

Fluoride ion emission, shear bond strength, and adhesive remnant index of calcium fluoride nanoparticles-containing orthodontic primer: an *In Vitro* study

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Objectives: This study investigated fluoride ion emission, shear bond strength (SBS), and the adhesive remnant index (ARI) of orthodontic primers containing varying percentages of calcium fluoride nanoparticles (nCaF₂).

Methods: Four primers were prepared with nCaF₂ concentrations of 0%, 20%, 30%, and 40%, mixed with Transbond XT primer (3M-Unitek, Monrovia, USA). Twenty-eight extracted upper premolars were equally divided into four groups, and bonded with orthodontic brackets using the respective primers following a standardised protocol. Fluoride ion emission was measured daily for two weeks, followed by assessments of SBS and ARI.

Results: The mean fluoride ion released was significantly different between the four groups. All groups showed higher initial fluoride ion levels, which later stabilised. Notably, only the primers with 40% nCaF₂ consistently released fluoride ions above 0.010 ppm, reaching 0.014 ppm on most days and stabilising between 0.011 and 0.026 ppm from Day 6 to Day 14. SBS differed significantly between the groups [$F(3,24)=4.977, p=0.008$], with the 40% nCaF₂ group showing significantly reduced SBS, although not to a clinically significant extent. ARI was unaffected [$\chi^2(2, N=28) = 3.589, p=0.263$].

Conclusions: Orthodontic primers with 40% nCaF₂ maintained fluoride ion release levels that may be clinically effective in combating white spot lesions, without compromising the SBS and ARI.

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Introduction

With an incidence and prevalence ranging from 23% to 76% and 2% to 97%, respectively, across different epidemiological studies,¹⁻⁴ fixed orthodontic

appliance therapy has been associated with an increased risk and high prevalence of early enamel demineralisation, known as a white spot lesion (WSL). The variable ranges depend on factors related to patient oral hygiene and treatment duration.^{2,4}

Various preventive measures have been introduced to reduce the risk of WSLs during orthodontic treatment, including the regular use of fluoride-containing products, chlorhexidine rinses, dietary modifications, and calcium-based remineralisation products. However, poor patient compliance, particularly among younger individuals who constitute the majority of orthodontic patients, limits the effectiveness of these approaches.^{4–7} Therefore, the development of effective strategies that do not rely on patient compliance could be a breakthrough in WSL prevention. One such approach involves using resin-modified glass ionomer cements (RMGICs) as orthodontic adhesives due to their fluoride-releasing properties. However, fluoride release from RMGICs declines rapidly after an initial release and is insufficient to suppress biofilm metabolism in the long term. Additionally, RMGICs have been reported to exhibit lower shear bond strength (SBS) and are prone to bond failure.^{8–11} Therefore, the development of new orthodontic materials capable of sustained and effective fluoride release is essential for preventing WSLs.

Nanotechnology has revolutionised dentistry, by offering a promising pathway in the fight against dental caries. The introduction of nanomaterials has opened new possibilities by leveraging their increased surface area to enhance solubility and ion release, surpassing traditional macro-sized materials.¹² Various nanotechnological innovations, including silver nanoparticles (nAg), zinc oxide nanoparticles (nZnO), gold nanoparticles (nAu), and nitrogen-doped titanium oxide (TiO₂) nanoparticles, have been explored to determine their effects on caries formation. Studies have shown that nAg is an effective antimicrobial agent against *Streptococcus mutans* by exhibiting superior bactericidal properties compared to nZnO and nAu, as both nZnO and nAu require a higher concentration to be effective. In addition, nAg has cosmetic drawbacks, as it can cause enamel discolouration, and at toxic levels, may lead to argyria.^{13–16} Similarly, nTiO₂ has been reported to possess antimicrobial properties, but its effectiveness is limited in the absence of light, and its strong tendency to aggregate due to high surface energy complicates dispersion.¹⁷ Furthermore, the need for robust long-term clinical efficacy, safety assurance, and a comprehensive understanding of the impact of these anti-cariogenic nanoparticles on bond strength remains, and necessitates further investigation.¹⁸

