



Comparison of the Fluoride Release of Silver Diamine Fluoride, Fluoride Varnish, Acidulated Phosphate Fluoride Gel on Extracted Teeth over Various Time Intervals in Artificial Saliva

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Authors' contributions

This work was carried out in collaboration among all authors. Author TT designed the study, performed the statistical analysis and wrote the protocol. Authors PKL and MK managed the analyses of the study and wrote the final draft of the manuscript. Author BS managed the literature searches and editing. Authors PD and RS did the proofreading. All authors read and approved the final manuscript.

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ABSTRACT

Silver Diamine Fluoride (SDF) has been documented to effectively arrest dental caries and reduce dental hypersensitivity. SDF promotes remineralization and harden the carious lesion. SDF increases fluoride concentration in saliva and increase the bioavailability of fluoride in saliva. After SDF application, fluoride ion promotes remineralization and silver ion is available for antimicrobial action.

Aim: The study aims to determine and compare the amount of fluoride released from various fluoride releasing materials in artificial saliva after 24 hours, 7th day and 14th day of the study.

Materials and Methods: 96 premolars free of any caries, fractures, or any other defects were

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sterilized in 10% formalin for 2 weeks. Then they were rinsed in tap water to remove any fixative from its surface and then stored in deionised distilled water for a period of 30 days prior to testing. Tooth samples were divided into four groups- Group 1: 38% SDF, Group 2: 1.23% APF gel, Group 3: Fluoride varnish and Group 4: Control. All the teeth specimens were blot dried and subjected to their respective material. Fluoride release was analysed using a Fluoride ion-selective electrode after 24 hours, 7days and 14 days of suspension in artificial saliva.

Results: Mann-Whitney U Test for inter-group comparison was used for statistical evaluation. 24 Hours fluoride release: The maximum amount of fluoride was released from Fluoride Varnish followed by SDF then APF Gel and least by artificial saliva alone (control) ($p < 0.001$). 7th Day fluoride release: The maximum amount of fluoride was released from SDF followed by Fluoride Varnish then APF Gel and least by artificial saliva alone (control) ($p < 0.001$). 14th Day fluoride release: The maximum amount of fluoride was released from Fluoride Varnish followed by SDF then APF Gel and least by artificial saliva alone (control) ($p < 0.001$).

Keywords: Fluoride release; silver diamine fluoride; artificial saliva.

1. INTRODUCTION

Dental caries continues to plague the majority of the world's population with giant unmet treatment needs. It places a monetary, health, and time burden most frequently on those least able to bear it [1]. In the developing countries, caries prevalence is increasing as dietary habits of industrialized nations are adopted, the basic needs of the population are not met and the problem of dental diseases receives low priority [2,3].

Attempts at controlling caries by manpower approaches requires more training and better dentists which results in more fillings but does not reduce the prevalence of the disease [4,5] Clearly the answer to this major public health problem is prevention. Fluoride is the pivot of preventive dentistry and continues to be the cornerstone of modern caries prevention philosophy [6]. CaF_2 acts as a fluoride reservoir on the tooth surface and it is formed only during treatment with high concentration fluoride solutions [4,7-13]. Topical fluorides work (i.e., directly on erupted teeth) by promoting remineralization and through antibacterial action to a lesser degree. In 1941, when the era of topical fluorides began, the first clinical study by Bibby with 0.1% NaF solution was carried out [6].

1.23% APF Gel contains 12,300 ppm in the form of sodium fluoride. It is usually applied by professionals in a tray, with dental floss, or with cotton wool. It requires less chair-time than solutions. Semi-annual application of 1.23% APF for 4 minutes helps reduce caries by 28% [14].

Fluoride varnishes act as a slow-releasing reservoir of fluoride because it adheres to the

tooth surfaces for longer periods and thus prevents the immediate loss of fluoride after application. The ADA guideline 2013 recommends the application of fluoride varnish to both primary and permanent teeth in those subjects at elevated caries risk at least every 6 months [15]. Silver diamine fluoride (SDF) is one of the newest fluoride products. The combination of silver and fluoride has a hypothesized ability to cease the caries process and simultaneously prevent new caries where fluoride ions act mainly on the tooth structure while the silver ions act mainly on cariogenic bacteria.

SDF was cleared by the Food and Drug Administration in the United States in 2014 [16]. SDF are available in a range of SDF concentrations. Two prospective randomized control trials [17,18] have compared the effect of 38% and 12% SDF in their ability to arrest caries.

