

# 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

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## ABSTRACT

**Aim:** To evaluate and compare the effect of potassium iodide (KI) and glutathione (GSH) on tooth discoloration after application of 38% silver diamine fluoride (SDF) in primary molars.

**Method:** Total of 30 primary molars were randomly divided into three groups of 10 each. Teeth were prepared and divided into: Group A—SDF only, Group B—SDF followed immediately by application of KI, and Group C—SDF was mixed with 25 mg of GSH. Final restoration was done using glass ionomer cement. Visual examination and color assessments using spectrophotometer were recorded at three time interval points, that is, day 1, 1 week, and 4 weeks.

**Results:** Statistical analysis was done using a repeated measures analysis of variances (ANOVA) test. The spectrophotometer results showed that Group A (SDF) exhibited the greatest amount of discoloration at all time intervals, while Group C (SDF + GSH) group was effective in decreasing the discoloration. Whereas, Group B (SDF + KI) significantly reduced the discoloration over the period of time. ( $p = 0.008$ ).

**Conclusion:** KI can effectively reduce discoloration after application of 38% SDF. GSH can also be used as an alternative.

**Clinical Significance:** This two-step treatment for arresting caries can be a practical and low-cost option in areas with limited access to comprehensive dental care.

**Keywords:** Glutathione, Potassium iodide, Silver diamine fluoride, Spectrophotometer, Tooth discoloration

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## INTRODUCTION

Dental caries are most commonly known as dental decay, which is a multifactorial oral disease caused as a result of imbalance between remineralization and demineralization of the tooth.<sup>1</sup> Margolis et al. stated the importance of dental plaque for the caries development. In their study, they observed that on exposure to fermentable carbohydrates, rate of demineralization of tooth was high and also a rapid loss of calcium phosphates in plaque was noticed. This was majorly observed due to production of lactic acid and plaque fluid depletion, eventually leading to development of caries.<sup>2</sup> Epidemiological studies have confirmed dental caries as a chronic widespread disease in children commonly seen in developing and developed countries.<sup>3</sup> Due to the low socioeconomic status, less exposure to basic oral hygiene, expensive dental procedures, and limited financial resources in developing countries, children are affected by untreated dental caries. This in turn has an impact on their education, overall health, and social development.<sup>4</sup>

The conventional approach for management of dental caries involves excavation of demineralized dentinal structure and restoration with a biocompatible material. Management of deep dentinal caries can be sometimes formidable, as it requires high cost of armamentarium, state of art dentist's skills, and good patient compliance toward the dental treatment. Treating young children present with dental caries is a conundrum for the clinician owing to their inadequate coping abilities.<sup>5</sup>

In order to achieve improved oral health, it is an imperative necessity to find different approaches to modify biofilm in a beneficial way. By augmenting the remineralization process of

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tooth structure, the occurrence of dental caries can also be altered. This leads to a paradigm shift in dental caries management and prevention. There is a requirement for more efficient, less expensive, approachable, and safer dental procedures that can be easily performed in high-risk population in different clinical settings.<sup>6</sup>

During 1960s, silver diamine fluoride (SDF) was first approved for therapeutic use in Japan. From 1960s to 1990s, in countries like Argentina, Australia, Brazil, and China, SDF has been used to prevent progression of dental caries. Recently in August 2014, the first SDF agent for commercial use was approved by Food and Drug Administration (FDA). In literature, SDF successfully prevented dental caries in primary and young permanent teeth in children and also arrested root caries in elderly patients. Alternatively, SDF has also been used for management of dentinal hypersensitivity. According

to Zhao et al., SDF is a clear, bactericidal solution which promotes the remineralization process of demineralized tooth structures.<sup>7</sup>

However, the inherent limitation of SDF is the discoloration of enamel and dentin, which in turn restricts its clinical use owing to its esthetic apprehensions. According to Knight et al., the use of potassium iodide (KI) has been advocated to reduce discoloration. The iodide crystals of KI reacts with the free silver ions of SDF in order to form a creamy white precipitate, thus reducing the discoloration caused by SDF.<sup>5</sup> Recently, glutathione (GSH) has been developed as an alternative agent to KI. When mixed with SDF, GSH preserves silver ions within SDF as well as on dental substrate. Previously, GSH has been used to promote interactions between complex biosystems.<sup>8</sup>

The aim of the present study was to compare and evaluate effect of KI and GSH on tooth discoloration after application of 38% SDF in primary molars. The objectives were to individually evaluate the effect of KI and GSH and compare its effect on tooth discoloration after application of 38% SDF in primary molars.

