The Effect of Various Fluoride Products on Dentine Lesions during pH-Cycling

Marwa M. Alhothali\textsuperscript{a,b}  Rob A.M. Exterkate\textsuperscript{c}  Maxim D. Lagerweij\textsuperscript{a}  A.J.P. van Strijp\textsuperscript{a,c}  Mark J. Buijs\textsuperscript{c}  Cor van Loveren\textsuperscript{a,c}

\textsuperscript{a}Department of Cariology at the Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; \textsuperscript{b}Department of Dentistry, Comprehensive Specialized Clinics and Hospital of Security Forces, Mecca City, Saudi Arabia; \textsuperscript{c}Department of Preventive Dentistry at the Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Keywords
Dentine · Demineralization · Remineralization · pH-cycling · Silver diammine · Titanium · Varnish · Fluoride

Abstract
This study compared the effect of topically applied fluoride products on dentine lesions in an in vitro experiment. Demineralized bovine dentine specimens were treated once with either SDF solution (35,400 ppm F), NaF varnish (22,600 ppm F), TiF\textsubscript{4} solution (9,200 ppm F), SnF\textsubscript{2} gel (1,000 ppm F), no treatment (control), or preserved as baseline lesions. After the application and subsequent removal of the fluoride products, the specimens were subjected to pH-cycling. Calcium loss and uptake in the de- and remineralization buffers were assessed daily. Fluoride release into the buffers was analyzed on days 1, 2, 3, 5, 8, and 13. After the pH-cycling period, mineral distribution throughout the lesion depth was analyzed using transversal microradiography (TMR). X-ray energy-dispersive spectroscopy (EDS) examined the deposition of silver, titanium, and tin after application of SDF, TiF\textsubscript{4}, and SnF\textsubscript{2}, respectively. Overall, calcium loss and uptake analysis in the de- and remineralization buffers revealed that the SDF product was the most effective in inhibiting lesion progression, followed by the TiF\textsubscript{4}, NaF, and SnF\textsubscript{2} products. Fluoride analysis disclosed a steep reduction of the amount of fluoride released into de- and remineralization buffers with time. The fluoride effects on de- and remineralization continued beyond the days that fluoride was released into the buffers. TMR analysis showed significant remineralization in the outer zone of the dentine lesions for all fluoride products, with SDF giving hypermineralization in this zone. In the inner zone, lesions developed in all fluoride groups, with the smallest in the SDF group. EDS showed silver and titanium deposition in depth up to 85 μm and 8 μm, respectively, while no tin deposition was observed. The silver in the dentine lesions did not contribute significantly to the density of the TMR profiles in the SDF group. In conclusion, all topical fluoride products protected the dentine lesions against lesion progression, but at different degrees. SDF showed a superior effect in protection against further demineralization and enhancement of remineralization. This was probably attributed to its fluoride concentration that was the highest among the fluoride products.

Introduction
In traditional restorative therapy in dentistry, clinicians treated the symptoms rather than the causes of the disease [Gao et al., 2016]. This approach does not neces-
The Effect of Various Fluoride Products on Dentine Lesions

SDF is more effective [Suzuki et al., 1974]. Crowns and roots were separated using a water-cooled diamond blade (Buehler Isomet, Lake Bluff, IL, USA). Standardized cylindrical coronal specimens of 6 mm in diameter were obtained by using a water-cooled hollow diamond burr (Diamant Boart, Vi-"naren, The Netherlands). Dentine specimens of approximately 3-mm thickness were cut just underneath the dentine-enamel junction using a diamond-coated wire saw of 220-μm thickness (Well type 3242; Ebner, Mannheim, Germany). Subsequently, the specimens were embedded in methylmethacrylate (Vertex; Denti-"mex, Zeist, The Netherlands) and after that ground flat with silicon carbide abrasive papers (grit 240–600) under H₂O and then stored in distilled water at 4°C until use.