Fluoride, the ionic form of fluorine, is a well-established anti-caries agent.^{19–22} Calcium fluoride (CaF₂) is a commonly used fluoride compound in oral care products and has been shown to effectively reduce enamel demineralisation.^{23,24} Dental enamel contains an inorganic component, primarily calcium phosphate crystals, well known as hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂). Ionic exchange can occur between the enamel and the environment of the oral cavity. Fluoride ions can replace the hydroxyl ions in the crystalline lattice, producing more stable and acid resistant crystals known as fluorapatite, which are harder compared to the original form of hydroxyapatite.^{25,26} This structural modification enhances enamel resistance to acid attacks, thereby reducing the risk of demineralisation. Additionally, fluoride promotes enamel remineralisation by facilitating the redeposition of calcium and phosphate ions and aiding in the repair of early enamel lesions. Furthermore, fluoride exhibits antimicrobial properties by inhibiting bacterial metabolism and reducing acid production by cariogenic bacteria such as *Streptococcus mutans*. These combined effects help maintain enamel integrity and may prevent or minimise the formation of WSLs in orthodontic patients.²⁷

In its nanoform, calcium fluoride nanoparticles (nCaF₂) show promise in reducing the formation of WSLs when incorporated into the Transbond XT orthodontic primer and demonstrating acceptable cytotoxicity, adequate SBS, and a favourable adhesive remnant index (ARI).²⁸ However, the fluoride ion release from nCaF₂-containing orthodontic primers has not yet been studied nor reported. This serves as the fundamental basis for research on nCaF₂-containing dental materials for the prevention of WSL. Therefore, the present study aimed to investigate the fluoride ion release from orthodontic primer enhanced with various percentages of nCaF₂, as well as SBS and ARI.

Materials and methods

The ethical approval for the present study was obtained from the Faculty of Dentistry Medical Ethics Committee (FDMEC), Faculty of Dentistry, Universiti Malaya (IRB No: DF CD2201/0008(P)).

The sample size was computed in G*Power 3.1 (Heinrich Heine Universität, Dusseldorf, Germany) based on an alpha level of 0.05, a power of 0.95, and

effect size of 1.96, which was derived from a standard deviation (SD) of 0.5 reported by a previous study conducted by Suebsureekul and Viteporn (2017), which investigated the fluoride ion released from orthodontic primers containing traditional calcium fluoride.²⁹ Therefore, a total of 28 extracted sound human upper premolar teeth ($N = 28$) were collected and divided into four groups of seven extracted teeth in each group ($n = 7$). The teeth were disinfected by soaking in 10% formalin for one week. Each tooth underwent meticulous cleaning to eliminate calculus, plaque, and debris. The buccal surface of the tooth was polished with a rubber cup and non-fluoridated pumice with water for 10 sec. Subsequently, the tooth was rinsed with normal saline and stored in bottles filled with normal saline to avoid dehydration, prior to the bracket bonding procedure.

Preparation of nCaF₂-containing orthodontic primer

The nCaF₂-containing orthodontic primers were prepared according to the method described by Al Tuma and Yassir (2021).²⁸ Three millilitres of Transbond XT primer (3M-Unitek, Monrovia, USA) and the respective nCaF₂ powder (Nanoshel LLC, India) per group were weighed using a four-digit sensitive balance (Ohaus PA 214C Pioneer Series Analytical Balance, Cole-Palmer, Vernon Hills, IL, USA). nCaF₂ powder was weighed according to the percentage per group (20%, 30%, and 40%, respectively) related to the weight of the Transbond XT primer. The nCaF₂ powders were mixed with 3ml of Transbond XT primer using a magnetic stirrer (IKA RCT Basic Magnetic Stirrer, IKA-Werke GmbH & Co, Staufen, Germany) at 1500 rotations per minute (rpm) under atmospheric pressure and room temperature for 5 minutes. The nCaF₂-containing orthodontic primers were covered with aluminium foil and stored in a dark room to prevent evaporation and polymerisation of Transbond XT primer, before they were used to prime the teeth prior to bracket bonding.

