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Original Article

Optimal concentration of potassium iodide to reduce the black staining of silver diamine fluoride

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KEYWORDS
Black staining;
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Abstract *Background/purpose:* Potassium iodide (KI) is used for reducing the degree of black staining occurred after silver diamine fluoride (SDF) application. However, the optimal KI concentration remains unknown. This study aimed to identify the optimal concentration of KI that effectively reduces black staining after SDF application.
Materials and methods: Twenty-four extracted teeth with similar pattern of carious lesions were assigned into 6 groups as follows: 1) SDF only, 2) SDF+7.5%KI, 3) SDF+10%KI, 4) SDF+15%KI, 5) SDF+20%KI, and 6) SDF+saturated KI. The KI solution was applied immediately after SDF application. Tooth images were obtained for color measurement at different time points as followed; before SDF application, immediately after SDF application, immediately after KI application, 1, 3, 7 and 14 days after SDF+KI application. The photographs were analyzed for mean gray value using the ImageJ program.
Results: The KI groups demonstrated a dose-dependent significant immediate reduction in black staining after KI application, except the saturated KI group. The teeth in the 20% KI group had the highest Δ mean gray value compared with other groups immediately after KI application, whereas a reduction in black staining in the saturated KI group appeared 1 day after KI application. The Δ mean gray value in all groups decreased over time. After 7 and 14 days, the reduction in black staining was not clearly different between KI groups.
Conclusion: KI application was able to reduce the degree of black staining in a dose-dependent manner, but the subsequent color change was minimal over the period of 14 days.

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Introduction

Dental caries is realized to be the most common oral health problem worldwide affecting over 80% of the population in many countries and affects their on quality of life.[1] Dental caries is a multifactorial disease that is caused by host, bacteria and environmental factors.[2] The bacteria metabolize sugar and produce lactic acid that dissolves the calcium and phosphate in the tooth causing demineralization. Demineralization occurs in the enamel or dentine causing a cavity in the tooth.[3] To prevent this problem, dental caries should be treated when it is in the initial stages. The most common treatment for dental caries is removing the carious tissue and restoring it with a material. However, an early carious lesion can be treated using non-invasive approaches, such as fluoride application, anti-caries agents, xylitol and silver diamine fluoride (SDF).[2] Currently, the preferred dental treatment is one that uses a minimally invasive approach. One of these approaches is applying SDF rather than removing carious tissue.

SDF is a liquid agent consisting of 24.4%—28.8% silver and 5.0—5.9% fluoride.[4] SDF is a topical fluoride that effectively arrests caries and decreases tooth sensitivity.[5] SDF is used for the non-operative treatment of active caries. Active caries treated with SDF usually becomes arrested caries, which is normally brown or black, hard, glossy, and non-progressive. SDF inhibits tooth demineralization and promotes remineralization.[4,6] After applying SDF to a carious lesion, it forms a silver protein conjugate on the carious surfaces.[7] SDF increases the resistance to acid dissolution and increases mineral density and hardness. A rich mineralized layer can be found on the surface of arrested carious lesions.[8] In addition to arresting caries, SDF also has an antimicrobial effect. It inhibits the metabolism of carbohydrates in acidogenic bacteria. A study found that the silver ions in SDF reduced biofilm formation.[4] Silver ions interfere with the glucosyltransferase, inhibiting the synthesis of glucan that is important in biofilm adhesion.[4] Other research revealed that SDF prevents the destruction of dentine collagen by inhibiting collagenases enzyme.[9] Furthermore, SDF is also inexpensive and easy to use. Many studies evaluated SDF for dental caries management in children and adolescents.[10] Several studies applied 38% SDF on cavitated carious lesions to arrest caries.[5,9,11,12] However, carious lesion applied with SDF have permanent black staining, resulting in esthetics concerns.[4,11] SDF releases free fluoride ions and silver ions. The silver precipitate causes black staining on the tooth.[4,9] The black staining occurs within 2 min and increases degree of staining for up to 6 h after application.[11]