### Null Hypothesis

The hypothesis stated that there was no significant difference in the effect of KI and GSH on tooth discoloration after application of 38% SDF in primary molars.

## MATERIALS AND METHODS

This was an *in vitro* experimental study conducted in the Department of Pediatric and Preventive Dentistry, Navi Mumbai, India. Ethical approval was obtained from Institutional Review Board (TDCEC/09/2019).

Sample size was determined in concordance to results from a previous study through G\* power software (version 3.0.10).<sup>8</sup> The level of significance ( $\alpha$  error) was set at 5% (0.05) and the power of the study ( $1-\beta$ ) at 80% (0.8). Hence, the total sample size was calculated to 10 per group. Teeth were collected from the institution and private clinics. These teeth were extracted due to pathologic mobility, over retained molars or for orthodontic consideration. According to inclusion and exclusion criteria, 45 primary molars were collected and 30 of them were included in the study.

### Inclusion Criteria

- Extracted carious primary molars
- Primary molars with carious lesions involving enamel and dentin on radiographic examination.

### Exclusion Criteria

- Teeth with internal resorption
- Extracted primary molars with restorations
- Primary molars with developmental disturbances.

All 30 teeth were subjected to scaling and root planing. Selected teeth were stored in distilled water to prevent dehydration and later immersed for 1 week in 0.5% sodium hypochlorite for disinfection. The teeth were then mounted in alginate mold till the cemento-enamel junction such that the crown structure was visible.

The specimens were divided into three groups using simple random technique according to solution application.

- Group A: Silver diamine fluoride (SDF)
- Group B: Silver diamine fluoride (SDF) + Potassium iodide (KI)
- Group C: Silver diamine fluoride (SDF) + Glutathione (GSH).

Complete excavation of carious lesion was carried out in teeth of all the groups. The cavity was prepared using a high-speed handpiece (NSK, Japan) and cylindrical diamond point (SS White, New Jersey). The walls of the prepared cavity were kept slightly divergent and caries free.

### Procedure

All the materials (SDF, KI, and GSH) were applied according to manufacturer's instructions.

Group A: 38% SDF (Fagamin, Argentina)—

Silver diamine fluoride was applied and agitated for 1 minute using micro brush applicator tip to the tooth surface, which was left for 2 minutes. It was then rinsed for 30 seconds with water copiously.

Group B: SDF followed by KI (Lugol's solution, India)—

A saturated KI solution was immediately applied after application of SDF. Repeated application of KI was done until the creamy white precipitate changed its color to clear (Fig. 1). This precipitate was then rinsed for 30 seconds with water copiously.

Group C: SDF with GSH (Health Vit, West Coast Pharmaceutical Works Ltd., India)—

A total of 25 mg GSH by weight was added to 3 drops of SDF in a dappen dish and mixed vigorously. Continuous mixing of both the agents was done till the mixture was clear and free of any precipitates. The application of this mixture was applied onto the tooth surface same as Group A (Fig. 2).

Teeth of all the groups were then restored with glass ionomer cement (GC corporation, Tokyo, Japan).

### Data Collection

Visual examination was done with photographs using a camera (Canon 600D DSLR, Japan) and the teeth were assessed for any color change at three different time intervals: day 1, 1 week, and 4 weeks. Color change was analyzed using a spectrophotometer (UV-NIR-3600 Shimadzu, Japan) with a range of 400–700 nanometers (nm). Three-dimensional CIELAB color system was used to record and explain each color change in the tooth.

The color difference ( $\Delta E$ ) for all the samples was evaluated and calculated with the help of following formula:

$$\Delta E = [(\Delta L)^2 + (\Delta a)^2 + (\Delta b)^2]^{1/2}$$



Fig. 1: Silver diamine fluoride (SDF) immediately followed by application of potassium iodide (KI)

**Statistical Analysis**

Comparison of the three groups at different time intervals on mean ΔE was statistically analyzed using multivariate ANOVA test. The significant p value <0.05 (p ≤ 0.05) was set for the present study. All the tests were statistically analyzed using SPSS® software (SPSS Inc. version 18, Chicago III, USA).

**RESULTS**

On comparison between all the three groups, it was seen that Group A (SDF) showed greatest amount of discoloration at different time intervals: day 1, 1 week, and 4 weeks. Mean values with standard deviation for color changes (ΔE) onto the tooth surface of all groups at different time intervals are presented in Table 1.