Homogeneity assessment of nCaF₂-containing orthodontic primer

A thin layer of nCaF₂-containing orthodontic primer was spread over a glass slab using a plastic spatula and cured for 15 sec using a light cure unit (LED curing

light, Kerr Demi Ultra, Kerr, Brea, CA, USA). The specimen was placed into a petri dish and closed tightly. The homogeneity of the nCaF₂-containing orthodontic primer was noted under a Field Emission Scanning Electron Microscope (FESEM) (FEI Quanta FEG 650, Missouri, USA).

Bonding of orthodontic bracket using nCaF₂-containing orthodontic primer

The buccal surface of each tooth was etched with 37% phosphoric acid for 30 sec, washed with de-ionised water, and air-dried using a triple syringe until a frosty white surface appearance was seen. Based on the grouping, each tooth was primed with a thin coat of their respective 0%, 20%, 30%, or 40% nCaF₂-containing orthodontic primer that had been prepared earlier. Each tooth was primed using an applicator by dipping into the orthodontic primer once and applying on the tooth using one stroke. Next, the orthodontic primer was gently air-dried for 2 sec and light-cured for 15 sec. A thin layer of Transbond XT adhesive (3M-Unitek, Monrovia, CA, USA) was applied to the bonding surface of the orthodontic bracket (Gemini MBT loose bracket, 3M-Unitek, Monrovia, CA, USA). The bracket was placed at the facial axis point (FA point), which is the most prominent point of the clinical crown and compressed against the tooth surface using a probe. Excess Transbond XT adhesive was removed around the bracket using the same probe. The adhesive resin was light cured for 20 sec using the same unit placed at a distance of no more than 3mm from the bracket surface. After bracket bonding, each tooth was soaked in an individual closed centrifugal tube containing 3 ml of de-ionised water at room temperature for 24 hr to study the fluoride ion release behaviour.

Fluoride ion release

A fluoride selective electrode (Radiometer Analytical, Copenhagen, Denmark) was used to measure released fluoride ions by measuring the fluoride ion concentration in the existing de-ionised water of each sample. Standard calibration solutions containing 0.1, 1.0, and 10 ppm fluoride were prepared from 1000 ppm fluoride. These calibration solutions were used to calibrate the fluoride selective electrode prior to each test of the fluoride ion released from the samples.

To study the behaviour of fluoride ion release, the solution from each centrifugal tube was mixed with 3 ml of TISAB III (Thermo Fisher Scientific, Waltham, MASS, USA). The solution was stirred and after measurement, was discarded, and 3 ml of fresh de-ionised water was added into each centrifugal tube to resoak the treated tooth.

These steps were repeated daily for all samples to measure the fluoride ion released over a period of two weeks.

Shear bond strength and adhesive remnant index

The shear bond strength (SBS) and adhesive remnant index (ARI) of all samples were tested after completing the fluoride ion release test.

The roots of the teeth for each sample were mounted into resin bases after which the samples were stored in distilled water before testing.

The SBS test was performed using a universal testing machine (AGS-X Series Shimadzu, Shimadzu Europa GmbH, Kyoto, Japan) with a load cell of 5000 N and 0.5 mm/min crosshead speed. A knife-edge rod was applied on the occluso-gingival aspect of the bracket-enamel interface. After the brackets debonded, the load at failure for each sample was recorded by the measuring software (Trapezium Lite X, Shimadzu Corp, Kyoto, Japan).

The enamel surface of each sample was examined under a stereomicroscope (Olympus BX51, Tokyo, Japan) and the amount of adhesive remaining on the tooth was scored according to Årtun and Bergland (1984)³⁰:

0. No adhesive left on the tooth;
1. Less than half of the adhesive left on the tooth;
2. More than half of the adhesive left on the tooth;
3. All of the adhesive left on the tooth, with a distinct impression of the bracket mesh.

Statistical analysis

IBM Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp, Armonk, NY, USA) was used for statistical analysis. The Shapiro-Wilk test revealed that the data of fluoride ion release for 0%, 20%, 30%, and 40% nCaF₂-containing orthodontic primer were not normally distributed

(Supplementary I–VI). Therefore, a non-parametric Kruskal Wallis ANOVA test was applied to assess the differences in the mean fluoride ion released between the groups. The pairwise differences in the mean fluoride ion released between the four groups were assessed using Friedman ANOVA.