To solve this problem, Potassium iodide (KI) is used for reducing the degree of black staining in carious lesion by applying KI immediately after SDF application.[11] KI is a salt consisting of 76% of iodine and 23% of potassium that generates white or transparent hexahedral crystals. KI is photosensitive and is slightly hygroscopic properties, being highly soluble in water.[13] Applying KI with SDF creates a silver iodide precipitate that is yellow, insoluble and does not cause black staining on the tooth.[4,9,14] Application of KI does not affect or minimally affects the effectiveness of SDF in arresting caries.[4] However, several studies demonstrated that KI reduces the anti-caries effects of SDF by reducing the number of silver ions.[4,9] A studies applied 10% KI to decrease the degree of black staining in arrested caries.[4] In addition, using KI can cause some side effects, such as a metallic taste in the mouth, swollen glands, nausea, diarrhea, vomiting, stomachache, headache and allergic reactions. KI also causes desquamation if it comes in contact with soft tissue.[15] However, the optimal KI concentration remains unknown. Therefore, the aim of this study was to determine the optimal concentration of potassium iodide that effectively reduces black staining after SDF application.

Materials and methods

The experimental protocol was approved by Dent CU-IBC (018/2019) and the Ethical Committee (HREC-DCU 2019-064) following diagram (shown in Fig. 1).

Sample preparation

Tooth preparation

Twenty-four extracted teeth from the Chulalongkorn University Mobile Dental Unit were stored in normal saline solution. Teeth with active carious lesions were selected and rinsed with normal saline solution. The teeth with a similar carious lesion size and location were randomly divided into 6 groups (n = 4).

Potassium iodide (KI) preparation

Saturated KI and 20% KI solutions were prepared by the Department of Pharmacology, Faculty of dentistry, Chulalongkorn University. A series of 7.5%, 10%, 15% KI solutions was prepared just before use by diluting the 20% KI solution with deionized water.

Experimental groups

The carious lesions were applied with 10 μl 38% SDF (Topamine™ Dental life, Ringwood, Australia) for 2 min using a microsponge brush. The teeth were randomly assigned into 6 groups using different KI concentrations. Six groups were as follows:

