Effect of silver diamine fluoride application on fluoride concentration in saliva

T A Widianti¹, A Bahar¹*, D A Maharani¹, E C Tumen² and I Yavuz²

¹Department of Dental Public Health and Preventive Dentistry, Faculty of Dentistry, Universitas Indonesia, Jakarta 10430, Indonesia
²Department of Pediatric Dentistry, Faculty of Dentistry, Dicle University, Diyarbakir 21280, Turkey

*Email address: armsbah@hotmail.com

Abstract. Silver diamine fluoride can increase fluoride concentration in saliva, facilitate remineralization, and increase the bioavailability of fluoride in saliva. The purpose of this study was to analyze the difference in fluoride concentration in saliva before and after silver diamine fluoride application on enamel. Stimulated saliva of four subjects was collected, and the concentration of fluoride was measured. The results showed that there were significant differences in the fluoride concentration (p<0.05) before, immediately after, and one hour after silver diamine fluoride application on enamel. It can be concluded that fluoride concentration reached its peak immediately after silver diamine fluoride application on enamel and that it had returned to the baseline one hour after application.

1. Introduction

The most common dental disease in Indonesian society is dental caries. According to national health research results, caries prevalence was 53.2% in 2013. This has increased since 2007, when the prevalence was 43.7%. This high prevalence indicates that awareness of the importance of dental health is still lacking among Indonesians. In addition, this finding is supported by the fact that the Indonesians brush their teeth correctly only 2.3% of the time. Therefore, additional preventive treatment is needed. One material that can be used in preventive treatment is the widely used topical agent silver diamine fluoride (SDF). SDF is a new material that can be used to increase enamel remineralization and decrease dentin hypersensitivity [1-3]. Ag(NH₃)₂F or SDF is a colorless liquid solution containing silver and fluoride ions [4]. One drop of SDF liquid can be used to treat five teeth and has a silver diamine fluoride content of 9.5 mg [5]. SDF is safe to use because doses used for treatment are one four-hundredth of the lethal dose, which is 520 mg/kg administered orally and 380 mg/kg administered subcutaneously [5]. It was reported that the advantages of using SDF include pain and infection control, affordable cost, easy manipulation, minimum requirement of tools and materials, and non-invasive application [5,6]. One disadvantage of SDF is the black spots produced on the teeth. In addition, SDF can stain the clothing and skin of users [4].

Fluoride is an element that can be used in dentistry to prevent caries. Fluoride ions can be topically or systemically used in adults and improve the process of enamel remineralization [2,7]. Studies have shown that topical fluoride application in adults not only stops the process of caries but also makes the enamel surface more resistant to any fluid [7]. In addition, the presence of systemic fluoride ions in
saliva will provide ions that can affect the tooth surface and prevent caries [7]. Enamel remineralization is a process of returning minerals into teeth [8]. This can occur by neutralizing the pH in the oral environment and increasing the concentration of calcium and phosphate ions. The existence of these ions will replenish crystals in demineralized enamel [9]. Demineralization is the process of dissolving dental minerals due to low pH [9]. Demineralization will cause a decrease in tooth surface hardness [10]. This occurs as enamel reacts with acid ions that dissolve hydroxyapatite into calcium, water, and phosphate ions. These acids are derived from acids produced by Streptococcus mutans, exposure to acidic food and beverages, and dental health problems such as caries or tooth erosion [8]. Demineralization can be affected by variety factors, such as the consumption of foods and beverages that contain high levels of acid, sugar consumption, bacteria in plaque, and salivary acidity.