In Group A (SDF), the mean ΔE values were 3.2461 at day 1, 3.2979 at 1 week, and 3.3245 at 4-week time interval (p = 0.085). In Group B (SDF+KI), the discoloration significantly reduced over time (p = 0.00) whereas Group C (SDF+GSH) showed minor color changes at baseline, which darkened after 4 weeks but it was nonsignificant (p = 1.000) (Fig. 3).

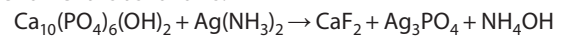
In intergroup comparison at day 1, difference found between Group A (SDF) and Group C (SDF+GSH) was statistically significant (p = 0.045). Whereas, at 1 week, there was a statistically significant difference between Group A (SDF) and group C

(SDF + GSH) (p = 0.040) as well as Group A (SDF) and Group B (SDF+KI) (p = 0.008). Similar findings were noticed even at 4 weeks between the three groups (Table 1).

On visual examination, it was noticed that the discoloration intensified over time in Group A and no discoloration was seen in Group B, whereas in Group C, only marginal discoloration was appreciated (Fig. 4).

**DISCUSSION**

Recent literature including randomized clinical trials and systematic reviews suggests that SDF application is an effective method for arresting carious lesions in children.<sup>9,10</sup> The reaction between SDF [Ag(NH<sub>3</sub>)<sub>2</sub>F] and hydroxyapatite of tooth [(HA)(Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(OH)<sub>2</sub>) leads to the formation of calcium fluoride (CaF<sub>2</sub>) and silver phosphate (Ag<sub>3</sub>PO<sub>4</sub>). These reaction products contribute to the arrest and prevention of dental caries. The chemical reaction depicting the phenomena is as follows.<sup>11,12</sup>



A white precipitate of Ag<sub>3</sub>PO<sub>4</sub> is formed onto the tooth surface, which is insoluble. The role of CaF<sub>2</sub> is to help in the formation of fluorapatite (FA) [Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>F<sub>2</sub>] by providing a fluoride reservoir. FA is highly resistant to demineralization as compared to HA.<sup>13</sup> The free fluoride ions from SDF promote remineralization of the tooth



Fig. 2: A mixture of silver diamine fluoride (SDF) and glutathione (GSH) applied on prepared tooth surface

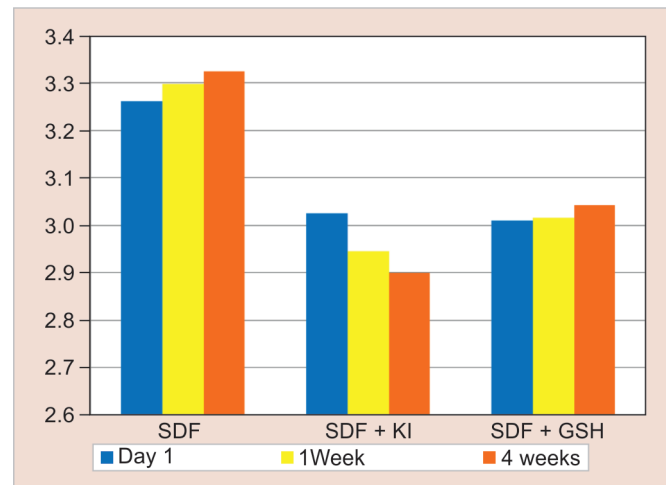


Fig. 3: Bar chart showing mean and SD for ΔE for different tested groups at all the time interval points

Table 1: Mean and SD for ΔE for different tested groups at all the time interval points

	DAY 1			1 WEEK			4 WEEKS		
	MEAN	SD	p-VALUE	MEAN	SD	p-VALUE	MEAN	SD	p-VALUE
GROUP A SDF	3.2461	.33338	0.065	3.2979	.40407	0.008*	3.3245	.41815	0.002*
GROUP B SDF + KI	3.0247	.08265		2.9448	.04444		0.040*	2.9000	
GROUP C SDF + GSH	3.0103	.07461	1.000	3.0150	.07294	1.000	3.0426	.06534	0.617

