International Journal of Clinical Dentistry
Volume 15, Number 4
ISSN: 1939-5833


# INHIBITION OF SILVER DIAMMINE FLUORIDE INDUCED TOOTH DISCOLORATION – A LITERATURE REVIEW

***Md. Sofiqul Islam***, Noor Sayed Majed Salman*†*,***
***Zainab Mohamed Ahmed*‡*,***
***and Mohammed Mustahsen Rahman*§
RAKCODS, RAK Medical and Health Sciences University,
Ras Al-Khaimah, United Arab Emirates

## ABSTRACT

*Objectives:* Silver Diammine Fluoride (SDF) is a safe dental caries-preventing and arresting agent. The main downfall of SDF is the permanent black staining on tooth-treated surfaces. This study aimed to investigate the literature for methods available to alleviate SDF-induced dental staining.

*Materials and methods:* A literature review was performed using the PubMed online database. The search employed the following keywords "silver diammine fluoride" OR "silver diammine fluoride" AND "discoloration" OR "staining." Inclusion criteria included studies published in English, from 2015 to 2020, and studies discussing methods for reduction of SDF-induced staining.

*Results:* The database search identified 38 publications, of which 29 articles were excluded. 8 articles met the inclusion criteria and were included in this literature review. These included 6 *in-vitro* studies, 1 systematic review, and 1 case report. A common method of reducing SDF-induced staining among the included studies was the use of potassium iodide (KI) immediately following the SDF application. Another intervention was reported by one laboratory study using a mixture of SDF with %20 glutathione (GSH).

*Conclusions:* The literature indicates that the commonly used method for stain reduction on SDF-treated teeth is the use of KI. The use of glutathione-SDF mixture was also proposed.

*Clinical significance:* The use of SDF as a preventive and therapeutic aid for caries getting popular around the world. This review will help the clinician to minimize the SDF

* Corresponding Author: Dr. Md Sofiqul Islam, RAKCODS, RAK Medical and Health Sciences University, P.O Box: 12973, Ras Al-Khaimah, United Arab Emirates.
E-mail: sofiqul.islam@rakmhsu.ac.ae; soheltmd@gmail.com
† E-mail: noorsmajid@hotmail.com
‡ E-mail: zainabthamer1997@gmail.com
§ E-mail: mustahsen@rakmhsu.ac.ae

induced tooth discoloration in a best possible manner in their routine dental practice using SDF.

**Keywords:** silver diammine fluoride, tooth discoloration, potassium iodide, glutathione

## INTRODUCTION

Dental caries is an infectious, bacterial, multifactorial, dynamic disease of dental hard tissue, and is considered to be one of the most common oral diseases amongst all populations [1]. Enamel and dentin demineralization occurs due to the effect of carious bacteria and the biofilm that produces acidic mineral-dissolving byproducts leading to an imbalance between the demineralization and re-mineralization processes of dental hard tissue [2]. A caries lesion can be reversed or arrested if diagnosed early with the help of various re-mineralizing agents [3]. Silver compounds have been used in dentistry for over a century, like silver nitrate (AgNO3) and silver fluoride (AgF) [4]. They have initially been used for the management of dental caries in deciduous teeth, and then their use was extended to include prevention of dental caries on permanent teeth [5].

Silver Diammine Fluoride (SDF), introduced in Japan by Yamaga et al., in the late 1960's is a topical cost-effective, efficient, safe, non-invasive caries preventing and arresting medicament that can be used especially for coronal caries in children and root caries in elderly patients [6] SDF meets the criteria of the World Health Organization's Millennium Goals for 21st century medical care [7]. It serves as an antibacterial agent that has an inhibitory effect on cariogenic biofilm, matrix metalloproteinase and cysteine cathepsin, which in turn prevents further progression of demineralization and collagen degradation and helps promote re-mineralization of dental hard tissue [8, 9, 10]. Application of SDF has been shown to increase the mineral density and the micro-hardness of the carious dentin lesions [11]. In addition, annual or biannual application SDF was proven to be more effective in the prevention and re-mineralization of carious lesions than the application of fluoride varnish quarterly [12]. SDF is colorless highly alkaline solution (pH 12.5) mainly containing about 25% silver (255,000 ppm) and high concentrations of fluoride (44,880 ppm) [13]. Silver acts as an antimicrobial agent that simultaneously strengthens the underlying dentin and fluoride is the active ingredient in SDF that arrests dental caries and helps in preventing new carious lesions [14].