Remineralization may occur due to salivary buffer processes occurring in the oral cavity, which occur because saliva contains phosphate ions (HPO$_{4}^{-}$) and bicarbonate ions (HCO$_{3}^{-}$) [9]. Calcium and phosphate ions in saliva can inhibit the process of dissolving minerals through the ion effect [7]. Saliva is a clear and slightly acidic exocrine solution [11] collected from major and minor salivary glands and gingival fluids, which contain oral bacteria and food waste [12]. Saliva is a very diluted liquid because it contains 99% water and 1% electrolytes, namely sodium, potassium, calcium, magnesium, bicarbonate, and phosphate [11]. Although fluoride may be present in saliva in amounts of 1 μmol/L or 0.01 ppm – 0.08 ppm [11]. The fluoride concentration in saliva in the oral cavity depends on the intake of fluoride from drinking water and topical fluoride treatment [13]. One agent is SDF, in which fluoride content improves the remineralization process. This is supported by previous research stating that products that increase the concentration of fluoride ions can increase the remineralization potential of enamel lesions and increase the bioavailability of fluoride ions in saliva [14]. Therefore, the present study investigated the effect of SDF application on tooth enamel surfaces on the concentration of fluoride ions in saliva.

2. Methods
This was a clinical and experimental laboratory research. The subjects of this study were young adult female subjects aged 20–30 years old with no history of systemic diseases and who were willing received SDF application; the subjects provided informed consent. The subjects were divided into three groups; fluoride concentration in saliva before SDF application, immediately after SDF application, and one hour after SDF application. To stimulate saliva, the subjects were asked to chew parafilms distributed by the researchers and to expectorate stimulated saliva until 20 mL was collected. These samples were then diluted as much as five times using Aquadem. Then, 20 mL of disbursed saliva was mixed with 10 mL of Aquadem and 10 mL of TISAB IV. A 40 mL sample was tested using an ion selective electrode to determine fluoride concentration in the sample in ppm.

Data obtained in this study were numerical data that were statistically analyzed using SPSS. Data normality testing was completed using the Shapiro–Wilk test because the number of data points was less than 50. For normally distributed data, dependent t-tests were performed, while for non-normally distributed data, the non-parametric Wilcoxon test was performed.

3. Results
The Shapiro–Wilk test showed that almost all data had normal distribution (p > 0.05). Data with normal distribution included fluoride concentration in saliva before SDF application and immediately after SDF application. Tables 1 shows the fluoride concentration results.
Table 1. Fluoride concentration in saliva before and after SDF application.

| Time                      | Experiment 1 | Subject 1 | Subject 2 | Subject 3 | Subject 4 | Mean±SD       |
|---------------------------|--------------|-----------|-----------|-----------|-----------|---------------|
| Baseline                  |              | 0.058     | 0.054     | 0.036     | 0.028     | 0.0439±0.142 |
|                           | Experiment 2 | 0.072     | 0.085     | 0.055     | 0.038     |               |
| Immediately after SDF     | Experiment 1 | 8.700     | 9.250     | 5.900     | 4.315     | 7.0412±2.336  |
| application               | Experiment 2 | 3.450     | 9.980     | 4.890     | 0.786     |               |
| 1 hour after SDF          | Experiment 1 | 0.153     | 0.056     | 0.045     | 0.044     | 0.0745±0.053  |
| application               | Experiment 2 | 0.246     | 0.091     | 0.062     | 0.068     |               |

After normality testing was conducted, comparative tests were performed between the groups using the paired sample t-test. From the comparative test results (Table 2), there was a significant difference (0.021) between saliva fluoride concentration before and immediately after SDF application. The comparative test results showed the mean and significance difference (0.018), which was statistically significant for fluoride concentration before and one hour after SDF application and fluoride concentration immediately after and one hour after SDF application.