GSH, glutathione; KI, potassium iodide; SDF, silver diamine fluoride



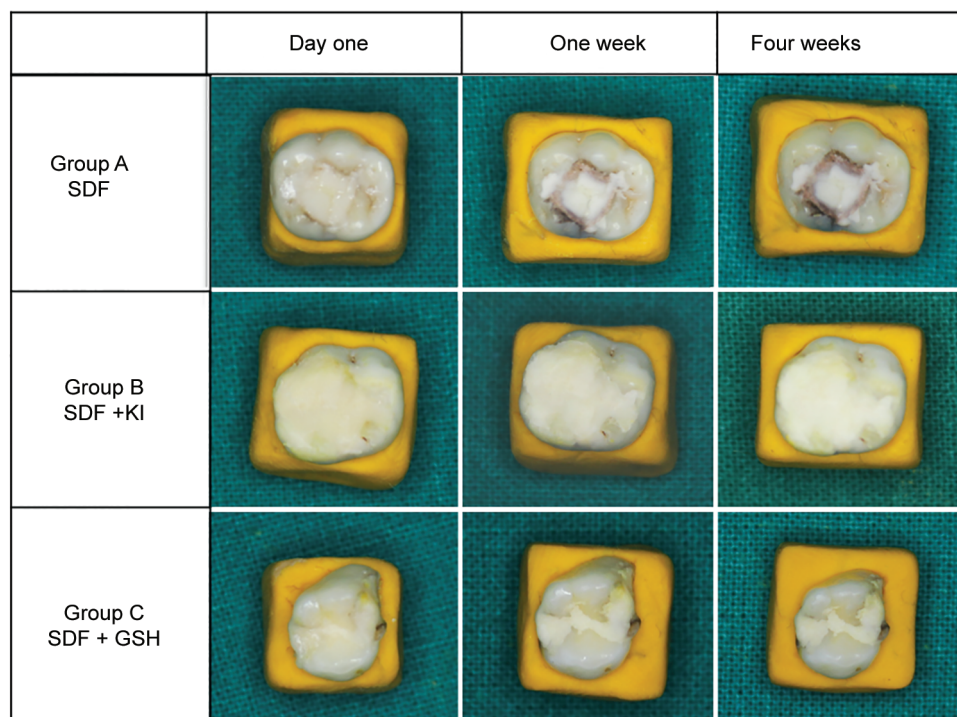


Fig. 4: Visual examination at all the time interval points

whereas the silver component of SDF causes discoloration. This has led to esthetic limitations among parents and clinicians.

Silver diamine fluoride leads to surface color changes on tooth structure, as it is sensitive to light. Hence, the spectrophotometer was selected to evaluate the color changes. A spectrophotometer is a digital instrument, which can measure the full visible spectrum of light and complex color of tooth with high accuracy, reproducibility, and reliability.<sup>14</sup>

Potassium iodide has been used as an agent to overcome tooth discoloration associated with SDF. When a saturated solution of KI interacts with SDF, a creamy white precipitate of silver iodide crystals was formed on tooth surface. Free silver ions from SDF are no longer available to form black precipitates onto the teeth thus avoiding discoloration.<sup>15</sup>

Glutathione is a commonly occurring reducing agent in human cells, which is also an antioxidant that acts as a metal chelator too.<sup>16</sup> The thiol group of GSH has a superior tendency to adsorb onto metal surfaces.<sup>17</sup> This helps in reducing the release of silver ions by forming a layer around silver particles, which in turn play an important role in decreasing the discoloration of an SDF coated tooth over time.<sup>18,19</sup>

Carious teeth involving enamel and dentin were used in the present study. In the present study, Group B (SDF + KI) showed insignificant color change between different time intervals. This could be attributed to the low number of free silver ions as most of them had already reacted with KI. Similar studies by Sayed et al., Zhao et al., and Nyugen et al., have stated that SDF and KI caused little or no discoloration over time.<sup>8,20,21</sup> However, Miller et al. had observed significant discoloration at long-term intervals.<sup>22</sup>

Group C showed a significant decrease in discoloration at 1 day, which showed effective reduction of discoloration even at 1 week and 4 weeks. In the present study, GSH and KI were effective in decreasing discoloration, thus rejecting the null hypothesis. In this study, 25 mg GSH by weight was added to three drops of SDF.

Perhaps, this amount of GSH was insufficient to cover all the silver particles completely.

Silver diamine fluoride has a wide variety of applications in pediatric dentistry. However, the use of SDF has been limited owing to its only drawback, which is tooth discoloration. More research on KI, GSH or any other agents which could help reduce the discoloration should be conducted.

## CONCLUSION

The following conclusions can be drawn from the findings of the present study:

- Group A (SDF) showed highest discoloration as compared to Group B (SDF and KI) and Group C (SDF and GSH)
- Group B (SDF and KI) significantly reduced the discoloration as compared to other groups
- Group C (SDF and GSH) also effectively reduced discoloration and can be used as an alternative to KI.

The use of this two-step noninvasive technique for arrest of caries can be a practical, more acceptable, low-cost option for children lacking cooperation, and children with special health care needs or for low-income pediatric patients with restricted access to dental care.

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