Original Article

An *In-vitro* Evaluation of Tooth Discoloration and Shear Bond Strength of Glass Ionomer Cement Bonded to Tooth Surface Pretreated with Silver Diamine Fluoride and Glutathione Biomolecule

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Abstract

Background: Silver diamine fluoride (SDF) is employed in caries prevention and treatment; however, tooth discoloration post treatment is a significant disadvantage, which can be reduced using glutathione (GSH), a water soluble tripeptide. **Aim:** To evaluate and compare the effect of glutathione biomolecule (GSH) and potassium iodide (KI) along with SDF on tooth discoloration and shear bond strength of glass ionomer cement (GIC) on the tooth surface. **Methods:** Artificial caries were created on 48 extracted unblemished premolars and divided into four groups (SDF, SDF + KI, SDF + GSH, and Water). The solutions were applied according to the manufacturer's instructions, and the samples were incubated for 24 hours. The color assessment was recorded on days 1, 7, and 14 by using a spectrophotometer. Following the color assessment, all the treated samples were bonded with GIC. The shear bond strength was evaluated using a universal testing machine. **Results:** Mixing SDF with GSH initially reduced tooth discoloration. Although there was an increase in the discoloration after 2 weeks, it was still less when compared to the SDF group. The application of GSH and KI post SDF application had no significant difference in the shear bond strength of GIC on the tooth surface. **Conclusions:** The use of GSH along with SDF helps in reducing the discoloration without compromising the shear bond strength.

Keywords: *Glass ionomer cement, glutathione biomolecule, shear bond strength, silver diamine fluoride, tooth discoloration*

Introduction

Dental caries is a localized, irreversible disorder that dissolutes teeth due to acidic biofilm.[1,2] It is a burden on society, and caries prevention is crucial in reducing this burden and improving children's lives. In the past, caries treatment focused on removing decayed tissue with mechanical preparation and restoring cavities. This destroyed healthy tooth structure. The current caries management strategy has progressed from traditional to minimally invasive.[3-5] Dental practitioners and researchers are exploring the use of silver diamine fluoride (SDF) for caries prevention.

In 659 AD, Chinese dentists used silver compounds as an efficient antibiotic. Antibacterial fluoride is also known to remineralize early carious lesions. Silver and fluoride were believed to prevent cavities.[1,6] Yamaga and Nishino from Japan were the first to use

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ammoniacal silver fluoride to arrest caries, leading to the first commercial SDF product, "Saforide."[7,8] Since then, several studies on SDF have proven its anticaries efficacy.[9] SDF is a colorless solution of diamine-silver and fluoride ions.[10,11] 38% SDF has the highest fluoride content of any fluoride agent at 44,800 ppm. (remaining things do not need any correction). SDF and hydroxyapatite interact to generate nanoscopic metallic silver particles, which oxidize and discolor teeth.

SDF is used to treat ECC, prevent secondary caries, and manage molar incisor hypo-mineralization and dentin hypersensitivity. SDF has several advantages, but the discoloration of teeth after treatment is a big negative. Earlier attempts to fix discoloration have failed miserably. Zinc fluoride and ammonium hexafluorosilicate were previously employed; however, they did not reduce dentin collagen breakdown and demineralization.[12,13] The black discoloration was reduced using a saturated potassium iodide (KI) solution after SDF application.[14] KI reduces SDF's free silver ions, thus reducing its benefits as an antibiotic. Glutathione (GSH) is a low-molecular-weight sulfhydryl-thiol molecule. It acts as a radical quencher and metal chelator.[15] Glutathione (GSH) is a water-soluble tripeptide that contributes to intracellular non-protein thiols. GSH's sulfhydryl group binds silver ions;[16] it also covers silver particles, preventing aggregation and regulating ion release. GSH applied to an SDF-treated tooth may reduce discoloration over time.

Cavitated lesions should be treated optimally to reduce subsequent caries. Some research says SDF is compatible with glass ionomer cement (GIC) restorations.[14] Little is known about GIC's adherence to caries-affected dentin treated with SDF + KI or SDF + GSH. Hence, we attempted to evaluate the effect of GSH on the discoloration of SDF and its effect on the shear bond strength of GIC.

Material and Methods

Study design and location

The study was an invitro type, carried out in the Department of Pediatric and Preventive Dentistry at JSS Dental College and Hospital, Mysuru, India. The protocol of the study was approved by the institutional ethics committee (JSSDCH/IEC/no.: 61/2019).