Despite its many advantages, the main drawback of SDF is the irreversible black staining on teeth due to the deposition of metallic silver within the dental hard tissue structure creating an esthetic concern for many patients, especially when evident in the anterior esthetic region, limiting its use in clinical practice [15]. The dark discoloration forms after exposure of the silver part of SDF to reducing agents or sunlight [16]. In order to adopt SDF as a widely acceptable routine dental caries preventive aid, the researcher must find a suitable solution to eliminate the SDF induced tooth discoloration [17]. Starting from 2016 several researches have been conducted to find the potential ingredients or technique for this purpose [18]. Therefore, the main objective of this literature review is to investigate the literature for the methods available to inhibit or alleviate the SDF-induced tooth staining.

## MATERIALS AND METHODS

An online database search was performed using PubMed. The search included the keywords of: “Silver diammine fluoride” or “silver diammine fluoride” and “discoloration” or “staining.” The search result was refining by the filter of full-length article, published in the last 5 years, and the English language. The inclusion criteria involved any type of study design, studies including the aforementioned keywords, studies published in the English language, and studies published within the last 5 years. Exclusion criteria included non-English articles, studies not published within the last 5 years, and studies not discussing any methods used to alleviate the SDF-induced dental discoloration in their titles or abstracts. The sequence followed for eligibility was the screening of the retrieved publications' titles and abstracts followed by evaluation of full-text publications for final study selection based on the predetermined inclusion criteria. The data extraction included the methods used for the reduction of SDF-induced dental discoloration and the result of each. In addition, data extraction from the *in-vitro* studies included the sample type, sample size and grouping, color change measuring device or the scale and follow-up period.

## RESULTS

The initial literature search identified thirty-eight citations, of which two were excluded upon filter application. Thirty-six articles underwent title and abstract screening, of which twenty-eight articles were excluded based on the predetermined exclusion criteria. Eight studies underwent full text analysis to evaluate their eligibility for inclusion in the literature review according to the predetermined inclusion criteria. All eight articles have met the criteria for inclusion and were eligible to be included in this review: six *in-vitro* experimental studies, one systematic review, and one case report. The online database search process is illustrated in Figure 1. Details of the included articles are outlined in Table 1. The data extracted from the included *in-vitro* studies are outlined in Table 2. The main findings of the included studies are summarized in Table 3.

**Table 1. Details of included literature review articles**

| Author, Year [Ref] | PubMed ID (PMID) | Location | Study Design |
|---|---|---|---|
| Miller et al., 2016 [19] | 29178735 | USA | *In-vitro* |
| Zhao et al., 2017 [15] | 28178188 | China | *In-vitro* |
| Patel et al., 2018 [16] | 29974546 | Australia | *In-vitro* |
| Sayed et al., 2018 [23] | 29710829 | Japan | *In-vitro* |
| Sayed et al., 2019 [24] | 30381632 | Japan | *In-vitro* |
| Zander et al., 2019 [20] | 30791530 | USA | *In-vitro* |
| Garg et al., 2019 [21] | 31046649 | USA | Case Report |
| Roberts et al., 2020 [22] | 31900927 | Australia | Systematic Review |

All seven included studies discussed methods for alleviating the stains induced by 38% SDF treatment. Out of all seven studies included, six studies evaluated the effect of potassium iodide (KI) application following SDF treatment on staining reduction. Studies assessed the effectiveness of KI treatment immediately after SDF application, 1 study compared KI with other interventions like mixing SDF with 20% glutathione biomolecule (GSH) and 1 study compared the color changes between SDF-treated teeth exposed to light and SDF-treated teeth kept in dark conditions.

