards including only GIC restorations or no restorations rather than other restorative materials routinely used in dental practise (Table 7). Furthermore, the follow-up periods for the higher quality studies were limited to 30 days,[22] which is not representative of the time a restoration is expected to be present in the oral cavity. For instance, Glass Ionomer restorations, if not removed and replaced, have a 30–42 month survival rate in permanent dentition, while appropriately placed composite restorations potentially last up to 10 years.[34,35] Thus, results cannot be reliably extrapolated into clinical situations and caution should be exercised in drawing generalized conclusions.

Application of KI after SDF might not impact aesthetics alone, as concerns about KI reducing the beneficial effects of SDF have been raised.[30,36] For instance there is debate over whether it reduces the bond strength between GIC and dentine.[36,37] One group reported that the bond strength of GIC to be comparable or greater than SDF while the other reported a significant decrease in bond strength.[36,37] A decrease in bond strength, or lack of consistency in bonding, might lead to complete or partial bond failure thus resulting in premature loss of restoration or secondary decay.[36] Although SDF + KI has been shown to reduce secondary caries and inhibit biofilm formation, it was not as effective as SDF alone.[30] However, SDF + KI was reported to be the most effective at inhibiting *S mutans* migration through dentine, when compared to SDF alone.[37] Further research is therefore needed into these inconsistencies to aid dental practitioners to consider all possible clinical effects of this combination prior to opting for the SDF + KI over SDF alone.

Although there is limited evidence on the impact of KI on SDF staining in carious lesions, its beneficial effect in preventing staining during management of dentine hypersensitivity in non-carious teeth warrants clinical consideration.[22,38] However, evidence from studies on carious tooth structure are inconclusive and further research is required into different restorative situations with stringent controls on confounding variables, as well as *in vivo* studies.

Table 7. Number of teeth and their intervention across studies included

	Number of teeth
Total	195
Treated with SDF + KI	75
Treated with SDF	85
Treated with neither	35
Self-Cure GIC restoration	59
RM-GIC restoration	14
Composite restoration	9
No restoration	113

CONCLUSIONS

This systematic review established that application of KI after SDF might have some potential to reduce staining. While most studies reported a positive association between SDF + KI and minimal staining, the available evidence from the literature failed to show meaningful and statistical advantage of KI in the management of SDF-associated tooth staining. The articles included in this review had differing study designs and reported varying results; from no effect, to darkening over time and significant reduction in staining. Combined use of SDF with KI has been marketed as a potential stain reducer and considering some degree of evidence from the studies included in this review, potential advantages of minimal staining might be beneficial, at least in short-term. However, studies with long-term follow-up would be required to provide evidence-based guidelines for use of SDF + KI formulations in routine clinical practice.

DISCLOSURE

Nothing to declare.

REFERENCES

1. Colak H, Dulgergil CT, Dalli M, Hamidi MM. Early childhood caries update: A review of causes, diagnoses, and treatments. J Nat Sci Biol Med 2013;4:29–38.
2. Wright JT, White A. Silver diamine fluoride: changing the caries management paradigm and potential societal impact. N C Med J 2017;78:394–397.