Sample size estimation

A sample size of 12 samples per group was derived using data from a similar study[17] and assuming at least a difference of 2.38 units in ΔE across the four groups at an α-level of 5% and a confidence interval of 95%. The four-group study featured 48 samples.

Method of collection of data

The current study used 48 newly extracted premolars for orthodontic reasons, with undamaged crowns, free of cavities and fractures obtained with the parent's consent. The study excluded hypoplastic lesions, attrition, abrasion, erosion, intrinsic stains, restorations, and developmental anomalies.

Sample preparation

The teeth were sectioned along the occlusal plane to expose dentin just gingival to the dentino-enamel junction under continuous distilled water irrigation using a diamond disc (Diatech, CH- 9435, Lot: 9605) fixed to a slow-speed micromotor handpiece (NSK, Nakanishi, Japan) to obtain 48 samples. Each sample was mounted in a resin block. The dentin surface of the mounted samples was polished with 2000-grit micro-fine sandpaper under water to generate a homogeneous surface.

Formation of artificial carious lesion

According to Ten-Cate and Dujister's methodology, 1 L of demineralizing solution (calcium chloride: 2.2 mM, potassium dihydrogen orthophosphate: 2.2 mM, acetic acid: 0.05 mM, and distilled water; pH adjusted to 4.5 by using 50% sodium hydroxide) was freshly made.[18] To simulate artificial caries, the samples were immersed in the demineralizing solution and incubated at 37°C for 7 days. The solution was changed daily.

Randomization and stratification

The samples were divided into four groups of 12, after 7 days of demineralization. One investigator placed the samples in similar containers, while another, unrelated to the experiment, randomly assigned them to different groups using a simple randomization technique using random number table. The samples were numbered for identification after being divided into four groups.

Group 1	38% SDF
Group 2	38% SDF + Saturated KI
Group 3	38% SDF + 20% GSH
Group 4	Water

Baseline color assessment using a spectrophotometer

Using a portable spectrophotometer (eXact Advanced, X-rite, PANTONE), all samples were color-tested. Equipment parameters were as follows: aperture: 4 mm; Illuminant D50/2°; and spectral range: 400–700 nm. The device was calibrated before each inspection, following the manufacturer's instructions. Dry samples were cantered over the device aperture.

The Commission International del'Eclairage (CIE) system (1976) was utilized to three-dimensionally explicate the color by recording the L* a* b* color coordinates. The L* axis indicated lightness from black (0) to white (100), the a* axis indicated red (+a*) to green (-a*), and the b* axis indicated yellow (+b*) to blue (-b*) (18). The values were recorded thrice, and the average was taken.

Application of the solutions to be tested

The protocol for the application of different solutions was as follows:

Group 1 – 38% SDF: Each Air-dried sample received one drop of commercial 38% SDF (FAgamin®). SDF was applied using a micro-applicator tip to the demineralized dentin and agitated for 1 minute. After 2 minutes, it was rinsed for 30 seconds with pure water.

Group 2 – 38% SDF + Saturated KI: A saturated solution of KI was freshly prepared in a glass dappen dish by mixing 1 g of KI in 1 mL of distilled water (10% by weight).

The application protocol for group 2 was as follows: Each air-dried sample received one drop of commercial 38% SDF (FAgamin®). SDF was applied with a micro-applicator tip onto the demineralized dentin and agitated for 1 minute, which was then followed by the immediate application of one drop of a saturated solution of KI to the treatment site until a creamy precipitate turned clear. It was then rinsed for 30 seconds with distilled water.

Group 3 – 38% SDF + 20% GSH: SDF + GSH solution was freshly prepared by mixing 0.2 g of GSH with 1 mL of SDF (20% by weight) under vigorous stirring until the solution became clear without the presence of any precipitates. The samples were air-dried. For every sample, one drop of the freshly prepared SDF + GSH solution was topically applied on the surface of the demineralized dentin and agitated for 1 minute. It was kept for 2 minutes and then rinsed for 30 seconds with distilled water.

Group 4 – Water: The samples were air-dried. For every sample, one drop of distilled water was topically applied to the demineralized dentin surfaces.