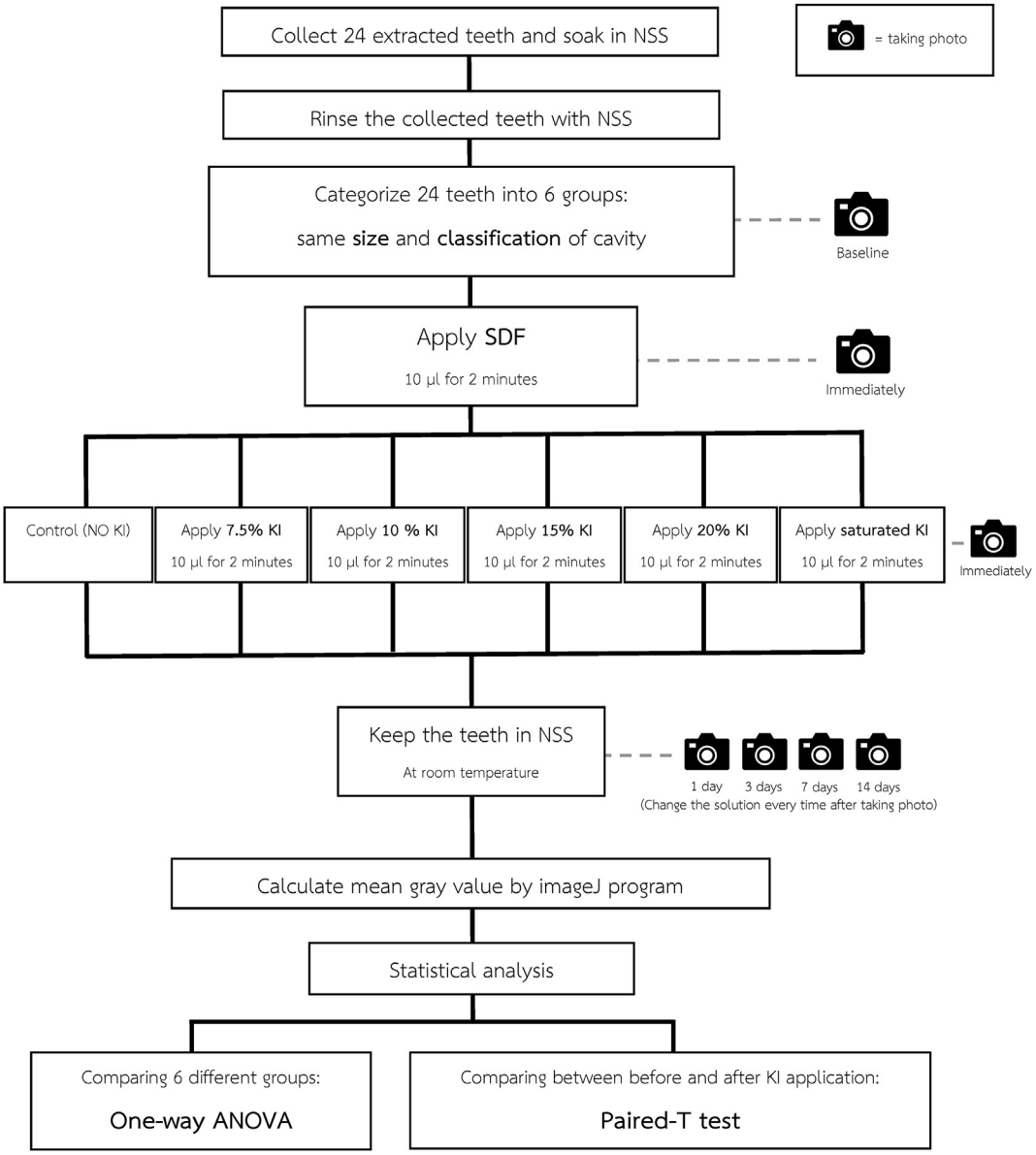

Figure 1 Schematic of the experimental flow.

Group 1: SDF application (as a control).

Group 2: SDF application and using 7.5% KI immediately afterwards.

Group 3: SDF application and using 10% KI immediately afterwards.

Group 4: SDF application and using 15% KI immediately afterwards.

Group 5: SDF application and using 20% KI immediately afterwards.

Group 6: SDF application and using saturated KI immediately afterwards.

Ten µL of KI solution was applied for 2 min immediately after SDF application using a microsponge brush. The experiments were performed by the same person. The teeth were stored in the normal saline solution for 14 days. The normal saline solution was changed every time after taking photographs. A schematic of the experimental flow is seen in Fig. 1.

Degree of black staining and image analysis measurement

The teeth were photographed using the Digital camera (OM-D E-M10, Olympus Corp., Tokyo, Japan) in the same controlled light conditions and positions. The time points for taking photographs were before SDF application, after SDF application, immediately after KI application, 1, 3, 7, and 14 d after KI application. The images were imported and calibrated using ImageJ software (WS Rasband, National Institute of Health, Bethesda, MD, USA). The images were selected, the carious area was isolated, and analyzed for mean grey values by one examiner for validity and reliability. The intra-observer reliability was determined using the intraclass correlation coefficient (ICC = 0.99) indicating high reliability of the black staining measurement within the same examiner.

The mean gray value was the average gray value within the selected area. The grey value ranges from 0 to 255 (0: black, 255: white). A high mean gray value is whiter than a low mean gray value.

The Δ mean gray value is the difference in mean gray values between after KI application and before KI application. A higher Δ mean gray value is whiter than before KI application.