An *in-vitro* pilot study performed by Miller et al., utilizing KI for SDF-staining reduction of glass ionomer restorations reported no significant differences between control and experimental groups [19]. Another *in-vitro* study by Zhao et al., found significantly less staining of SDF+KI treatment when compared to SDF treatment alone, but the staining slightly increased over the follow-up period of 14 days following the intervention [15]. Similarly, Zander et al., reported immediate visual change on KI-treated teeth to light grey compared to SDF-treated teeth which were colored dark black [20]. The only in-vivo case report included in this literature review performed by Garg et al., showed that KI+SDF treatment significantly minimized the staining. However, in the long term and over a 6 months period, some amount of greying was clearly observable [21]. In addition, one systematic review had varying outcomes reported; from no effect to darkening over time, and significant staining reduction. The combined use of SDF with KI has been announced as a possible stain reducer in the short term [22]. Another *in-vitro* study comparing the effect of KI + SDF use with the use of SDF + %20 GSH for stain reduction found that KI-treated teeth showed insignificant color changes over time, while GSH was effective in decreasing the color changes especially in enamel and to a lesser extent in dentin [23]. The results of an *in-vitro* laboratory study evaluating the effect of light exposure on the discoloration of root dentin reported that the groups exposed to light showed more color change in comparison to those kept in light-proof containers [24].

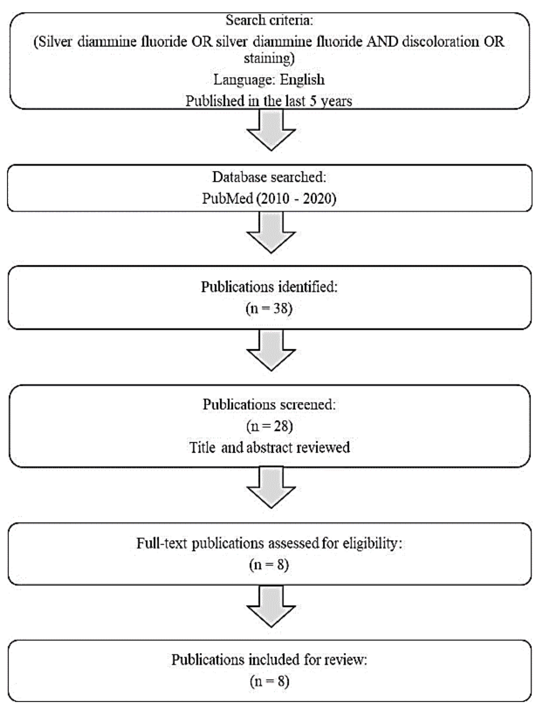


Figure 1. Flowchart of literature search for methods available to inhibit SDF-induced dental discoloration.

**Table 2. Data extracted from the included *in-vitro* studies**

| Author, Year [Ref] (Country) | Sample Type | Sample Size and Grouping | Measuring Device/ Scale | Follow-Up Period |
|---|---|---|---|---|
| Miller et al., 2016 [19] (USA) | Human extracted teeth with frank cavitated carious lesions | Total: 20<br>1. Control group (SDF only, then restored with GIC): 10<br>2. Experimental group (SDF + KI applied before GIC restoration): 10. | Subjective 0-5 scale by reviewers | 30 days |
| Zhao et al., 2017 [15] (China) | Intact human extracted premolars | Total: 30<br>1. SDF + KI: 10<br>2. Positive control group (SDF only): 10<br>3. Negative control group (no treatment): 10 | Dental spectrophotometer | 14 days |
| Patel et al., 2018 16 (Australia) | Extracted carious primary molars | Total: 35<br>Group 1: SDF only.<br>Group 2: KI immediately after SDF application.<br>Group 3: 38% SDF compared with 12% SDF.<br>Group 4: Enamel compared with cementum. | DSLR camera image using Image J software | 1, 2, 3, 4, 5, 10, 15, 30, 45, 60, 90, 120 minutes, 3, 4, 5, 6, 12, 24, 48, 72, 120, 168 h |
| Sayed et al., 2018 [23] (Japan) | Bovine teeth (6×6 mm enamel and dentin blocks), free of cracks or caries | Total: 120 (60 enamel and 60 dentin)<br>1. Control group (SDF only): 40<br>2. SDF + KI: 40<br>3. SDF mixed with 20% GSH: 40 | Dental spectrophotometer | 14 days |
| Sayed et al., 2019 [24] (Japan) | Bovine teeth (5×5×2 mm root dentin blocks), free of cracks or caries | Total: 80<br>1. Control group (no treatment): 20<br>2. 30 min EDTA demineralized group: 20<br>3. 5 h EDTA demineralized group: 20<br>4. 13 h EDTA demineralized group:20 | Dental spectrophotometer + photographs using digital camera | 14 days |
| Zander et al., 2019 [20] (USA) | Bovine incisors | Total : 32<br>1. Negative control (rinsed with deionized water): 8<br>2. 5% NaF varnish: 8<br>3. SDF: 8<br>4. SDF + KI (1.44 g/mL KI): 8 | Subjective visual analysis | None |