Assessment of color

All the samples were incubated for 24 hours at 37°C. Color assessment of all treated samples was recorded at three time interval points, namely 1st day, 7th day, and 14th day, by using the spectrophotometer. The L* a* b* color coordinates for all treated samples were recorded. The following mathematical equation was used to calculate the difference in color (ΔE) for every sample between the baseline and each time-interval point:[19]

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

Shear bond strength assessment

Placement of GIC

Following the color assessment, all treated samples were bonded with GIC (GC GOLD LABEL-9). To make cylindrical GIC buttons, a customized jig made of Teflon with a hole of 4-mm diameter and 2-mm height was used. The jig could be adjusted vertically and horizontally with the help of screws to ensure proper contact of the GIC with the treated dentin surfaces. For every sample, GIC was mixed according to the manufacturer's instructions and with the help of the jig, bonded to the treated samples forming a cylindrical button of 4-mm diameter and 2-mm height. After bonding, the samples were kept at 37°C for 24 hours for GIC to completely harden.

Shear bond strength analysis

Following the placement of GIC, the samples were evaluated for the shear bond strength of GIC to the treated samples. The test was performed using a flat edge loading head universal testing machine (Lloyd Instruments, UK, EZ-20). The crosshead speed was 0.5 mm/min. A shear force perpendicular to the GIC cylindrical button was applied. The load required to debond the GIC cylinder was measured in Newtons. By dividing the load at failure by the bonded surface area in square millimeters, the bond strength was determined in MPa.

Statistical analysis

Continuous variables were presented using the mean and standard deviation. ANOVA with post-hoc Bonferroni's test for multiple group comparisons was performed. Intragroup statistical comparisons employed RMANOVA. SPSS 24.0 was used for the analysis of data.

Results

Table 1 depicts the mean, SD, intragroup, and intergroup statistical comparison of the L* values at different periods among all the groups.

Intragroup statistical comparisons of mean L* value

According to Table 1, the SDF group resulted in tooth color that was darker compared to the baseline value, and the difference was significant (P value < 0.05). The L* value continued to decrease further on days 7 and 14 (shift to the darker side) but was statistically insignificant (P value > 0.05). The SDF + KI group resulted in tooth color that was lighter compared to baseline, and this difference was statistically significant (P value < 0.05). However, the L* value significantly decreased (shift to the darker side) by the 14th day compared to day 1 (P value < 0.05). The SDF + GSH group resulted in tooth color that was darker compared to baseline, and this difference was statistically significant (P value < 0.05). The L* value continued to decrease significantly (shift to the darker side) by the 7th and 14th day (P value < 0.05). The water group (negative control) did not change color from baseline in the provided time span (P value > 0.05).

Intergroup statistical comparison of mean L* value

The results as shown in Table 1 infer that the distribution of mean L* values at baseline did not significantly differ across the four study groups (P value > 0.05 for all). The SDF group resulted in a tooth color that was darker compared to all the other groups. This difference was statistically significant across all the groups on the 1st day, 7th day, and 14th day (P value < 0.05 for all). The SDF + KI group resulted in a tooth color that was lighter compared to all the groups. The difference was significant statistically across all the groups. The SDF + GSH group showed L* values that were darker compared to the SDF + KI and water groups but lighter when compared to the SDF group, and the difference was statistically significant across all the groups.

Intergroup statistical comparison of the mean ΔL value

Table 2 depicts the mean, SD, and intergroup statistical comparisons of the mean Δ L values at different periods among all the groups.

A statistically significant change in color was observed at each time interval when comparing distinct groups

Table 1: Distribution of mean and SD of L* values at different periods among all four groups

L* value	SDF (n=12)		SDF + KI (n=12)		SDF + GSH (n=12)		Water (n=12)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Baseline	$66.25^{a,A}$	2.01	$65.69^{a,A}$	1.03	$65.05^{a,A}$	2.99	$67.52^{a,A}$	4.47
Day 1	$38.66^{b,A}$	3.69	$89.32^{b,B}$	2.17	$58.88^{b,C}$	3.03	$66.95^{a,D}$	2.12
Day 7	$39.38^{b,A}$	5.57	$85.82^{c,B}$	2.81	$53.87^{c,C}$	3.94	$65.98^{a,D}$	3.29
Day 14	$39.93^{b,A}$	5.50	$83.14^{d,B}$	3.30	$46.73^{d,C}$	4.04	$64.61^{a,D}$	2.05

L* value: represent the lightness of color from black (0) to white (100). Different superscript lowercase letters (a, b, c, d) indicate a significant difference in the intragroup comparisons among the group within one column (P<0.05). Different superscript uppercase letters (A, B, C, D) indicate a significant difference in the intergroup comparisons between the groups within one row (P<0.05)

Table 2: Distribution of mean and SD of ΔL values at different periods among all four groups