Lesion Formation
Sixty-four specimens were glued by nail varnish in groups of 8–10 specimens to the bottom of a glass tray (length × width × height; 9.5 × 7.5 × 6 cm). Then, 150 mL of 8% methylcellulose gel was poured over the specimens. After 1 day, the methylcellulose gel was covered with a filter paper sheet, and subsequently 150 mL of 0.1 mol/L lactic acid at pH 5.0 was poured over the filter paper sheet and the gel [ten Cate et al., 1995]. The trays were stored for 17 days at 37°C to demineralize the specimens.

pH-Cycling Conditions
After completing 17 days of demineralization, specimens were subjected to 3 days of pH-cycling to determine the baseline values of calcium loss and uptake. At the end of this cycling period, the specimens were sorted based on the net calcium loss values (on average 1.70 ± 0.14 μmol/cm²), while the outliers were discarded. Subsequently, forty of forty-eight matched specimens were randomly treated once with either SDF solution, NaF varnish, TiF₄ solution, or SnF₂ gel or received no treatment (control) and were subsequently placed in a pH-cycling robot for 15 days [ten Cate et al., 1995]. The remaining 8 specimens were not cycled and kept in distilled water at 4°C to be used later for determining baseline lesions using TMR analysis.

The pH-cycling conditions were standardized at a daily schedule of six cycles; each cycle included 0.5-h demineralization and 2.5-h remineralization. The night period comprised 6 h of remineralization. In between the cycles, specimens were placed in 3 mL of rinsing buffer for 10 s. The experiment was conducted in 3 consecutive weeks (21 days), each including pH-cycling for 5 weekdays followed by a no-cycling weekend.

The remineralization buffer was composed of 1.5 mmol/L CaCl₂, 0.9 mmol/L KH₂PO₄, 130 mmol/L KCl, and 20 mmol/L Hepes, adjusted to pH 7.1. The demineralization buffer was composed of 1.5 mmol/L CaCl₂, 0.9 mmol/L KH₂PO₄, and 50 mmol/L acetic acid, adjusted to pH 4.8. The rinsing buffer was composed of 1.5 mmol/L CaCl₂ and 0.9 mmol/L KH₂PO₄ [ten Cate et al., 2006]. Each specimen was cycled in 3 mL aliquots of both buffers. The buffers were refreshed daily, except for the weekends.

Fluoride Products
Details of the fluoride products and application methods are presented in Table 1. SDF solution (35,400 ppm F), NaF varnish (22,600 ppm F), and SnF₂ gel (1,000 ppm F) were commercially available products. SnF₂ gel was not marketed to prevent dentine caries, but it was introduced in the current study based on our expectations that it could be beneficial in dentine caries management. TiF₄ solution (1.5%; 9,200 ppm F; 0.48 M F, 0.12 M Ti, pH 1.2) was prepared in our lab by mixing 1.5 g of titanium tetrafluoride powder (Sigma-Aldrich Chemie GmbH, Schnellendorf, Germa-
ny) with 100 mL MilliQ water. The current concentration of TiF$_4$ has been chosen based on the commonly used concentrations of TiF$_4$ solutions for caries prevention that ranged from 1% to 4% [Wiegand et al., 2010].

**Calcium Analysis**

Calcium loss and uptake were determined in the de- and remineralization buffers. Daily samples of 200 μL were taken and diluted into 3 mL of 36 mmol/L La(NO$_3$)$_3$ solution and analyzed using atomic absorption spectroscopy (PerkinElmer Analyst 100; PerkinElmer, Waltham, MA, USA). The daily calcium data were cumulated over the experimental period to give cumulative calcium loss, cumulative calcium uptake, and net calcium change (the difference between calcium loss and calcium uptake).

**Fluoride Analysis**

Fluoride analysis was performed using gas chromatography (GC-2010; Shimadzu, Kyoto, Japan) [Alhothali et al., 2021]. Samples were taken from the de- and remineralization buffers collected on days 1, 2, 3, 5, 8, and 13.

**Transversal Microradiography**

After the pH-cycling period, three sections of 200-μm thickness were cut from the middle of each specimen using a diamond-coated wire saw. Two of these sections were subjected to TMR analysis [Lagerweij et al., 1994; van Strijp et al., 1995], and the remaining one was analyzed using X-ray energy-dispersive spectroscopy (EDS; XFlash® 6-30; Bruker, Karlsruhe, Germany). For TMR, four scans were analyzed per section, and then the 8 scans of the two sections of each lesion were averaged. The data obtained from the TMR analysis were mineral distribution profiles, the integrated mineral loss (IML and ΔIML), and the mineral content of the surface layer.