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3. Horst JA, Ellenikiotis H, Milgrom PL. UCSF protocol for caries arrest using silver diamine fluoride: rationale, indications and consent. J Calif Dent Assoc 2016;44:16–28.
4. Crocombe LA, Stewart JF, Brennan DS, Slade GD, Spencer AJ. Is poor access to dental care why people outside capital cities have poor oral health? Aust Dent J 2012;57:477–485.
5. Austrailan Institute of Health and Welfare. Australia's Health 2016: Web report: Australian Government; 2016 Available at: https://www.aihw.gov.au/reports/australias-health/australias-health-2016/contents/determinants
6. Sanders A. Social determinants of oral health: conditions linked to socioeconomic inequalities in oral health in the Australian population. Adelaide: Australian Institute of Health and Welfare, 2007.
7. Austrailan Institute of Health and Welfare. Oral health and dental care in Australia: key facts and figures 2015. Australian Institute of Health and Welfare; 2016.
8. Nguyen V, Neill C, Felsenfeld J, Primus C. Potassium Iodide. The solution to silver diamine fluoride discoloration? Health 2017;5:555655.
9. Targino AG, Flores MA, dos Santos Junior VE, de Godoy Bene Bezerra F, de Luna Freire H, Galembeck A. An innovative approach to treating dental decay in children. A new anti-caries agent. J Mater Sci Mater Med 2014;25:2041–2047.
10. Crystal YO, Marghalani AA, Ureles SD, *et al.* Use of silver diamine fluoride for dental caries management in children and adolescents, including those with special health care needs. Pediatr Dent 2017;39:E135–E45.
11. Mei ML, Lo EC, Chu CH. Clinical use of silver diamine fluoride in dental treatment. Compend Contin Educ Dent 2016;37:93–8; quiz100.
12. Fukuoka BM. Clinical use of silver diamine fluoride. Decisions in Dentistry 2018;4:35–36.
13. Rajendra A, Veitz-Keenan A, Oliveira BH, *et al.* Topical silver diamine fluoride for managing dental caries in children and adults. Cochrane Database Syst Rev 2017(7): CD012718.
14. Nelson T, Scott JM, Crystal YO, Berg JH, Milgrom P. Silver diamine fluoride in pediatric dentistry training programs: survey of graduate program directors. Pediatr Dent 2016;38:212–217.
15. Mei ML, Ito L, Cao Y, Li QL, Lo EC, Chu CH. Inhibitory effect of silver diamine fluoride on dentine demineralisation and collagen degradation. J Dent 2013;41:809–817.
16. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. J Dent Res 2002;81:767–770.
17. Yee R, Holmgren C, Mulder J, Lama D, Walker D, van Palenstein Helderman W. Efficacy of silver diamine fluoride for arresting caries treatment. J Dent Res 2009;88:644–647.
18. Hendre AD, Taylor GW, Chavez EM, Hyde S. A systematic review of silver diamine fluoride: effectiveness and application in older adults. Gerodontology 2017;34:411–419.
19. Llodra JC, Rodriguez A, Ferrer B, Menardia V, Ramos T, Morato M. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. J Dent Res 2005;84:721–724.
20. Tan HP, Lo EC, Dyson JE, Luo Y, Corbet EF. A randomized trial on root caries prevention in elders. J Dent Res 2010;89:1086–1090.
21. Crystal YO, Janal MN, Hamilton DS, Niederman R. Parental perceptions and acceptance of silver diamine fluoride staining. J Am Dent Assoc 2017;148:510–518.e4.
22. Miller MB, Lopez LA, Quock RL. Silver diamine fluoride, potassium iodide, and esthetic perception: an in vitro pilot study. Am J Dent 2016;29:248–250.
23. Southern Dental Industries. Riva Star: SDI; 2018. Available at: https://www.sdi.com.au/au/product/rivastar/
24. Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Medicine 2009;6 (7):e1000097.
25. Roberts A, Pachal T, Bradley J, Merkley S, Gopal JV, Sharma D. Enhancement of aesthetic outcome by using potassium iodide following silver diamine fluoride application in minimally invasive and preventive dentistry: a systematic review. PROSPERO 2018 CRD42018089715: National Institute for Health Research. Available at: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018089715
26. Oxford Centre for evidence-based medicine – levels of evidence (March 2009) 2009. Available at: https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/
27. Faggion CM, Jr. Guidelines for reporting pre-clinical in vitro studies on dental materials. J Evid Based Dent Pract 2012;12:182–189.
28. Luo JD, Miller C, Jirjis T, Nasir M, Sharma D. The effect of non-steroidal anti-inflammatory drugs on the osteogenic activity in osseointegration: a systematic review. Int J Implant Dent 2018;4:30.
29. Garg S, Sadr A, Chan D. Potassium iodide reversal of silver diamine fluoride staining: a case report. Oper Dent 2019;44:221–216.
30. Zhao IS, Mei ML, Burrow MF, Lo EC, Chu CH. Effect of silver diamine fluoride and potassium iodide treatment on secondary caries prevention and tooth discolouration in cervical glass ionomer cement restoration. Int J Mol Sci 2017;18:E340.
31. Zhao IS, Chu S, Yu OY, Mei ML, Chu CH, Lo ECM. Effect of silver diamine fluoride and potassium iodide on shear bond strength of glass ionomer cements to caries-affected dentine. Int Dent J 2019;69:341–347.
32. Patel J, Anthonappa RP, King NM. Evaluation of the staining potential of silver diamine fluoride: in vitro. Int J Paediatr Dent 2018;28:514–522.
33. Banerjee A. 'MI'opia or 20/20 vision? Br Dent J 2013;214:101–105.
34. Gaengler P, Hoyer I, Montag R. Clinical evaluation of posterior composite restorations: the 10-year report. J Adhes Dent 2001;3:185–194.
35. Fernandes NA, Vally ZI, Sykes LM. The longevity of restorations – A literature review. S Afr Dent J 2015;70:410–413.
36. Koizumi H, Hamama HH, Burrow MF. Effect of a silver diamine fluoride and potassium iodide-based desensitizing and cavity cleaning agent on bond strength to dentine. Int J Adhes Adhes 2016;68:54–61.
37. Knight GM, McIntyre J. The effect of silver fluoride and potassium iodide on the bond strength of auto cure glass ionomer cement to dentine. Aust Dent J 2006;51:42–45.
38. Craig GG, Knight GM, McIntyre JM. Clinical evaluation of diamine silver fluoride/potassium iodide as a dentine desensitizing agent. A pilot study. Aust Dent J 2012;57:308–311.

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