ΔL	SDF (n=12)		SDF + KI (n=12)		SDF + GSH (n=12)		Water (n=12)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
T1−T0	-27.85^{A}	3.15	23.63^{B}	1.56	-5.74^{C}	4.00	0.43^{D}	4.46
T2−T0	-27.22^{A}	5.08	20.12^{B}	2.69	-11.09^{C}	5.36	-3.54^{D}	4.42
T3−T0	-26.68^{A}	5.41	17.45^{B}	3.39	-17.89^{C}	5.57	-3.16^{D}	6.51

ΔL: Difference in the shift of color of the black/white scale between two different time intervals. T1−T0: Difference between baseline values and 1 day post application of the material to be tested. T2−T0: Difference between baseline values and 7 days post application of the material to be tested. T3−T0: Difference between baseline values and 14 days post application of the material to be tested. Different superscript uppercase letters (A, B, C, D) indicate a significant difference in the intergroup comparisons between the groups within one row (P<0.05)

Table 3: Distribution of mean and SD of ΔE values at different periods among all four groups

ΔE	SDF (n=12)		SDF + KI (n=12)		SDF + GSH (n=12)		Water (n=12)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Day 1	27.89^{a}	3.31	20.75^{a}	3.59	7.77^{a}	3.99	3.88^{a}	2.38
Day 7	27.23^{a}	5.29	19.35^{a}	4.97	17.27^{b}	3.28	4.98^{a}	3.28
Day 14	27.51^{a}	5.09	22.06^{b}	3.80	26.09^{c}	5.38	6.32^{a}	4.17

ΔE: Difference in the total color change between two different time intervals. Different superscript lowercase letters (a, b, c, d) indicate a significant difference in the intragroup comparisons among the group within one column (P<0.05)

Table 4: Distribution of mean shear bond strength among four groups

	SDF (n=12)		SDF + KI (n=12)		SDF + GSH (n=12)		Water (n=12)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Shear bond strength (MPa)	1.56^{A}	0.08	1.68^{A}	0.17	1.60^{A}	0.25	1.56^{A}	0.27

The same superscript uppercase letters (A, B, C, D) indicate no significant difference in the intergroup comparison among the groups within the row (P>0.05) of ΔL values, as indicated by the table results. These groups included those measured at day 1 (T1 − T0), day 7 (T2 − T0), and day 14 (T3 − T0).

Intragroup statistical comparison of the mean ΔE value

Table 3 represents the mean, SD, and intragroup statistical comparisons of the mean ΔE values.

According to the results, all the groups except the water group (negative control) showed an obvious color change on 1st day compared to their respective baseline values, and the difference was statistically significant (P value < 0.05 for all). There was an insignificant difference in the ΔE values between the 7th-day and 14th-day follow-ups in the SDF group, SDF + KI group, and water group, suggesting that there was no further overall color change among these groups (P value > 0.05). However in the SDF + GSH group, the distribution of the mean ΔE on the 7th day and 14th day was significantly higher compared to ΔE on the 1st day and 7th-day follow-ups, respectively, suggesting that the SDF + GSH group continued to show a change in the total color at the 7th and 14th-day follow-up (P value < 0.05 for all).

Shear bond strength of GIC applied to the tooth surface

Table 4 depicts the mean, SD, and intergroup statistical comparisons of the shear bond strength of GIC applied to the tooth surface post the application of the solutions.

The mean shear bond strength in the SDF group, SDF + KI group, SDF + GSH group, and water group was 1.56, 1.68, 1.60, and 1.56 MPa, respectively. There was no statistically significant difference in the mean shear bond strength of the GIC applied to the pretreated tooth surfaces in the four study groups (P value > 0.05 for all).

Discussion

Dental caries in children is a public health concern. Minimally invasive treatments are becoming more common these days. SDF has been demonstrated to arrest and prevent caries with minimum intervention. It has been proposed as a non-aerosol dental caries treatment, thus reducing COVID-19 pandemic transmission.[20] Gao *et al.*[21] found that SDF arrested cavities in 81% of primary teeth after a 6–30-month follow-up study. According to Chibinski *et al*., SDF was found to be 89% more efficient than other medications in reducing caries due to its ability to release free silver and fluoride ions.[1,22] Jabin *et al.*[23] established that utilizing 38% SDF to prevent dental caries in deciduous teeth is a safe and effective strategy.