Statistical methods

In this study we considered an increment mean gray value of carious lesions among six groups. The sample size calculation using the G*power computer program indicated that a total sample of 24 teeth for 6 groups would be needed to detect small effects (effect size = 0.33) with 80% power using one-way ANOVA tests between means with an alpha at 0.05. The data were analyzed using the Statistical Package for the Social Sciences 22.0 (IBM Corp., Armonk, NY, USA).

One-way ANOVA tests followed by Post-hoc tests were performed to compare the mean gray value between 6 different groups. Statistical analyses for comparing between before and after KI applications were performed using the Paired t-test. The differences at $p < 0.05$ were considered statistically significant.

Results

Twenty-four teeth were applied with SDF and randomly assigned into 6 groups; control, 7.5%, 10%, 15%, 20%, or saturated KI. Photographs of the teeth were taken before SDF application, after SDF application, immediately after KI application, 1, 3, 7, and 14 d after KI application (Fig. 2). Immediately after applying KI, the black staining of the teeth was whiter, except in the saturated KI groups. However, the black staining was less white after 7 and 14 d. We calculated the mean gray value and standard deviation of the different concentrations of KI at different time points (before KI, immediate, 1, 3, 7, 14 d) (Fig. 3). The KI groups demonstrated a significant reduction in black staining immediately after KI application ($p < 0.05$) compared with before KI application, except for the control and saturated KI groups that demonstrated little change. However, after 1 day, these 2 groups presented a significant reduction in black staining. All the KI groups exhibited a gradual reduction in the effectiveness in reducing black staining over 1, 3, 7 and 14 d.

Figure 4 presents the Δ mean gray value and standard deviation of the different concentration KI groups at different time points. The teeth in the 20% KI group had the highest Δ mean gray value compared with the other groups immediately after KI application followed by the 15%, 10%, 7.5%, saturated KI and control groups. In contrast, the saturated KI group demonstrated the highest Δ mean gray value 1 and 3 d after KI application followed by the 20%, 15%, 10%, 7.5%, and control groups. After 7 and 14 d, the reduction in black staining was not clearly different between the KI groups. The Δ mean gray value significantly decreased over time.

The Δ mean gray value in the 6 KI groups was significantly different (ANOVA $p < 0.05$) in at least one group at every time point (Table 1). Table 2 shows the pairwise comparisons of the Δ mean gray value. At the immediate time point, the Δ mean gray value between the no KI group and each concentration group except for the saturated KI group were significantly different ($p < 0.05$). There was no significant difference between the 7.5% KI and 10% KI groups, the 7.5% and saturated KI groups, the 10% KI and 15% KI groups, or the 15% KI and 20% KI groups at the immediate time point. After 7 and 14 d, the reduction in black staining was not significantly different between the groups, except for the No KI and saturated groups and the 7.5% KI and saturated KI groups.

Discussion

The present study evaluated the optimal concentration of potassium iodide (KI) that effectively reduces black staining after silver diamine fluoride (SDF) application. The results indicated that all KI application groups demonstrated a significant reduction in black staining immediately after KI application, except for the control and saturated KI groups. It is possible that the silver ions from SDF and the iodide ions from KI form silver iodide (AgI), which is yellowish-white and insoluble in water. Thus, the application of KI can minimize the SDF black staining and improve the esthetic problem.[4,14]

Similar to our findings, a number of studies found that treatment with KI following SDF significantly reduced staining compared with SDF treatment.[4,11] KI enhanced the esthetic outcome by reducing the black stain, thus making SDF an appropriate choice for preventing caries.[15] In contrast, a study indicated that KI application did not reduce the black staining.[16] These disparate results may be due to different evaluation time points. In a previous study, KI was ineffective when evaluated at 12, 24, 30 months, which are long-term periods.[16] In the present study, there was a significant reduction in black staining after KI application, however, KI application had no long-term effect on reducing the black staining after 7 and 14 d. There is a possibility that the silver iodide is photosensitive and becomes darker when exposed to the light from the camera flash.[4,15]