The Shapiro-Wilk test showed that SBS results were normally distributed (Supplementary I–VI). Therefore, a parametric one-way analysis of variance (ANOVA) was used to compare the mean SBS differences between the test groups. The homogeneity of data was assessed using the Levene test and the results showed that the data between the groups were homogenous ($p > 0.05$) (Supplementary I–VI). Therefore, Tukey's Honest Significant Differences (Tukey HSD) test was selected as a post-hoc test for further pairwise comparison. A Chi-square/Fisher's Exact test was used to investigate any significant differences in ARI scores between the test groups.

Results

Homogeneity and distribution of nanoparticles within the primer

On visual observation, the resulting mixture was light yellowish in colour and translucent. The nCaF₂ powder and the orthodontic primer appeared to be well mixed with no obvious sediment nor particles in the mixture.

The FESEM results supported the feasibility of preparing nCaF₂-containing orthodontic primer using the current mixing method. nCaF₂-containing orthodontic primer showed a homogeneous distribution of the nanoparticles within the primer with no significant agglutination (Figure 1).

Fluoride ion release

Table I shows the mean, standard deviation, and range (minimum-maximum) of the fluoride ion released for each group throughout the 14-day observation period. Based on the data in Table I, the mean fluoride ion release from the four groups was plotted against the observation days to monitor the release trend, as shown in Figure 2. The control orthodontic primer released 0.019 ± 0.007 ppm of fluoride ions on Day 1 and 0.004 ± 0.005 ppm on Day 2, before showing negligible fluoride release until Day 14. The orthodontic primers containing

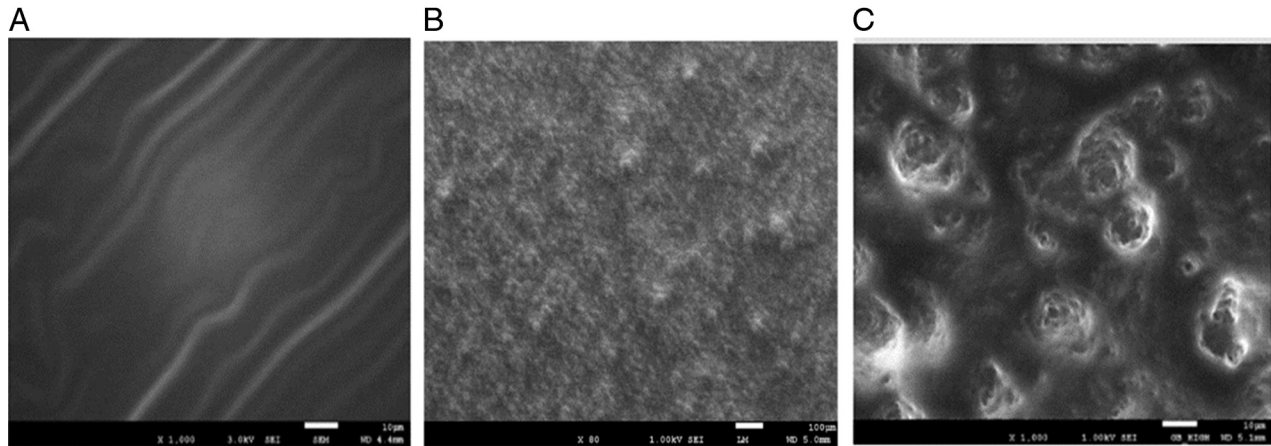


Figure 1. FESEM view of (A) Control primer at a magnification of X 1000; (B) nCaF₂-containing orthodontic primer with a concentration of 30% nCaF₂ at a magnification of X 80; and (C) nCaF₂-containing orthodontic primer with a concentration of 30% nCaF₂ at a magnification of X 1000.

20% nCaF₂ released 0.066 ± 0.010 ppm of fluoride ions on Day 1 and 0.041 ± 0.009 ppm on Day 2, before stabilising at a relatively consistent fluoride release level between 0.007 and 0.016 ppm from Day 3 to Day 14. For primers containing 30% nCaF₂, the fluoride ion release was 1.329 ± 0.206 ppm on Day 1, 0.869 ± 0.385 ppm on Day 2, 0.083 ± 0.018 ppm on Day 3, and 0.036 ± 0.024 ppm on Day 4, before stabilising at a relatively consistent level between 0.003 and 0.013 ppm from Day 5 to Day 14. Lastly, for primers containing 40% nCaF₂, the fluoride ion release was 1.971 ± 0.111 ppm on Day 1, 1.086 ± 0.107 ppm on Day 2, 0.120 ± 0.022 ppm on Day 3, 0.051 ± 0.042 ppm on Day 4, and 0.043 ± 0.035 ppm on Day 5, before stabilising at a relatively consistent level between 0.011 and 0.026 ppm from Day 6 to Day 14 (Table I and Figure 2).