Both studies found that 38% SDF was more effective in arresting caries than 12% SDF. The American Academy of Pediatric Dentistry (AAPD) published guidelines for the use of SDF in 2017, which supports the use of 38% SDF for the arrest of cavitated caries lesions in primary teeth as part of a comprehensive caries management programme [19]. 38% SDF solution contains 44,800 ppm of fluoride and one drop of SDF liquid can be used to treat five teeth surfaces [20].

The application times from 10 sec to 3 min have been used in most of the clinical studies. Two randomized control trials [18,21] have found that a six-monthly SDF application is more effective at arresting caries than yearly applications. Products showing greater fluoride release overtime are effective in preventing and

controlling dental caries. Thus, the aim of this study was to evaluate the concentration of fluoride in artificial saliva, after the topical application of professional use fluoridated products to assess their efficacy.

2. MATERIALS AND METHODS

The study was conducted in the Department of Pediatric and Preventive Dentistry, Guru Nanak Dental College and Hospital, Kolkata. It was an in vitro laboratory experimental research protocol.

This study consisted of 96 premolars free of any caries, fractures, or any other defects, which had been extracted due to orthodontic reasons. Tooth samples were sterilized in 10% formalin for 2 weeks.

10% Neutral buffered formalin (NBF) is the most commonly used fixative for light microscopy. 10% NBF requires a relatively short period of fixation, but can also be used for the long-term storage of tissue.

Over-fixation of tissues can produce false-negative results due to excessive cross-links, but the negative effects of over-fixation can often be reversed with an appropriate antigen retrieval procedure. The effects of over-fixation are somewhat dependent on the cellular location of the target antigen; over-fixation of nuclear antigens may not be reversible while cytoplasmic antigens may not be affected by over-fixation or can be recovered after antigen retrieval.

Under-fixation of tissues may result in cross-links forming only on the exterior of a sample and the center of the sample remaining unfixed. This can result in an inconsistent gradient of staining that is difficult to interpret. In addition, under-fixed tissues are more susceptible to damage or distortion caused by antigen retrieval methods.

The tooth samples were rinsed in tap water to remove any fixative from its surface and then stored in deionised distilled water for a period of 30 days prior to testing. Tooth samples were divided into four groups according to the respective materials used in the study.

Each tooth is coated with acid-resistant nail varnish (Revlon, Miami, FL) in two layers, leaving one square window of 5x5 mm on an intact labial surface. All the teeth specimens were blot dried

and subjected to their respective material. The following materials were used:

- 38% Silver Diamine Fluoride - e-SDF, Kids-e-Dental LLP
- Fluoride varnish - Bifluorid 10, Voco
- 1.23% Acidulated phosphate fluoride gel - Fluocall Gel, Septodont

F1- 38% SDF was applied with a micro-brush and allowed it to soak in for 1-3 minutes and excess was removed with a cotton pellet or roll [20].

F2- 1.23% APF Gel was applied for 4 minutes with a micro brush.

F3- Bifluorid 10 varnish was thinly coated and allowed to be absorbed for 10-20secs then air dried.

F4- control group, were not subjected to any fluoride treatment.

Artificial saliva was prepared according to the formula:

NaCl 0.400 g, KCl 0.400 g, CaCl₂·H₂O 0.795 g, NaH₂PO₄ 0.69 g, Na₂S_x9H₂O 0.005 g, Urea 1 g, distilled water 1000 ml. The pH was adjusted to 7 with the help of KOH solution and the volume adjusted to 500 ml.

The teeth were then placed in individual plastic containers at room temperature, containing artificial saliva at a pH of 7. Fluoride release was analyzed using a fluoride ion-sensitive electrode after 24 hours, 7 days and 14 days of suspension in artificial saliva. Data on fluoride ion concentrations was analyzed statistically using the Statistical Package for the Social Sciences.

Continuous variables were compared using unpaired t-test/One Way ANOVA if the data follows normal distribution or Median and Interquartile Range and compared using Mann-Whitney U test if the data does not follow the normal distribution. Over time comparison was done using a paired t-test if the data follows normal distribution or Wilcoxon Sign Rank Test if the data does not follow the normal distribution. An alpha level of 5% has been taken, i.e. if any p-value is less than 0.05 it will be considered as significant.

3. RESULTS

Mann-Whitney U test was performed for inter-group comparison. 24 Hours Fluoride Release: SDF was 1.52± 0.01 ppm, APF Gel was 1.25± 0.01 ppm, Fluoride varnish was 7.20± 0.04 ppm

and Artificial saliva was 0.16± 0.00 ppm. The difference of mean 24 hours fluoride, fluoride in four groups was statistically significant (p<0.001) (Table 1).