**Table 3. Results of the studies using different methods aiming to inhibit SDF-induced dental discoloration**

| Author, Year [Ref] (Country) | PubMed ID (PMID) | Study Design | Method Used to Inhibit SDF-Induced Dental Discoloration | Main Results/Summary Findings |
|---|---|---|---|---|
| Miller et al., 2016 [19] (USA) | 29178735 | *In-vitro* | Potassium iodide (KI) after SDF application. | KI application may improve initial esthetic outcome, but there was no significant difference in staining after GIC restoration placement following the use of SDF alone or the use of SDF + KI prior to GIC restoration. |
| Zhao et al., 2017 [15] (China) | 28178188 | *In-vitro* | Potassium iodide (KI) application immediately after SDF treatment. | - Although the staining still could be detected, KI application on SDF-treated teeth decreased the discoloration intensity but also decreased the effectiveness of SDF in preventing secondary caries under cervical glass ionomer (GIC) restorations.<br>- The use of KI in preventing the discoloration of SDF is not effective in the long term. |
| Patel et al., 2018 [16] (Australia) | 29974546 | *In-vitro* | Potassium iodide (KI) application immediately after SDF treatment. | (i) Onset of black staining occurred within two minutes, was noticeable after five minutes, and increased in value for up to 6 h post-application,<br>(ii)Use of KI immediately after SDF application resulted in no noticeable staining of the carious dentine or surrounding enamel<br>(iii)No significant differences were evident in the staining potential between the different SDF concentrations (38% and 12%)<br>(iv)Root surface and cementum was found to stain darker and more readily when compared with the coronal enamel surface,<br>(v)SDF reacted with sodium chloride in the artificial saliva resulting in the formation of silver chloride, an insoluble white precipitate that masked the underlying staining. |
| Sayed et al., 2018 [23] (Japan) | 29710829 | *In-vitro* | 1. 20% Glutathione biomolecule (GSH) mixed with 38% SDF.<br>2. Potassium iodide solution (KI) (2.36 mol/L) applied following the application of SDF. | - GSH application decreased the color changes effectively in both light and dark conditions in enamel and to a lesser extent in dentin.<br>- KI resulted in insignificant immediate color changes. However, darkening occurred over time. |
| Sayed et al., 2019 [24] (Japan) | 30381632 | *In-vitro* | Storage of SDF-treated teeth in light-proof containers. | - Teeth unexposed to light showed less color changes than those exposed to light. - Degree of dentin demineralization before SDF application significantly increased the rate of dentin color changes; sound dentin recorded the least color changes. |
| Zander et al., 2019 [20] (USA) | 30791530 | *In-vitro* | 1.44 g/mL KI immediately after SDF application. | - KI-treated samples appeared light grey, while those only treated by SDF were colored dark black.<br>- KI did not affect the anti-demineralization properties of SDF. |
| Garg et al., 2019 [21] (USA) | 31046649 | Case Report (*in-vivo*) | 1 g/mL saturated KI solution immediately after SDF application. | KI reverses the SDF-induced staining to a large extent. However, restoration margins may still be at risk of staining. |
| Roberts et al., 2020 [22] (Australia) | 31900927 | Systematic Review | Potassium iodide (KI) after SDF application. | Positive effect of KI reported by some studies. However, insufficient evidence exists to support the benefit of KI use on dental staining following SDF treatment. |

## DISCUSSION

SDF received its FDA approval for clinical use as a dental desensitizing agent in addition to its off-label use as a dental caries-preventing and halting agent [25]. Besides the simplicity of its use, its low-cost and its advantage in allowing management of fearful and anxious patients, SDF effectiveness in caries prevention and arrest has been reported in the literature [26, 5]. A single drop of SDF solution is capable of treating 5 tooth surfaces. Due to its minimally invasive nature, SDF is commonly indicated for the management of dental caries in those individuals who cannot tolerate the conventional methods of restoring carious lesions such as behaviorally or medically-challenging patients, frail elder patients and extreme caries risk like early childhood caries (ECC) and xerostomia [27]. However, the main adverse effect of SDF use is the dark black staining on the treated teeth which does not seem to be reversible in nature, restricting its use in clinical practice [28].