The Kruskal Wallis ANOVA showed that there were significant differences in the mean fluoride ion released between the four groups for all 14 days ($p < 0.05$) (Table II). The pairwise differences in the mean fluoride ion released between the four groups were assessed using Friedman ANOVA and shown in Table III. The results confirmed a significant difference in the mean fluoride ion released for all pairwise groups (Table III).

Shear bond strength and adhesive remnant index

Table IV shows the mean, standard deviation (S.D.), and range (minimum–maximum) of shear bond strength (SBS) for the four groups. The SBS

of 20% group (10.70 ± 3.00 MPa) and 30% group (9.61 ± 1.74 MPa) were comparable to the control group (9.50 ± 2.08 MPa). The 40% group had the lowest mean SBS (5.44 ± 3.72 MPa). The one-way ANOVA test indicated that the SBS was significantly different between the groups [$F(3,24) = 4.977$, $p = 0.008$]. Therefore, the Post-hoc Tukey HSD analysis was conducted and revealed that the SBS of the 40% nCaF₂ group was significantly lower compared to the three other groups, as shown in Table V.

Table VI shows the distribution of the adhesive remnant index (ARI) scores. The Chi-square/Fisher's Exact test revealed no significant differences between the ARI scores of the four tested groups [$\chi^2(2, N = 28) = 3.589$, $p = 0.263$].

Discussion

The use of fixed bracketed orthodontic appliances has been associated with an increased incidence of WSLs. This is primarily attributed to the accumulation of dental plaque, which occurs due to the difficulty in maintaining optimal oral hygiene around the components of fixed orthodontic appliances. Acidogenic bacteria within the plaque metabolise fermentable carbohydrates and produce acids that lower the pH of the oral environment below the remineralisation threshold, leading to enamel demineralisation.^{2,6} The acids produced by the acidogenic bacteria, primarily lactic and acetic acids, diffuse into the interprismatic spaces of the enamel, where hydrogen ions are released and remove the mineral content of the enamel surface.³¹ The

Table 1. Mean, standard deviation, and range (minimum – maximum) of the fluoride ion releases for each group

	Control				20% nCaF ₂				30% naFC ₂				40% nCaF ₂			
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Day 1	0.019	0.007	0.01	0.03	0.066	0.010	0.05	0.08	1.329	0.206	1.10	1.60	1.971	0.111	1.80	2.10
Day 2	0.004	0.005	0.00	0.01	0.041	0.009	0.03	0.05	0.869	0.385	0.90	1.10	1.086	0.107	1.00	1.30
Day 3	0.000	0.000	0.00	0.00	0.011	0.004	0.01	0.02	0.083	0.018	0.06	0.11	0.120	0.022	0.09	0.15
Day 4	0.000	0.000	0.00	0.00	0.016	0.008	0.01	0.03	0.036	0.024	0.01	0.07	0.051	0.042	0.00	0.11
Day 5	0.000	0.000	0.00	0.00	0.011	0.004	0.01	0.02	0.013	0.008	0.00	0.02	0.043	0.035	0.00	0.09
Day 6	0.000	0.000	0.00	0.00	0.014	0.010	0.00	0.03	0.006	0.005	0.00	0.01	0.026	0.025	0.00	0.07
Day 7	0.000	0.000	0.00	0.00	0.010	0.006	0.00	0.02	0.010	0.006	0.00	0.02	0.021	0.015	0.01	0.05
Day 8	0.000	0.000	0.00	0.00	0.010	0.006	0.00	0.02	0.011	0.004	0.01	0.02	0.026	0.008	0.02	0.04
Day 9	0.000	0.000	0.00	0.00	0.011	0.004	0.01	0.02	0.013	0.008	0.01	0.03	0.017	0.008	0.01	0.03
Day 10	0.000	0.000	0.00	0.00	0.011	0.004	0.01	0.02	0.009	0.004	0.00	0.01	0.014	0.008	0.01	0.03
Day 11	0.000	0.000	0.00	0.00	0.011	0.004	0.01	0.02	0.009	0.004	0.00	0.01	0.011	0.004	0.01	0.02
Day 12	0.000	0.000	0.00	0.00	0.009	0.004	0.00	0.01	0.009	0.004	0.00	0.01	0.013	0.005	0.01	0.02
Day 13	0.000	0.000	0.00	0.00	0.007	0.005	0.00	0.01	0.003	0.005	0.00	0.01	0.019	0.009	0.01	0.03
Day 14	0.000	0.000	0.00	0.00	0.007	0.008	0.00	0.02	0.007	0.005	0.00	0.01	0.019	0.007	0.01	0.03