Because the black staining was not reduced by KI application over the long term, a restoration with glass ionomer cement (GIC) after SDF and KI application may solve this problem. A resin-modified glass ionomer (RMGI) can improve the esthetic outcome and mechanical properties of a restoration. A study found that applying SDF and KI before restoring with GIC did not affect the bond strength of the GIC to dentin and did not interfere with the fluoride uptake into the demineralized dentin.[17] Moreover, SDF and KI both have an antibacterial and caries arresting effect[18] and its remineralization potential is expected to improve when combined with RMGI.[15]

The effect of SDF and KI in arrested caries is unresolved. Knight et al. found that applying a saturated solution of KI immediately after applying SDF, minimized the staining of the carious lesion, while the caries arresting effect of SDF is not affected.[19] In contrast, Li et al. reported that SDF and

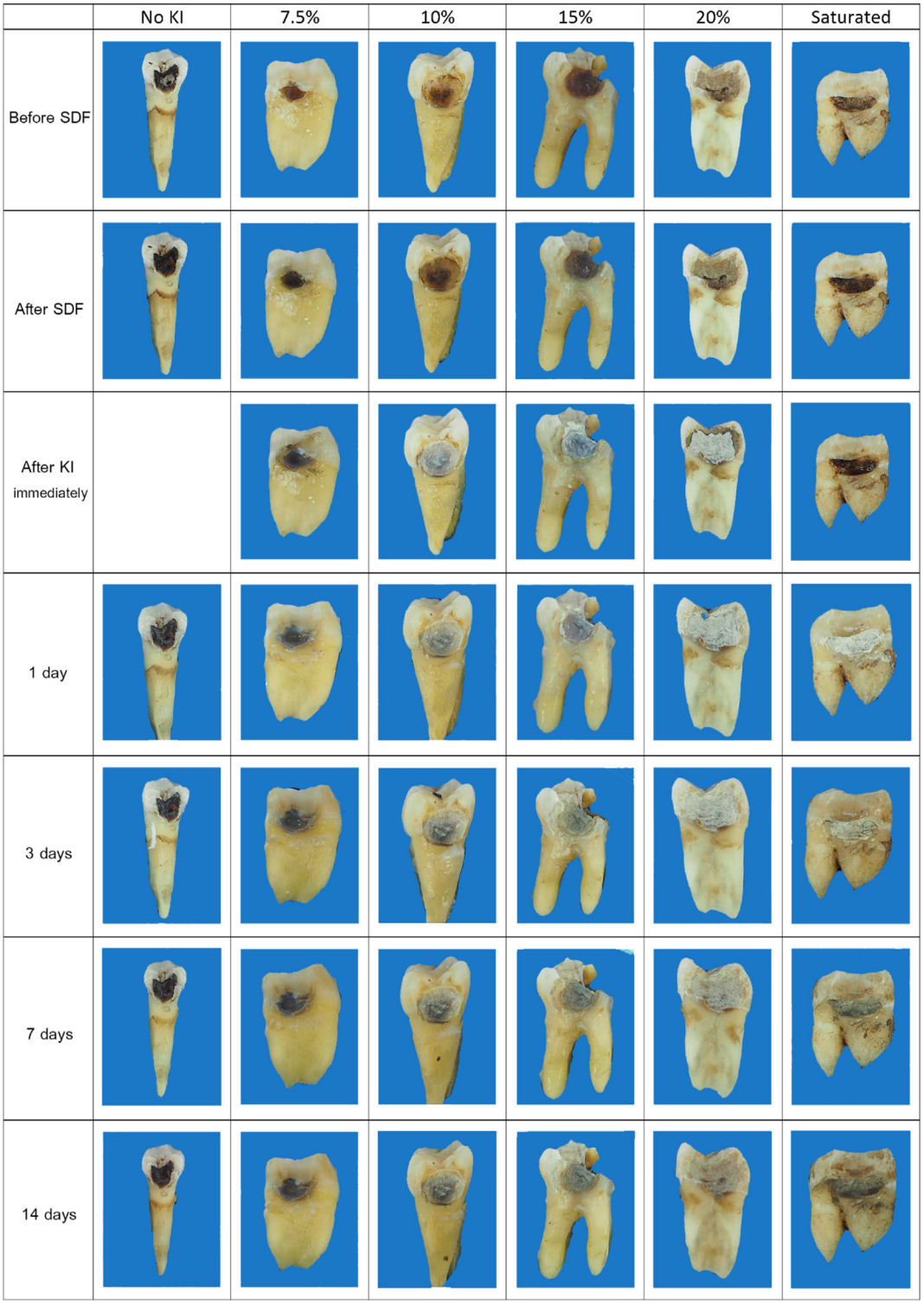

Figure 2 Representative images of the teeth applied with SDF and different concentrations of KI over time.