38% SDF [Ag $(NH_3)$ 2 F] is composed of 24-27% silver, 8.5-10% ammonia and 5-6% fluoride.4 SDF releases large amounts of free silver ions ($Ag^+$) and fluoride ions ($F^-$) when applied to teeth. The ions released from SDF can penetrate enamel up to 20 micrometers, forming mainly calcium fluoride ($CaF_2$), silver phosphate ($Ag_3PO_4$), and a small quantity of metallic silver. In case of dentin, the ions can penetrate up to 50-200 micrometers, mainly forming metallic silver attached to protein (silver protein), $CaF_2$ and $Ag_3PO_4$ in lesser amounts. Because silver ions are good electron acceptors, silver has a high affinity for proteins (i.e., collagen). Moreover, silver has a high polarizing power facilitating strong bond formation with nitrogen and sulfur groups of cysteine and histidine in proteins. Reduction of the silver ions results in their precipitation and the formation of dark black stains on the tooth surface [29].

KI solution has been used in dentistry as an antimicrobial agent especially following dental hygiene and scaling procedures to reduce the risk of tissue damage and inflammation. In addition, Iodine potassium iodide (IPI) has been used as an antifungal agent against Candida albicans and an antimicrobial irrigant in endodontics [30, 31]. KI saturated solution was suggested as an additive to alleviate the staining properties of SDF and has been described as a promising approach to solve the discoloration problem [21]. The mechanism of the short-term staining reduction was explained by the formation of a bright yellow solid compound, silver iodide (AgI), as a reaction product resulting from the interaction of SDF with KI. This reaction is thought to decrease the excess free silver ions that cause the black staining [15]. Upon KI application immediately after SDF treatment, AgI crystals aggregate and precipitate as a creamy white participate on the surface allowing a short-term reduction in staining. Garg et al., explained the mechanism of KI in stain reduction by the formation of two different white powders as a result of its reaction with the byproduct of the SDF + HA reaction, silver phosphate ($Ag_3PO_4$). The first powder that is thought be the major cause of stain reduction is tripotassium phosphate ($K_3PO_4$). The other photosensitive yellowish-white powder, which is a double-reaction product, is silver iodide (AgI) [21]. Some studies reported that KI effect on color change was only temporary as darkening of the SDF-treated teeth still occurred, showing insignificant color changes over time [19]. Previous studies reported no adverse effects of KI on SDF's anti-caries performance, except one laboratory study by Zhao et al., which reported that SDF+KI was slightly less effective in preventing caries than SDF alone [15].

Sayed et al., developed an alternative method for managing SDF-induced dental staining by mixing SDF with %20 glutathione. Glutathione, a tri-peptide biomolecule, is a reducing agent and an antioxidant serving as a metal chelator and a radical quencher [32, 33]. One use of GSH was coating silver particles to increase its water solubility by decreasing the aggregation of its particles and controlling their rate of release. Because it contains a thiol group (-SH), it is considered as the best candidate with silver, making it a potential intervention for reducing SDF-related color changes [34]. The *in-vitro* study reported that GSH was effective in decreasing the color changes especially in enamel and to a lesser extent in dentin. When compared to enamel, the greater dentin color change was ascribed to the greater amount of metallic silver formation in dentin than that in enamel. Furthermore, it was assumed that dentin requires an increased concentration of GSH to inhibit the color change more effectively [23].

Majority of the studies included in this literature review were *in-vitro* laboratory studies, therefore their findings do not necessarily represent the findings that would be there in the complex oral environment. Variations in the methodology of the *in-vitro* studies included must be considered. The only in-vivo study included in this literature review did not involve a control group for comparison, thus decreasing its level of evidence. In general, the use of KI as a method for alleviating SDF-induced staining seems to have a positive effect in the short-term. On top of that, the newly developed method of SDF + %20 GSH mixture expands the possibility of improving the esthetic outcome of SDF treatment on teeth. As dentists must be aware of the potential drawbacks of any intervention, the interaction of KI and GSH with SDF, their effects on its effectiveness and their mechanisms of action need to be further investigated in future research. In addition, more research needs to be done in regards to developing new methods to solve the SDF-induced staining problem in order to increase its acceptability and use in clinical practice.