Table 2. Mean and significant difference of fluoride concentration before and immediately after SDF application.

| Time                      | Mean  | p-value |
|---------------------------|-------|---------|
| Before Application        | 0.044 | 0.021   |
| Immediately After Application | 7.041 |         |
| Before Application        | 0.044 | 0.018   |
| 1 Hour After Application  | 0.075 |         |
| Immediately After Application | 7.041 | 0.018   |
| 1 Hour After Application  | 0.075 |         |

4. Discussion

This study investigated the effect of SDF application on tooth enamel surfaces on fluoride concentration in saliva. The effect was determined by calculating fluoride concentration changes after SDF application. SDF is a colorless liquid solution containing silver ions, fluoride ions, and ammonia [4]; fluoride ions support the remineralization process. In general, SDF is used to stop caries and reduce dentine hypersensitivity [14]. Each 38% SDF contains 24.4–28.8% silver and 5.0–5.9% fluoride, containing 55,800 ppm fluoride ion; 249,000 ppm silver ion; and pH of 10.2; therefore, if SDF is applied to multiple teeth, it is suspected that fluoride concentration in the body increases [15]. The mechanism of action of SDF involves both fluoride and silver ions; these ions are released to minimize mineral loss. Researchers have used stimulated saliva as a sample because the collection of unstimulated saliva is more time consuming and its viscosity made saliva more difficult to examine.

The concentration of fluoride in saliva in the oral cavity depends on fluoride intake from drinking water and topical fluoride treatment. By not consuming foods or beverages containing fluoride over a period of time, the difference between the fluoride concentration in saliva before and after fluoride treatment can be attributed to fluoride applied topically on tooth enamel surfaces as a caries prevention measure [16]. In the present study, the average fluoride concentration of saliva before SDF application
was 0.044 ppm, and it reached the maximum level shortly after SDF application. Fluoride concentration immediately after SDF application averaged 7.041 ppm. One hour after SDF application, saliva fluoride concentration was 0.075 ppm. Based on statistical tests, fluoride concentrations during the three time frames were significantly different, which means that the correlation was strong and positive. This shows that the time difference has a real effect on fluoride concentration in saliva. This agrees with the results of a previous study showing that saliva fluoride concentration reach edited maximum level less than an hour after topical fluoride application [17].

This also agrees with the findings of previous publications who stated that the highest increase in fluoride concentration in saliva occurs shortly after topical fluoride application and that the concentration returns to the initial level one hour after SDF application [17]. There are some studies that have shown a different result, with saliva fluoride concentration increasing shortly after SDF application and then returning to the initial concentration after six hours [18]. There is one subject in our study who had a higher fluoride concentration in saliva than the other three subject sat one hour after SDF application. This may happen because of fluoride bioavailability, which depends on various factors [12] including fluoride intake, fluoride production, and saliva flow rates [14].

This study has implications for enamel remineralization that occurs in the oral cavity. The results obtained agree with those of previous studies, suggesting that products that increase the concentration of fluoride also increase remineralization potential and increase fluoride bioavailability in saliva [14]. SDF application will lead to CaF$_2$ layer formation on the enamel surface, and this CaF$_2$ layer will later release bioavailable fluoride ions [14]. In the present study, SDF was applied to healthy enamel, which is free of caries and has no dentin exposed. This may be a limitation of this study because SDF is recommended for at-risk caries treatment, treatment in which subjects cannot medically or psychologically tolerate standard treatment, carious lesions that are difficult to treat, and subjects with dentin hypersensitivity. The mechanism of action of SDF is exerted through silver particles and fluoride ions contained in its constituent; SDF inhibits the formation of cariogenic biofilms, where high silver-containing deposits and fluoride ions enter the tubular hole that results from SDF and helps minimize mineral loss [8]. In addition, silver and fluoride ions (25 microns) that enter into tooth enamel and the ions (50–200 microns) that enter into dentine can affect saliva concentration after SDF application [5]. Another limitation may be the small number of subjects due to time constraints. The present study examined the capacity of stimulated saliva buffer and did not use unstimulated saliva. Although unstimulated saliva represents the state of saliva daily, unstimulated saliva collection takes more time and its viscosity makes it more difficult to examine.

5. Conclusion
SDF application can increase fluoride concentration in saliva, which in turn can inhibit the tooth demineralization process. SDF is best administered to people who have caries or have dentin hypersensitivity. However, the application of SDF in healthy subjects is sufficient to demonstrate the purpose of this study, which was to measure increases in fluoride concentration in saliva.

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