KI treatment inhibited the development of secondary caries on GIC restorations, however, it was not as effective as SDF treatment alone[16] Zhao et al. revealed that KI influenced the effectiveness of SDF in preventing secondary root caries. This may be because applying KI reduced the amount of silver ions that are important in the antimicrobial effects of SDF in inhibiting caries progression.[9]

There are few adverse effects of SDF and KI. Using of SDF does not cause any acute or serious systemic illness.[11] However, silver allergy is being a contraindication. Some adverse effects such as ulcerative gingivitis can occur if soft tissue is not protected but the symptom will relieve in 48 h.[15] Using KI in cases of overdose can cause side effects, such as a metallic taste in the mouth, swollen glands,

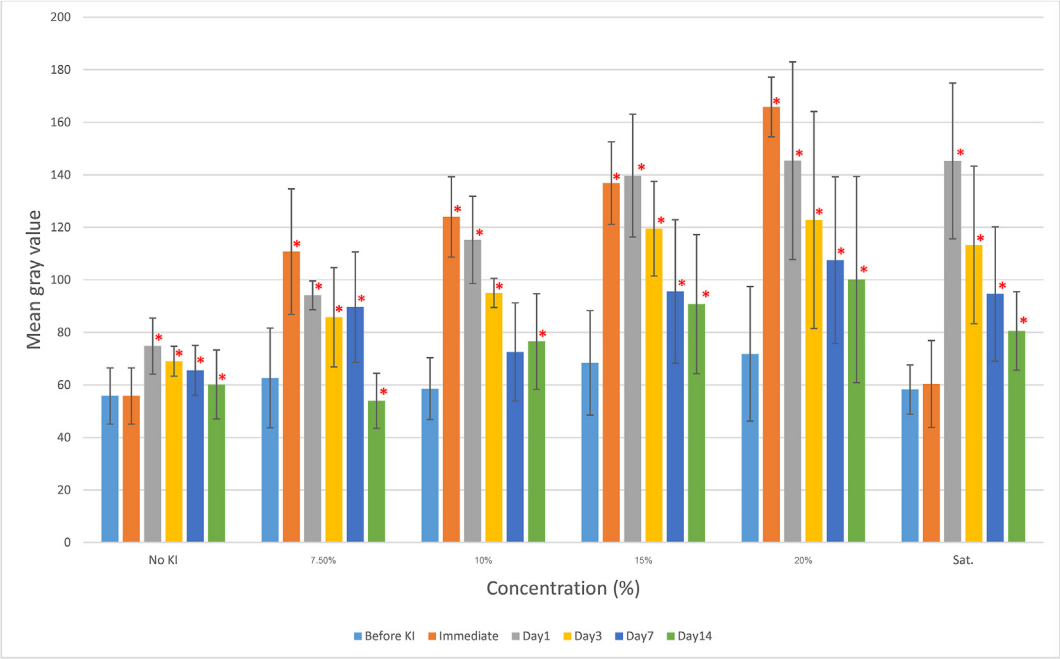

Figure 3 The mean gray value and standard deviation of the different concentrations of KI at different time points. *indicates a significant difference from before KI using Paired t-test.