**Elemental Analysis (EDS) of Dentine Lesion Treated with SDF, TiF$_4$, and SnF$_2$**

The sections were placed in an oven of 37°C and dehydrated for 18 h. No gold coating was applied to the sections. The sections were then placed on a multi-pin specimens-mount using double-sided bonding carbon tape. Elemental composition from 0- to 400-μm depth was analyzed at 3-nm resolution, ×500 magnification, at 30 kV. Secondary electron detector and the EDS mapping mode were used to detect the silver, titanium, and tin in weight percentage.

In a control experiment, EDS analysis was done on 3 additional specimens immediately after the SDF application and not subjected to pH-cycling. Half of each of these specimens surface was covered with translucent nail varnish to preserve the baseline. The other half was treated with SDF (following the same treatment protocol as described before). Next, one section was cut from the middle of each specimen, and TMR images were made. Mineral distribution profiles were calculated from three sections of untreated and treated surfaces. From one of these sections, silver distribution was also analyzed using EDS.

**Sample Size Calculation**

Eight specimens per group were used in the current study. This number was based on previous pH-cycling experiments [ten Cate et al., 1995; ten Cate et al., 2006]. Power calculations revealed that the effect size for ANOVA and MANOVA would be 1.79 and 0.34, respectively, when assuming a power of 0.8, α 0.05, for 5 experimental groups (G*power 3.1.9.7; [Faul et al., 2007]).

**Statistical Analysis**

Data were analyzed by using IBM SPSS version 25.0. Daily calcium loss, uptake, and net calcium change were analyzed using multivariate analysis of variance (MANOVA). The cumulative calcium data at the end of the experiment, the differences in ΔIML after the pH-cycling period, and the mineral content of the surface layer were also analyzed using one-way ANOVA. MANOVA was also used to test the fluoride release in de- and remineralization buffers. Post hoc Tukey’s HSD test was used with each (M)ANOVA test to examine the differences between the experimental groups. The level of significance was set at 0.05 for all analyses.
**Fig. 1.** Fluoride released into demineralization buffers (a) and remineralization buffers (b) at selected days during pH-cycling ($n = 8$ specimens/group). Y-axis represents the fluoride content in parts per million, and X-axis represents cycling days. Different characters per day represent statistically significant differences at $p < 0.05$ (post hoc Tukey test).
Results

Calcium Analysis

Daily and cumulated calcium loss, calcium uptake, and net calcium change for 15 days of pH-cycling are shown in online supplementary Figures 1 and 2 (see www.karger.com/doi/10.1159/000521453 for all online suppl. material). The average cumulated net calcium change at the end of the experiment differed statistically significantly between all groups. The SDF product was the most effective in inhibiting lesion progression, followed by the TiF₄, NaF, and SnF₂ products (Table 2; ANOVA, Tukey post hoc test,  \( p < 0.05 \)).

Fluoride Analysis

Fluoride content in de- and remineralization buffers is shown in Figure 1. The statistical analysis showed significant differences among the groups in fluoride release into both de- and remineralization buffers (MANOVA, Tukey post hoc,  \( p < 0.05 \)). In the demineralization phase, the fluoride release from the SDF-treated dentine was significantly higher than in the other groups up to day 8. In the remineralization phase, SDF and TiF₄ showed no significant difference in fluoride released on day 1. The SDF product showed statistically significantly higher fluoride release than the other fluoride groups up to day 13, with 0.042 ± 0.0037 ppm versus 0.037 ± 0.0017 ppm for the control group. In the TiF₄ group, the fluoride release was not different from the other groups from day 3.

TMR Analysis

The mean mineral content (vol% ± SD) of the surface layer of the SDF-treated lesions (40 ± 3) was significantly higher than the mineral content of the baseline lesions (26 ± 3) (Fig. 2). NaF and SnF₂ showed no significant differences in this layer from the baseline lesion (30 ± 2, 28 ± 3, and 26 ± 3, respectively). No significant difference was found between TiF₄ and control (20 ± 2 and 18 ± 3, respectively), and both groups showed mineral loss in this layer compared to baseline (26 ± 3). All profiles in the fluoride-treated groups intersected the profile of the baseline lesion, indicating remineralization in the outer zone of the lesion (before the intersection point) and further demineralization in the inner zone of the lesion (beyond the intersection point). The mean depths ± SD of the intersection points differed statistically significantly between the TiF₄ (113 ± 20 μm) and SDF (103 ± 11 μm) groups at one hand and NaF (84 ± 9 μm) and SnF₂ (68 ± 6 μm) groups on the other hand (Fig. 2; ANOVA, Tukey post hoc,  \( p < 0.05 \)). In the outer zone of the lesion, significant remineralization was observed in the fluoride groups (Fig. 3; SDF > NaF = TiF₄ = SnF₂), while the control group showed demineralization at all depths of these zones. In the inner zone of the lesions, demineralization was observed in all experimental groups (Fig. 3; SDF < control; NaF = SnF₂ = TiF₄ = control). The sum of both zones in the SDF group showed significant remineralization. In contrast, a significant reduction of demineralization was observed in the dentine lesions treated with NaF, TiF₄, and SnF₂ compared to the control group.