The maximum amount of fluoride was released from Fluoride Varnish followed by SDF then APF Gel and least by artificial saliva alone (control).

After 7 days, fluoride release by SDF was 5.67± 0.07ppm, APF Gel was 1.54± 0.01 ppm, Fluoride varnish was 3.84± 0.07 ppm and Artificial saliva was 0.19± 0.01 ppm. The difference of mean 7th day fluoride, fluoride in four groups was statistically significant (p<0.001) (Table 2). The maximum amount of fluoride was released from SDF followed by Fluoride Varnish then APF Gel and least by artificial saliva alone (control).

After 14 days, fluoride release by SDF was 1.87± 0.01 ppm, APF Gel was 0.63± 0.02ppm, Fluoride varnish was 8.46± 0.06 ppm and Artificial saliva was 0.29± 0.01 ppm. The difference of mean 14th day fluoride, fluoride in four groups was statistically significant (p<0.001) (Table 3). The maximum amount of fluoride was released from Fluoride varnish followed by SDF then APF Gel and least by artificial saliva alone (control).

Wilcoxon Sign Rank Test is used for Comparison of the amount of fluoride release (ppm) in various groups at different time intervals. Mean value of fluoride release by SDF at 24hours was 1.52± 0.01 ppm, mean value of fluoride release by SDF after 7days was 5.67± 0.07 ppm, mean value of fluoride release by SDF after 14days was 1.87± 0.01 ppm.

Table 1. Inter-group comparison of the fluoride release (ppm) between various groups at 24th hour time interval

Group		24 hours fluoride
SDF	Mean	1.52
	Median	1.52
	Std. Deviation	0.01
APF GEL	Mean	1.25
	Median	1.25
	Std. Deviation	0.01
Fluoride varnish	Mean	7.20
	Median	7.22
	Std. Deviation	0.04
Artificial saliva(baseline)	Mean	0.16
	Median	0.16
	Std. Deviation	0.00
p Value	Overall	<0.001

Table 2. Inter-group comparison of the fluoride release (ppm) between various groups at 7 days time interval

Group		7 th day fluoride
SDF	Mean	5.67
	Median	5.70
	Std. Deviation	0.07
APF GEL	Mean	1.54
	Median	1.54
	Std. Deviation	0.01
Fluoride varnish	Mean	3.84
	Median	3.88
	Std. Deviation	0.07
Artificial saliva(baseline)	Mean	0.19
	Median	0.19
	Std. Deviation	0.01
p Value	Overall	<0.001

The difference of mean in the three groups was statistically significant (Table 4). Mean value of fluoride release by APF Gel at 24hours was 1.25± 0.01 ppm, mean value of fluoride release by APF Gel after 7days was 1.54± 0.01 ppm, mean value of fluoride release by APF Gel after 14days was 0.63± 0.02ppm. The difference of mean in the three groups was statistically significant (Table 5).

Mean value of fluoride release by Fluoride Varnish at 24 hours was 7.20± 0.04 ppm, mean value of fluoride release by Fluoride varnish after

7days was 3.84± 0.07 ppm, and mean value of fluoride release by Fluoride varnish after 14days was 8.46± 0.06ppm. The difference of mean in the three groups was statistically significant (Table 6).

Mean value of fluoride release by Artificial saliva at 24hours was 0.16± 0.00 ppm, mean value of fluoride release by Artificial saliva after 7days was 0.19± 0.01 ppm, mean value of fluoride release by Artificial saliva after 14days was 0.29± 0.01 ppm. The difference of mean in the three groups was statistically significant (Table 7).

Table 3. Inter-group comparison of the fluoride release (ppm) between various groups at 14 days time interval

Group		14 th day fluoride
SDF	Mean	1.87
	Median	1.87
	Std. Deviation	0.01
APF GEL	Mean	0.63
	Median	0.63
	Std. Deviation	0.02
Fluoride varnish	Mean	8.46
	Median	8.44
	Std. Deviation	0.06
Artificial saliva (baseline)	Mean	0.29
	Median	0.29
	Std. Deviation	0.01
p Value	Overall	<0.001

Table 4. Comparison of the amount of fluoride release (ppm) in group-I (SDF) at different time intervals