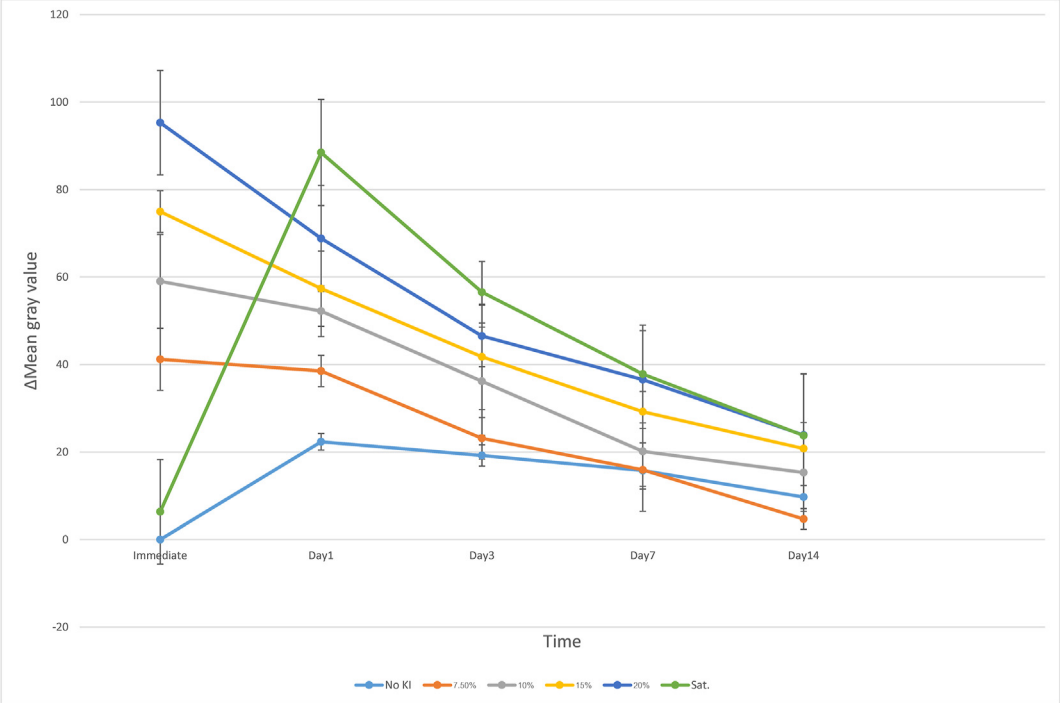

Figure 4 The Δ mean gray value and standard deviation of the different concentrations of KI at different time points.

nausea, diarrhea, vomiting, stomachache and headache. KI also causes desquamation if it contacts soft tissue.[15] To avoid these undesirable effects, the minimum effective dose of KI should be used.

Currently, there has been no report concerning the optimal concentration of KI. It has been shown that 10% KI solution effectively reduced black staining by SDF *in vitro*.[4] Furthermore some studies recommended that SSKI (potassium iodide oral solution, USP), which is a saturated solution of KI containing 1 g KI per milliliter, was effective in reducing the black staining by SDF.[15,20]

In the present study, we found that the 20% KI group had the greatest reduction in black staining immediately after KI application. However, saturated KI was more effective 1 d after KI application compared with the other groups (control, 7.5%, 10%, 15%, and 20% KI). It is unclear why the

Table 1 The Δ mean gray value of the different concentrations of KI at different time points.