EDS Analysis

EDS data showed that the silver levels were elevated up to the depth of 85 μm of the dentine lesion treated with SDF (online suppl. Fig. 3). The mineral composition in the hyper-remineralized area in the body of the pH-cycled dentine lesion treated with SDF contained 58 wt% calcium, 24 wt% phosphate, and only 16 wt% silver. Titanium level reached only 1 wt% at the depth 8 μm and was not detected in the deeper layers. EDS did not detect tin throughout the whole depth of dentine lesion treated with SnF₂.

Table 2. Average of cumulated data (µmol/cm²) at the end of the experiment from demineralization, remineralization, and net calcium change

| Experimental group (n = 8) | Average* ± SD | Statistics |
|---------------------------|---------------|------------|
|                           | Demineralization phases | Remineralization phases | Net calcium change** |
| TiF₄                      | −8.0±1.1      | a          | −3.8±2.1   | a          |
| SDF                       | −13.7±1.9     | b          | −7.8±1.9   | b          |
| NaF                       | −15.7±1.6     | c          | −13.1±1.2  | c          |
| SnF₂                      | −16.0±0.9     | c          | −17.9±2.2  | d          |
| Control                   | −19.2±1.0     | d          | −23.4±2.2  | e          |
|                           | Remineralization phases | Net calcium change** |
| SDF                       | +9.9±0.9      | a          | −3.8±2.1   | a          |
| NaF                       | +2.7±0.9      | b          | −7.8±1.9   | b          |
| TiF₄                      | +0.2±0.9      | c          | −13.1±1.2  | c          |
| SnF₂                      | −1.9±1.7      | d          | −17.9±2.2  | d          |
| Control                   | −4.2±1.3      | e          | −23.4±2.2  | e          |

Different characters represent statistically significant differences at  \( p < 0.05 \) (ANOVA post hoc Tukey test). * Negative values mean demineralization, and positive values mean remineralization. ** Net calcium change is the difference between calcium loss and calcium uptake.
Online supplementary Figure 4 shows the results of the TMR and EDS analysis of the penetration of silver ions immediately after the topical application of SDF together with the profiles after cycling. In the body of the pH-cycled lesions, a hyper-remineralized area was observed in the TMR profile at the depth of approximately 60 μm with a concomitant silver content of 20 wt%. In the no pH-cycled lesions immediately after the application of SDF, silver was detected in the surface of the lesion at approximately 43 wt% silver. At a depth of 60 μm, the no pH-cycling lesions contained about 20 wt% of silver, which did not alter the TMR profile compared to that of the baseline lesion at that depth.

Discussion

This study showed that the current variety of topical fluoride products was sufficient to protect dentine lesions against lesion progression under the chosen conditions. SDF showed a significant reduction in demineralization and enhancement in the remineralization of dentine lesions in both chemical and microradiographic analysis.

The current study selected a pH-cycling model of de- and remineralization buffers with pH 4.8 and 7.1, respectively. The control group showed as planned net demineralization after the pH-cycling. Net demineralization was also reported by ten Cate et al. [1995] after 10 days of pH-cycling under slightly different conditions of pH 5.0 and 7.0 in de- and remineralization buffers, respectively. In contrast to the findings of ten Cate et al. [1995], in the current study, calcium loss was observed during the remineralization phase in the control group. The source of this calcium loss is not clear. It might be that the mineral continues to demineralize, but it may also be that the concentration of calcium in the intratubular fluid is so high after the demineralization phase that besides causing remineralization, part of the calcium diffused out into the remineralization buffer. The first scenario suggests that the rinsing step between the two phases of pH-cycling might not be sufficient to neutralize or wash out the acid. Additionally, the subsequent remineralization solution might also not have been able to neutralize the remaining acid. The second scenario of the continuous leaking calcium out of the intratubular fluid may relate to the fact that the remineralization process is relatively slow compared to the demineralization process. Therefore, the calcium concentration may remain higher in the intratubular fluid than in the remineralization buffer, causing an efflux. The different results in this continued calcium loss between the study of ten Cate et al. [1995] and the present study might indicate that the small differences in de- and remineralization conditions may have a pronounced effect on lesion development in dentine.