Group		Amount of fluoride release			p value		
		24 hours fluoride	7 th day fluoride	14 th day fluoride	24 hr vs. 7 th Day	24 hr vs. 14 th Day	7 th Day vs. 14 th Day
SDF	Mean	1.52	5.67	1.87	0.012	0.009	0.012
	Median	1.52	5.70	1.87			
	Std. Deviation	0.01	0.07	0.01			

Table 5. Comparison of the amount of fluoride release (ppm) in group-II (APF gel) at different time intervals

Group		Amount of fluoride release			p value		
		24 hours fluoride	7 th day fluoride	14 th day fluoride	24 hr vs. 7 th Day	24 hr vs. 14 th Day	7 th Day vs. 14 th Day
APF	Mean	1.25	1.54	0.63	0.011	0.012	0.011
GEL	Median	1.25	1.54	0.63			
	Std. Deviation	0.01	0.01	0.02			

Table 6. Comparison of the amount of fluoride release (ppm) in group-III (fluoride varnish) at different time intervals

Group		Amount of fluoride release			p value		
		24 hours fluoride	7 th day fluoride	14 th day Fluoride	24 hr vs. 7 th Day	24 hr vs. 14 th Day	7th Day vs. 14 th Day
Fluoride varnish	Mean	7.20	3.84	8.46	0.012	0.012	0.012
	Median	7.22	3.88	8.44			
	Std. Deviation	0.04	0.07	0.06			

Table 7. Comparison of the amount of fluoride release (ppm) in group-IV artificial saliva (control/baseline) at different time intervals

Group		Amount of fluoride release			p value		
		24 hours fluoride	7 th day fluoride	14 th day fluoride	24 hr vs. 7 th Day	24 hr vs. 14 th Day	7th Day vs. 14 th Day
Artificial saliva (baseline)	Mean	0.16	0.19	0.29	0.012	0.012	0.011
	Median	0.16	0.19	0.29			
	Std. Deviation	0.00	0.01	0.01			

4. DISCUSSION

The purpose of this dissertation was to study the amount and pattern of fluoride ion released over various time intervals after topical fluoride application. The fluoride release was evaluated at neutral pH, as it is already known that the release of fluoride is greater in acidic pH, [22,23] but it is not clear whether fluoride is released in neutral pH as well. Hence the importance of fluoride release at neutral pH remains to be investigated, especially at different time intervals [24]. This in vitro study gives an indication of the cumulative amount of fluoride release possible at neutral pH at different time intervals which are not possible to record in vivo, since fluoride is lost during eating and swallowing activities and the exposure from other sources of fluoride cannot be controlled. There is also a possible reuptake of released fluoride into the tooth during the acid challenge.

Comparison of the amount of fluoride release (ppm) was also done at different intervals by each group. It revealed that, Mean value of fluoride release by SDF at 24hours was 1.52 ± 0.01 ppm, mean value of fluoride release by SDF after 7days was 5.67 ± 0.07 ppm, mean value of fluoride release by SDF after 14days was 1.87 ± 0.01 ppm. The difference of mean in the three groups (viz. 24 hours, 7 days, 14 days) was statistically significant.

This result was accordance to study done by DL Sari et al in 2017 [25] where there was a decrease in the concentration of fluoride ions in

urine from the baseline to 30 minutes after application, and an increase from baseline to two and three hours after the application of SDF. Although in the current study time intervals were different.

Mean value of fluoride release by APF Gel at 24hours was 1.25 ± 0.01 ppm, mean value of fluoride release by APF Gel after 7days was 1.54 ± 0.01 ppm, mean value of fluoride release by APF Gel after 14days was 0.63 ± 0.02 ppm. The difference of mean in the three groups (viz. 24 hours, 7 days, 14 days) was statistically significant.

Mean value of fluoride release by Fluoride Varnish at 24 hours was 7.20 ± 0.04 ppm, mean value of fluoride release by Fluoride varnish after 7days was 3.84 ± 0.07 ppm, and mean value of fluoride release by Fluoride varnish after 14days was 8.46 ± 0.06 ppm. The difference of mean in the three groups was statistically significant. Twetman S, Larsson K.S, Modeer T in 1999 [26] concluded there was a significant elevation of fluoride in saliva 1 hr after application of Bifluorid 12 and Duraphat, which lasted 6 hrs. There was a substantial increase of salivary fluoride within the first 2 hrs after the varnish application, which decreased with the time; however, after 168 hrs it was still higher compared to the baseline. This study was in accordance with the current study.