## Conclusion

In view of the findings in this literature review, the commonly used method for managing SDF-induced dental discoloration is the application of KI immediately following SDF treatment. Another newly proposed approach is the mixture of SDF with %20 GSH solution. Both interventions produced better esthetic results as compared to the use of SDF solely. Further research is needed to consolidate the findings of this literature review and caution is recommended viewing them.

## Ethical Compliance

The authors have stated all possible conflicts of interest within this work. The authors have stated all sources of funding for this work. If this work involved human participants, informed consent was received from each individual. If this work involved human participants, it was conducted in accordance with the 1964 Declaration of Helsinki. If this work involved experiments with humans or animals, it was conducted in accordance with the related institutions' research ethics guidelines.

## REFERENCES

[1] Kailembo A, Preet R, Stewart Williams J. Common risk factors and edentulism in adults, aged 50 years and over, in China, Ghana, India and South Africa: Results from the WHO Study on global AGEing and adult health (SAGE). *BMC Oral Health*. 2016;17(1):29. doi:10.1186/s12903-016-0256-2.

[2] Featherstone JDB. The caries balance: the basis for caries management by risk assessment. *Oral Health Prev Dent*. 2004. doi:10.3290/j.ohpd.a10163.

[3] Kidd E. The implications of the new paradigm of dental caries. *J Dent*. 2011. doi: 10.1016/j.jdent.2011.11.004.

[4] Peng JJY, Botelho MG, Matinlinna JP. Silver compounds used in dentistry for caries management: A review. *J Dent*. 2012. doi:10.1016/j.jdent.2012.03.009.

[5] 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(5):135-145.

[6] Rosenblatt A, Stamford TCM, Niederman R. Silver diamine fluoride: A caries "silver-fluoride bullet." *J Dent Res*. 2009:88(2):116-25. doi:10.1177/0022034508329406.

[7] Shah S, Bhaskar V, Venkatraghavan K, Choudhary P, M. G, Trivedi K. Silver Diamine Fluoride: A Review and Current Applications. *J Adv Oral Res*. 2014;5(1):25-35. doi:10.1177/2229411220140106.

[8] Mei ML, Li QL, Chu CH, Lo ECM, Samaranayake LP. Antibacterial effects of silver diamine fluoride on multi-species cariogenic biofilm on caries. *Ann Clin Microbiol Antimicrob*. 2013;12(4). doi:10.1186/1476-0711-12-4.

[9] Mei ML, Li QL, Chu CH, Yiu CKY, Lo ECM. The inhibitory effects of silver diamine fluoride at different concentrations on matrix metalloproteinases. *Dent Mater*. 2012;28(8):903-908. doi:10.1016/j.dental.2012.04.011.

[10] Mei ML, Ito L, Cao Y, Li QL, Lo ECM, Chu CH. Inhibitory effect of silver diamine fluoride on dentine demineralisation and collagen degradation. *J Dent*. 2013;41(9):809-817. doi:10.1016/j.jdent.2013.06.009.

[11] Firouzmandi M, Shafiei F, Jowkar Z, Nazemi F. Effect of Silver Diamine Fluoride and Proanthocyanidin on Mechanical Properties of Caries-Affected Dentin. *Eur J Dent*. 2019;13(2):255-260. doi:10.1055/s-0039-1693237.

[12] Chu CH, Lo ECM. Promoting caries arrest in children with silver diamine fluoride: a review. *Oral Health Prev Dent*. 2008;6(4):315-321. doi:10.3290/j.ohpd.a14177.

[13] Mei ML, Chu CH, Lo ECM, Samaranayake LP. Fluoride and silver concentrations of silver diammine fluoride solutions for dental use. *Int J Paediatr Dent*. 2013;23(4):278-285. doi:10.1111/ipd.12005.

[14] Mei ML, Chu CH, Low KH, Che CM, Lo ECM. Caries arresting effect of silver diamine fluoride on dentine carious lesion with S. mutans and L. acidophilus dual-species cariogenic biofilm. *Med Oral Patol Oral Cir Bucal*. 2013;18(6):e824-831. doi:10.4317/medoral.18831.

[15] Zhao IS, Mei ML, Burrow MF, Lo ECM, 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(2):340. doi:10.3390/ijms18020340.

[16] Patel J, Anthonappa RP, King NM. Evaluation of the staining potential of silver diamine fluoride: *In vitro*. *Int J Paediatr Dent*. 2018. doi:10.1111/ipd.12401.