$Ag(NH3)2F(aq) \rightarrow Ag(s) + 2NH3(g) + F - (aq)$.[20]

Reduced silver ions result in a black silver precipitate that discolors the teeth.[20] Tooth discoloration is one of SDF's key downsides, which limits its application. Attempts to treat discoloration in the past have been unsuccessful. Zinc fluoride and ammonium hexafluorosilicate have exhibited modest success in reducing dentin collagen breakdown and demineralization when compared to 38% SDF.[12,13] KI and SDF have been shown to minimize tooth discoloration. According to Patel *et al.*,[24] KI has been demonstrated to reduce SDF staining. Roberts *et al.*[25] conducted a systematic review to assess the efficiency of KI to reduce staining. Of the six articles included in the review, five reported stain reduction in the teeth treated with KI post SDF application. When KI ions combine with silver ions in SDF, a yellowish silver iodide precipitate forms, which helps to minimize discoloration.

$Ag(NH3)2F(aq) + KI\ (aq) \rightarrow AgI\ (s) + 2NH3(g) + F - (aq)$.[20]

According to Zhao *et al.*,[26] KI did not affect the aesthetic discoloration of the tooth in the long run, SDF + KI did not help prevent secondary caries, and KI reduced free silver ions needed for SDF's antibacterial and anticarcinogenic effects.

In terms of minimizing discoloration, GSH has been examined as a viable alternative to KI.[20] To investigate the color, a spectrophotometer that measures the whole spectrum with great precision, reliability, and consistency using the CIELAB system was used. During the process, changes in sample position can impact these measurements.[27] Hence, three consecutive readings were taken for each sample, with the average being considered to limit error.

ΔE stands for the whole color change. If ΔE is greater than 3.7 units (perceptibility threshold), tooth discoloration would be clinically noticeable.[28] According to the ΔE values, the SDF group had the most color shift when compared to the other groups. SDF + GSH had the smallest color change on day 1, but it increased over the next 2 weeks. These were equivalent to those found on bovine incisors by Sayed *et al.*[20] The ΔE number only denotes the entire color shift, not the change in the direction of color. Hence, interpreting differences in color qualities would be more useful.

SDF caused the darkest tooth discoloration in our study. The CIELAB L* value represents brightness from black (0) to white (100). SDF + KI reduced SDF-induced discoloration by increasing tooth lightness when compared to baseline values.[24,29] Over 2 weeks, this amount dropped, proving that KI is not effective in the long term.[30] GSH in combination with SDF reduced the darkness on day 1; however, after 2 weeks, the teeth returned to their prior state. The homeostatic feature of GSH, which controls the rate of silver ion release, could be the reason.[31] Silver ions over time generate darkness. GSH's slower release of silver ions compared to KI results in a long-lasting antibacterial response, thus increasing SDF's efficacy in preventing secondary caries.[26] After 2 weeks, SDF + GSH created less darkness than SDF alone.

The SDF group had the greatest difference in the color shift on a black/white scale between two independent time intervals, which was consistent with the study done by Hamdy *et al*.[20] The color shift in the SDF + GSH group was the smallest, albeit it grew over 2 weeks.

The use of a tooth-colored restoration would help to mask the staining while also restoring the teeth's function. When GIC restorations were placed on a tooth treated with SDF by using an ART approach, Jiang *et al*.[32] reported higher parental satisfaction. GIC bonds to dentin micromechanically and chemically.[33] Because of its acid content, GIC can be regarded as a self-etching restorative material, allowing enhanced micromechanical interlocking and adhesion to tooth structures. With the rising usage of SDF for caries prevention, it is crucial to understand how KI or GSH might alter dentin bond strength. Therefore, we wanted to evaluate how GSH and KI affected the shear bond strength of GIC to SDF-pretreated dentin.

GIC's shear bond strength was statistically insignificant in all four groups, implying that SDF, SDF + KI, and SDF + GSH do not affect dentin adhesion. This finding was consistent with prior research[14,34,35] on GIC's bond strength to SDF- and SDF + KI-treated dentin.

Thus, it can be stated that SDF induced the most tooth discoloration, which was visible during the first 24 hours of application. The use of KI soon after applying SDF helps to decrease discoloration. After 24 hours, SDF and GSH reduced tooth discoloration. However, discoloration increased slightly after 2 weeks, but it was still less than in the SDF group. GIC's shear bond strength to the tooth surface was unaffected by KI or GSH in SDF.

Hence, combining SDF with GSH may help overcome its drawbacks. Nonetheless, more clinical research is needed.

Limitations of the study

- The conclusions of this in-vitro study cannot be generalized and applied to clinical settings. The dynamic nature of the oral cavity, saliva, and chromogenic and nonchromogenic bacteria all affect tooth discoloration
- In addition, controlled laboratory conditions differ from the natural oral environment, which might influence GIC mechanical properties and bond strength.

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Conflicts of interest

There are no conflicts of interest.

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