The released fluoride from the treated dentine surfaces has been measured to examine the possibility of sat-
duration of the de- and remineralization buffers for fluoridated hydroxyapatite. The current findings showed that the amount of released fluoride steeply reduced from day 1 in both de- and remineralization phases in the SDF, the TiF₄, and the NaF groups. From day 2, the amount of fluoride in the de- and remineralization buffers was low for, respectively, NaF, TiF₄, and SDF, that we do not expect any protective effect by saturation to fluoride hydroxyapatite of the buffers. As the fluoride effects continued beyond these days as shown in online supplementary Figures 1 and 2, it was suggested that the effects were mainly related to fluoride associated with the mineral.

The TMR data showed remineralization in the outer zone of the lesion and further demineralization in the inner zone of the lesion for all fluoride products. The depths of the intersection points between re- and demineralization differed between the fluoride groups and were significantly deeper for the TiF₄ and SDF group than for NaF and SnF₂. The deeper effectivity of TiF₄ and SDF in the lesion might be related to specific features of these products. The acidity of TiF₄ (pH = 1.2) during the application of the product can produce a slight demineralization of the surface layer. This slight demineralization can facilitate the diffusion of fluoride ions due to the presence of hydrogen fluoride (HF) that may have carried the fluoride into deeper layers of the lesions [Gron, 1977]. Fluoride from SDF could probably easily diffuse deeply into dentinal tubules because of the high concentration [Wllershausen et al., 2015].

**Fig. 3.** The integrated mineral loss (ΔIML) of SDF, NaF, TiF₄, SnF₂, and control groups after the pH-cycling period (n = 8 specimens/group). Y-axis represents the ΔIML (vol%.μm). X-axis represents the outer zone of the lesion, the inner zone of the lesion, and the sum of both zones (total). For the control group, the transition from outer to inner zone was set at the average depth of this transition in the fluoride groups. Different characters per zone indicate statistically significant difference between the groups (ANOVA; p < 0.05).
SDF showed not only remineralization but also a significant hyper-remineralization in the body of the lesion as estimated from the TMR profile. The question arose to what extent silver contributed to this high-density mineral profile. EDS analysis revealed that in this area, silver was present at a concentration of 16 wt% compared to the calcium concentration of 58 wt%. To estimate whether this 16 wt% of silver would have influenced the density of the TMR profile, an additional experiment was conducted. In this experiment, TMR and EDS analyses were performed on specimens immediately after the SDF application. The mineral distribution profiles of the non pH-cycled SDF-treated specimens did not show hyperdensity in the body of the lesion, while the EDS analysis revealed an accumulation of silver ions, which was higher in the surface layer than in the pH-cycled specimens (online suppl. Fig. 4). Based on this control experiment, we concluded that silver played, if any, only a minor role in the hyper-density profile of the SDF specimens after the pH-cycling period.

In conclusion, the current variety of topical fluoride products was considered adequate to protect dentine lesions against progression. The current chemical and microradiographic analysis revealed that the SDF is significantly effective in reducing demineralization and enhancing remineralization of the dentine lesions compared to the other products. This finding raised the question of whether the superior effect of the SDF is attributed to its high fluoride concentration or the presence of the non-fluoride component (silver). Further studies are recommended to examine the anti-demineralizing and antimicrobial effect of SDF, since the pH-cycling model could not evaluate the microbial effect of SDF. In addition, further investigations are needed to examine the significance of the high fluoride concentration of the SDF product and whether this plays a pivotal role in the superior clinical effect of SDF.

Acknowledgment

The authors would like to thank Arie Werner from the Dental Material Science department, Academic Center of Dentistry (ACTA) Amsterdam, for his technical assistance in the X-ray energy-dispersive spectroscopy (EDS).