[17] Duangthip D, Fung MHT, Wong MCM, Chu CH, Lo ECM. Adverse Effects of Silver Diamine Fluoride Treatment among Preschool Children. *J Dent Res*. 2018;97(4):395-401. doi:10.1177/0022034517746678.

[18] Primus C. Potassium Iodide. The Solution to Silver Diamine Fluoride Discoloration? *Adv Dent Oral Heal*. 2017;5(1):1-6. doi:10.19080/adoh.2017.05.555655.

[19] Miller MB, Lopez LA, Quock RL. Silver diamine fluoride, potassium iodide, and esthetic perception: An *in vitro* pilot study. *Am J Dent*. 2016.

[20] Zander V, Chan D, Sadr A. Microcomputed tomography evaluation of root dentin caries prevention by topical fluorides and potassium iodide. *Sensors (Switzerland)*. 2019;19(4):874. doi:10.3390/s19040874.

[21] Garg S, Sadr A, Chan DCN. Potassium iodide reversal of silver diamine fluoride staining: A case report. *Oper Dent*. 2019;44(3):221-226. doi:10.2341/17-266-S.

[22] Roberts A, Bradley J, Merkley S, Pachal T, Gopal J V., Sharma D. Does potassium iodide application following silver diamine fluoride reduce staining of tooth? A systematic review. *Aust Dent J*. 2020:65(2):109-117. doi:10.1111/adj.12743.

[23] Sayed M, Matsui N, Hiraishi N, Nikaido T, Burrow MF, Tagami J. Effect of glutathione bio-molecule on tooth discoloration associated with silver diammine fluoride. *Int J Mol Sci*. 2018. doi:10.3390/ijms19051322.

[24] Sayed M, Matsui N, Hiraishi N, et al., Evaluation of discoloration of sound/ demineralized root dentin with silver diamine fluoride: *In-vitro* study. *Dent Mater J*. 2019;38(1):143-149. doi:10.4012/dmj.2018-008.

[25] Trieu A, Mohamed A, Lynch E. Silver diamine fluoride versus sodium fluoride for arresting dentine caries in children: a systematic review and meta-analysis. *Sci Rep*. 2019;9(1):2115. doi:10.1038/s41598-019-38569-9.

[26] Contreras V, Toro MJ, Eliás-Boneta AR, Encarnación-Burgos A. Effectiveness of silver diamine fluoride in caries prevention and arrest: A systematic literature review. *Gen Dent*. 2017:65(3):22-29.

[27] JUCSF protocol for caries arrest using silver diamine fluoride: rationale, indications, and consent. *Br Dent J*. 2017;44(1):16-28. doi:10.1038/sj.bdj.2017.311.

[28] Chu CH, Lo ECM, 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(11):767-770. doi:10.1177/154405910208101109.

[29] Lou YL, Botelho MG, Darvell BW. Reaction of silver diamine fluoride with hydroxyapatite and protein. *J Dent*. 2011;39(9):612-618. doi:10.1016/j.jdent.2011.06.008.

[30] Huang L, Szewczyk G, Sarna T, Hamblin MR. Potassium Iodide Potentiates Broad-Spectrum Antimicrobial Photodynamic Inactivation Using Photofrin. *ACS Infect Dis*. 2017;3(4):320-328. doi:10.1021/acsinfecdis.7b00004.

[31] Tello-Barbaran J, Nakata HM, Salcedo-Moncada D, Bramante CM, Ordinola-Zapata R. The antimicrobial effect of iodine-potassium iodide after cleaning and shaping procedures in mesial root canals of mandibular molars. *Acta Odontol Latinoam*. 2010;23(3):244-247.

[32] Jozefczak M, Remans T, Vangronsveld J, Cuypers A. Glutathione is a key player in metal-induced oxidative stress defenses. *Int J Mol Sci*. 2012:13(3):3145-3175. doi:10.3390/ijms13033145.
[33] Nassar M, Hiraishi N, Islam MS, Otsuki M, Tagami J. Age-related changes in salivary biomarkers. *J Dent Sci*. 2014;9(1). doi:10.1016/j.jds.2013.11.002.
[34] Taglietti A, Diaz Fernandez YA, Amato E, et al., Antibacterial activity of glutathione-coated silver nanoparticles against gram positive and gram negative bacteria. *Langmuir*. 2012;28(21):8140-8148. doi:10.1021/la3003838.