Min, Minimum; Max, Maximum ; SD, Standard deviation.

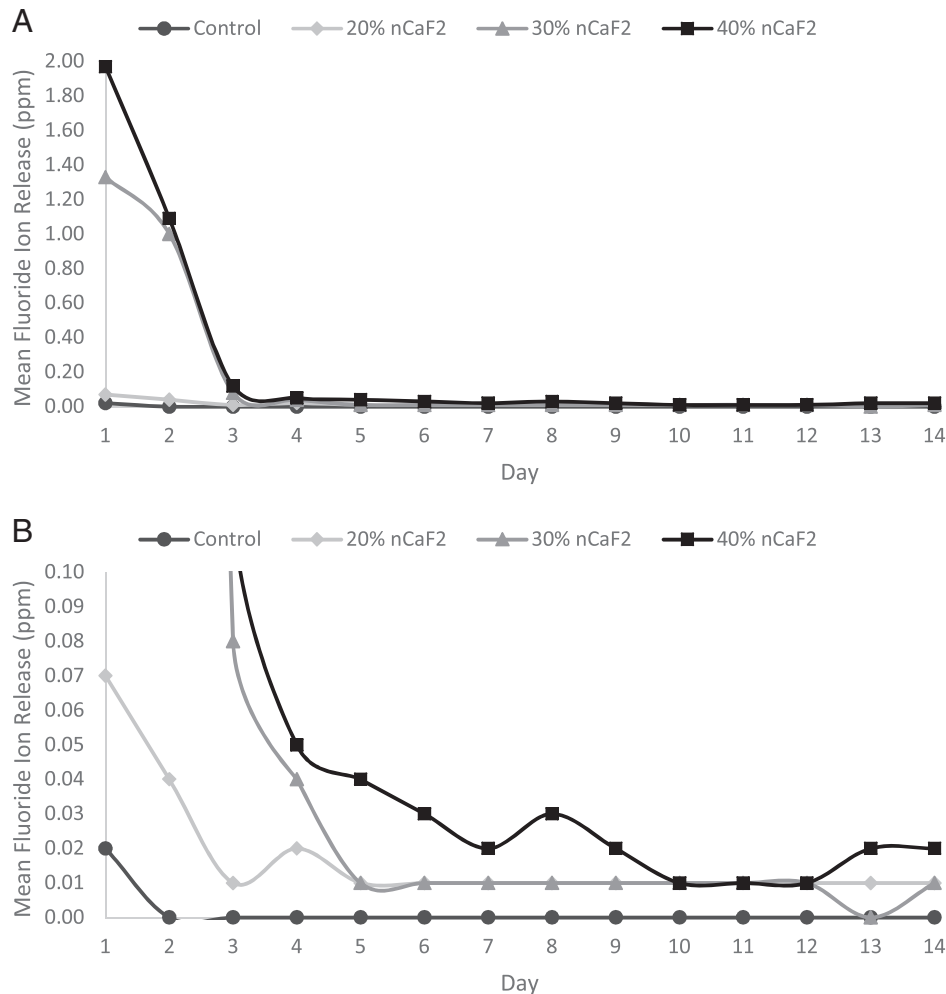


Figure 2. (A) and (B) Mean fluoride ion released from control, 20%, 30%, and 40% nCaF₂-containing orthodontic primer.