Time	Concentration	Mean	S.D.	P-value[a]
Immediate	No KI	0	0	<0.001*
	7.5% KI	41.195	7.078	
	10% KI	57.255	10.708	
	15% KI	77.455	4.782	
	20% KI	97.802	11.949	
	Sat. KI	6.35	14.975	
Day 1	No KI	22.342	1.894	<0.001*
	7.5% KI	38.532	3.546	
	10% KI	52.187	5.793	
	15% KI	57.34	8.604	
	20% KI	68.822	12.129	
	Sat. KI	88.465	23.748	
Day 3	No KI	19.217	2.444	0.001*
	7.5% KI	23.155	4.757	
	10% KI	36.2	12.365	
	15% KI	41.77	12.023	
	20% KI	46.525	7.027	
	Sat. KI	56.516	19.575	
Day 7	No KI	15.767	4.214	0.020*
	7.5% KI	15.917	3.742	
	10% KI	20.152	13.698	
	15% KI	29.235	7.127	
	20% KI	36.57	11.184	
	Sat. KI	37.846	13.296	
Day 14	No KI	9.71	2.623	0.035*
	7.5% KI	4.68	2.335	
	10% KI	15.305	8.843	
	15% KI	20.792	5.937	
	20% KI	23.88	14.041	
	Sat. KI	23.781	4.06	

Sat. KI: Saturated KI.
*Indicates significant relationship ($p < 0.05$).
[a] One-way ANOVA tests.

Table 2 Pairwise comparison of the Δ mean gray value between the different concentrations of KI at different time points.

Pairwise comparison		P-value[a]				
		immediate	Day 1	Day 3	Day 7	Day 14
No KI	7.5% KI	0.020*	0.005*	0.996	1	0.358
	10% KI	0.026*	0.005*	0.314	1	0.995
	15% KI	0.001*	0.015*	0.096	0.3	0.322
	20% KI	0.007*	0.020*	0.030*	0.338	0.887
	Sat.KI	1	0.052	0.002*	0.453	0.029*
7.5% KI	10% KI	0.554	0.063	0.584	1	0.765
	15% KI	0.004*	0.084	0.229	0.312	0.109
	20% KI	0.008*	0.061	0.079	0.353	0.662
	Sat. KI	0.163	0.106	0.006*	0.467	0.008*
10% KI	15% KI	0.313	0.903	0.979	0.995	0.998
	20% KI	0.035*	0.657	0.782	0.839	0.998
	Sat. KI	0.030*	0.319	0.16	0.835	0.917
15% KI	20% KI	0.413	0.657	0.99	0.997	1
	Sat. KI	0.020*	0.319	0.459	0.996	1
20% KI	Sat. KI	0.002*	0.695	0.804	1	1

Sat. KI: Saturated KI.
* Indicates significant relationship ($p < 0.05$).
[a] One-way ANOVA tests followed by Post-hoc tests.

effect of saturated KI has a slower onset. The effect of saturated KI on SDF needs to be investigated in future studies.

The control group, which received only SDF, also presented reduced black staining. This phenomenon may be because the extracted teeth were stored in normal saline solution (0.9% NaCl solution). When the silver ions from SDF combine with the NaCl solution, a white precipitate of silver chloride (AgCl) forms. Therefore, using normal saline solution may have affected the results of our study. Artificial saliva is a common tooth storage media, however, in our pilot study, we observed the formation of a precipitate and bad smell after 3 days of tooth storage. In future studies, other solutions, such as 0.1% thymol solution, and sterilization techniques, such as autoclaving, should be evaluated to prolong the period of tooth storage.[9]

Despite the rich data emerging from this study, limitations exist. This study attempted to control many factors for validity and reliability, including SDF and KI preparation and application by the same person and taking photographs in the same controlled light conditions and positions. The images were selected and the carious areas were isolated by one examiner. However, each measurement may be inexact because the irregular border of the carious lesion made it difficult for the examiner to define the area. Moreover, to confirm these results, a larger sample size and a longer experimental period should be used in future investigations. Furthermore, the present study was performed *in vitro*, which is different from the more complex clinical situation. The results cannot be extrapolated directly to the in vivo condition and caution is advised in the interpretation of the results.

Declaration of Competing Interest

The authors declare no conflicts of interest relevant to this article.

Acknowledgements

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