Mean value of fluoride release by Artificial saliva at 24 hours was 0.16 ± 0.00 ppm, mean value of fluoride release by Artificial saliva after 7days was 0.19 ± 0.01 ppm, mean value of fluoride

release by Artificial saliva after 14 days was 0.29 ± 0.01 ppm. The difference of mean in the three groups (viz. 24 hours, 7 days, 14 days) was statistically significant.

In this study, an inter-group comparison of fluoride release between various groups in artificial saliva was done after 24 hours, on 7th day and 14th day time intervals. It revealed that after 24 HOURS, the maximum amount of fluoride was released from Fluoride varnish followed by SDF then APF Gel and least by artificial saliva (control group). This result was in accordance to study by Delbem AC, Bergamaschi M, Sasaki KT, Cunha RF in 2006 [27] where the fluoride released by varnish showed greater interaction with sound enamel and provided less mineral loss when compared with silver diamine solution. Prasad, Thottathil AA, Neethu KS in 2019 [28] concluded that Fluor Protector varnish had an increased sustained release of fluoride ions when compared to APF gel. Retief, Harris BE, Bradley EL in 1985 [29] conducted where enamel acquired significantly more Fluoride from Fluor Protector and Duraphat than from APF. This was accordance to the current study where Fluoride varnish released more fluoride than APF Gel.

After 7 days, the maximum amount of fluoride was released from SDF followed by Fluoride Varnish then APF Gel and least by artificial saliva (control group). And after 14 days, the maximum amount of fluoride was released from Fluoride varnish followed by SDF then APF Gel and least by artificial saliva (control group).

This result varies from the in vivo study done by SG Shah et al. in 2014, [30] where significant fluoride content of enamel was found in SDF when compared to Fluoride varnish and APF gel. This research also varied from a study done by Soekanto SA, Dayanara P, Daviq H, Sarwono AT, Sahlan M in 2019, [31] where SDF released more fluoride ions than PPF from dentin within 60 days. This research varied from a study done by Widiyanti TA, Bahar A, Maharani DA, Tumen E.C, Yavuz I. 2018, [32] where 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. Bezerra et al 2019 [33] concluded that greater fluoride release was observed for Fluorine Acidulate Gel 1.23% (AG) and Fluorine Neutral Gel 2% (NG) groups after 1hr application compared to Cariostatic 12% (CA), Fluoridated Varnish 5% (FV).

Factors responsible for fluoride uptake and retentions are mainly concentration of fluoride, pH of the solution and barrier coating over the solution [24]. As SDF has the highest concentration of fluoride (44,800 ppm), so it can be assumed that fluoride on enamel is directly proportional to the amount of fluoride available. On the other hand, APF Gel with acidic pH has increased penetration power, and Fluoride Varnish forms a barrier coating which increased the contact period of fluoride with the tooth surface.

Fluoride varnish performed better than SDF may be attributed to the formation and dissolution of silver phosphate and silver proteinate and re-precipitation of silver chloride, silver oxide and metallic silver crystals during pH-cycling [34]. Silver may have interfered with the formation of fluoridated deposits and formed silver phosphate, which may compete with fluoride. In contrast, the main product formed after fluoride varnish application is the calcium fluoride, which may act as a fluoride reservoir. During the acid challenge, the calcium fluoride dissolves, and the Fluoride is released effectively to promote remineralization. The silver fluoride products are more often used in dentin caries, which present a greater amount of protein substrate, carbonates, and phosphates for the reaction. On the other hand, the enamel is short of these substrates in comparison with dentin, which may have decreased the silver diamine fluoride reactivity. This may contribute to the differences observed in the results of the present study [35].

5. CONCLUSION

Professionally applied fluorides have become clinical manoeuvres frequently offered by dental personnel in private practice, virtually on a routine basis. Professionally applied topical fluorides helps in the remineralization of the demineralized enamel along with making the adjacent tooth structure resistant to acidic attack. They are popular because of the ease of use by the operator with a relatively good financial return, acceptance by the patients, and effectiveness in caries reduction. Since the majority of the young population still suffer from high prevalence and incidence of dental caries, emphasis should now be placed on targeting these high-risk individuals who can receive maximum benefit from materials releasing fluoride and other caries controlling factors thereby arresting caries at an acceptable cost without significant harm.

The present study provides a prospect for its application in the clinical scenario since it guides the choice of fluoridated products by dental professionals following the patients' needs. Besides that, this study may guide the unification of resources and practices for the improvement of oral health.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The Study Protocol was approved by Ethical Committee of Guru Nanak Institute of Dental Sciences and Research, Kolkata, India.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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