subsequent loss of calcium and phosphate ions results in the formation of smaller enamel crystals, leading to optical changes that manifest as WSLs.^{2,6,8} If left untreated, WSLs may progress to cavitated carious lesions, which compromise dental aesthetics and necessitate restorative intervention.^{2,4,6,31}

CaF₂ is widely used as an antimicrobial agent and a remineralisation aid for teeth.³² In its nanoform, nCaF₂, it offers a larger surface area, higher solubility, and greater chemical and surface reactivity compared to conventional CaF₂, while maintaining biocompatibility and stability.³³ It has been reported that adding nCaF₂ to Transbond XT orthodontic primer results in acceptable cytotoxicity, adequate SBS, and favourable ARI. However, this *in vitro* study did not investigate the fluoride ions released from the nCaF₂-containing primer, which is fundamental to

material science and engineering.²⁸ The same research group recently reported a clinical study that an orthodontic primer containing nCaF₂ demonstrated a notable capacity for enamel remineralisation compared to the conventional primer after one month of application. However, its WSL-preventing effect appeared to be short-term, as there was no difference observed between the nCaF₂-containing orthodontic primer and a control primer related to decreasing demineralisation scores during the three and six-month observation periods. The authors attributed the relatively short-term effect of nCaF₂-containing orthodontic primer against WSL formation to the hydrophobic nature of the composite resin after polymerisation, which may act as a barrier for the interaction of the nanoparticles with the saliva and decrease the release of fluoride and calcium ions.³⁴

Table II. Kruskal Wallis ANOVA test results for differences of mean fluoride ion released between the four groups

Day	Kruskal–Wallis H	<i>p</i> -value
1	25.491	0.000*
2	20.590	0.000*
3	25.153	0.000*
4	16.195	0.001*
5	13.351	0.004*
6	11.750	0.008*
7	17.334	0.001*
8	22.755	0.000*
9	19.897	0.000*
10	19.890	0.000*
11	20.431	0.000*
12	18.680	0.000*
13	18.105	0.000*
14	16.819	0.001*

* Significant ($p < 0.05$).

This observation further indicates the need and importance of the present study. The literature reports that even low levels of fluoride are sufficient to prevent mineral loss from enamel. Margolis et al. (1986) found that as little as 0.024 ppm to 0.054 ppm fluoride provided consistent and remarkable protection of the enamel surface from demineralisation.³⁵ Lynch et al. (2004) discovered that even at a lower concentration of 0.014 ppm, there was a significant reduction in demineralisation compared to water controls. However, at 0.009 ppm fluoride, no significant reduction in demineralisation was observed.³⁶ Therefore, a minimum amount of 0.010 ppm fluoride is suggested to be clinically sufficient.³⁷ Moreover, only a small amount of fluoride ion is sufficient to combat WSL clinically, as the modified orthodontic primer is located precisely where the lesions are likely to develop. Additionally, the total amount of fluoride ions in the mouth is greater, as there are typically about 20 to 28 brackets intraorally present for each patient. Lynch et al. (2004) also reported that there were no significant differences between the reduction achieved by 0.2 ppm and 2.0 ppm fluoride, as the reduction appeared to approach a plateau (49%

Table III. Friedman ANOVA test results for pairwise differences in the mean fluoride ion released between the four groups

95% Confidence interval					
Group	Mean difference	Std error	p-value	Lower bound	Upper bound
Control					
20%	-0.0153	0.00091	0.000*	-0.0184	-0.0122
30%	-0.1701	0.01094	0.000*	-0.2102	-0.1300
40%	-0.2439	0.00766	0.000*	-0.2719	-0.2158
20%					
Control	0.0153	0.00091	0.000*	0.0122	0.0184
30%	-0.1548	0.01097	0.000*	-0.1948	-0.1148
40%	-0.2286	0.00770	0.000*	-0.2565	-0.2006
30%					
Control	0.1701	0.01094	0.000*	0.1300	0.2102
20%	0.1548	0.01097	0.000*	0.1148	0.1948
40%	-0.0738	0.01335	0.001*	-0.1159	-0.0317
40%					
Control	0.2439	0.00766	0.000*	0.2158	0.2719
20%	0.2286	0.00770	0.000*	0.2006	0.2565
30%	0.0738	0.01335	0.001*	0.0317	0.1159

*Significant ($p < 0.05$).