Statement of Ethics

This in vitro study did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was funded by Comprehensive Specialized Clinics and Hospital of Security Forces, Mecca City, Saudi Arabia.

Author Contributions

M.M.A., R.A.M.E., M.D.L., A.J.P.S., and C.L. designed the study; M.M.A., M.J.B., and R.A.M.E. performed the study; M.M.A. and R.A.M.E. analyzed the data. M.M.A. and M.D.L. performed the statistical analysis; M.M.A. and C.L. wrote the manuscript; A.J.P.S. commented on the manuscript; C.L. and A.J.P.S. revised the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further enquiries can be directed to the corresponding author.

References

Alhothali M, Exterkate R, Lagerweij M, Buijs M, van Loveren C, van Strijp AJP. The effect of equal fluoride concentrations in silver diamine fluoride and potassium fluoride on demineralized dentin during pH-cycling: chemical data. Eur J Oral Sci. 2021;129:e12789.
Buzalaf MAR, Pessan JP, Honório HM, Ten Cate JM. Mechanisms of action of fluoride for caries control. Monogr Oral Sci. 2011;22:97–114.
Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39:175–91.
Gao SS, Zhang S, Mei ML, Lo EC, Chu CH. Caries remineralisation and arresting effect in children by professionally applied fluoride treatment: a systematic review. BMC Oral Health. 2016;16:12.
Gron P. Chemistry of topical fluorides. Caries Res. 1977;11:172–204.
Grurryhuyen RIM. Non-restorative cavity treatment. Managing rather than masking caries activity. Ned Tijdschr Tandheelkd. 2010;117:173–80.
Innes NPT, Frencken JE, Bjorndal L, Maltz M, Manton DJ, Ricketts D, et al. Managing carious lesions: consensus recommendations on terminology. Adv Dent Res. 2016;28:49–57.
Lagerweij MD, de Josselin de Jong E, ten Cate JM. The video camera compared with the densitometer as a scanning device for microradiography. Caries Res. 1994;28:353–62.
Li Y, Liu Y, Psoter WJ, Nguyen OM, Bromage TG, Walters MA, et al. Assessment of the silver penetration and distribution in carious lesions of deciduous teeth treated with silver diamine fluoride. Caries Res. 2019;53:431–40.
Lippert F. Mechanistic observations on the role of the stannous ion in caries lesion de- and remineralization. Caries Res. 2016;50(4):378–82.

Peterson LG, Twetman S, Dahlgren H, Norlund A, Holm AK, Nordenram G, et al. Professional fluoride varnish treatment for caries control: a systematic review of clinical trials. Acta Odontol Scand. 2004;62:170–6.

Seifo N, Cassie H, Radford JR, Innes NPT. Silver diamine fluoride for managing carious lesions: an umbrella review. BMC Oral Health. 2019;19:145.

Suzuki T, Nishida M, Sobue S, Moriwaki Y. Effects of diammine silver fluoride on tooth enamel. J Osaka Univ Dent Sch. 1974;14:61–72.

ten Cate JM, Buijs MJ, Damen JJ. pH-cycling of enamel and dentin lesions in the presence of low concentrations of fluoride. Eur J Oral Sci. 1995;103:362–7.

ten Cate JM, Exterkate RA, Buijs MJ. The relative efficacy of fluoride toothpastes assessed with pH cycling. Caries Res. 2006;40:136–41.

van Strijp AJ, Buijs MJ, ten Cate JM. Contact microradiography of dentine under wet conditions to prevent lesion shrinkage. Caries Res. 1995;29:107–10.

Wiegand A, Magalhães AC, Attin T. Is titanium tetrafluoride (TiF4) effective to prevent carious and erosive lesions? A review of the literature. Oral Health Prev Dent. 2010;8:159–64.

Wierichs RJ, Stausberg S, Lausch J, Meyer-Lueckel H, Esteves-Oliveira M. Caries-preventive effect of NaF, NaF plus TCP, NaF plus CPP-ACP, and SDF varnishes on sound dentin and artificial dentin caries in vitro. Caries Res. 2018;52:199–211.

Willershausen I, Schulte D, Azaripour A, Weyer V, Briseño B, Willershause B. Penetration potential of a silver diamine fluoride solution on dentin surfaces. An ex vivo study. Clin Lab. 2015;61:1695–701.