Std error, Standard error.

Table IV. Mean, standard deviation, and range (minimum – maximum) of shear bond strength

Group	Mean	SD	Min	Max
Control	9.50	2.08	7.15	13.11
20%	10.70	3.00	7.65	16.28
30%	9.61	1.74	6.59	12.50
40%	5.44	3.72	1.95	11.93

Min, Minimum; Max, Maximum; SD, Standard deviation.

and 56%, respectively). In contrast, at 0.014 ppm and 0.025 ppm fluoride, the reductions were 19.7% and 31%, respectively. This indicates that at lower fluoride concentrations, a small increase in fluoride level can significantly reduce enamel dissolution compared to higher fluoride levels.³⁶ In the current study, only orthodontic primers containing 40% nCaF₂ consistently released fluoride ions above 0.010 ppm and above 0.014 ppm on most days (except for 0.011 ± 0.004 ppm on Day 11 and 0.013 ± 0.005 ppm on Day 12). The release of fluoride ions stabilised at a relatively consistent level between 0.011 and 0.026 ppm from Day 6 to Day 14.

A recent clinical study reported that an orthodontic primer containing nCaF₂ exhibited a significantly greater ability to prevent enamel demineralisation compared to a conventional primer after one month of application.³⁴ Although the present study observed fluoride ion release for only 14 days, it is speculated that fluoride release can be sustained clinically due to fluoride's ability to be recharged from the oral environment when patients use fluoridated products daily, in the form of fluoridated toothpaste and mouthrinse. In vitro studies have shown that fluoride-containing dental materials can be recharged by fluoridated products, and thereby maintain a continuously elevated level of fluoride ions.^{38,39} Nevertheless, the sustainability of fluoride ion release, including its rechargeability, beyond one month, warrants further investigation.

Fluoride ion release in de-ionised water is higher than in artificial or human saliva.^{40–42} The higher viscosity of artificial and human saliva reduces ion diffusion into and out of materials. In the natural oral environment, the presence of other ions in saliva can influence fluoride ion release from the surface of dental materials.⁴³ Moreover, in vitro studies have eliminated the influence of various factors that may affect fluoride ion release, and which are related to

Table V. Post-hoc pairwise comparison of shear bond strength

Group	Mean difference	p	95% Confidence interval	
			Lower bound	Upper bound
Control				
20%	-1.20	0.845	-5.249	2.848
30%	-0.11	1.000	-4.161	3.935
40%	4.06 *	0.049	0.015	8.111
20%				
Control	1.20	0.845	-2.848	5.249
30%	1.09	0.880	-2.961	5.135
40%	5.26 *	0.008	1.216	9.312
30%				
Control	0.11	1.000	-3.935	4.161
20%	-1.09	0.880	-5.135	2.961
40%	4.18 *	0.041	0.128	8.225
40%				
Control	-4.06 *	0.049	-8.111	-0.015
20%	-5.26 *	0.008	-9.312	-1.216
30%	-4.18 *	0.041	-8.225	-0.128

*Significant (p < 0.05).

the oral environment pH, the presence of proteins, and other ions like calcium and phosphate.⁴⁰ As an example, fluoride release is higher under acidic conditions compared to neutral conditions.⁴⁴ Therefore, the findings of the present in vitro study should be considered in context, and further in vivo studies are needed to confirm the clinical relevance.

The bond strength between orthodontic brackets and teeth must be robust to endure the forces of mastication and the orthodontic tooth movement exerted during the course of orthodontic treatment. SBS of 5.9 to 7.8 MPa are reported to be sufficient to withstand masticatory force and prevent bond failure.⁴⁵ However, certain studies have proposed a broader range, spanning from 2.8 to 10 MPa, as clinically acceptable.⁴⁶ It is influenced by circumstances such as the enamel condition, the composition of the adhesive, bracket material, bracket base, etching duration, oral environment, and even the clinician's skills. The bond strength between the bracket and the tooth can also be affected by

Table VI. Frequency of adhesive remnant index scores between groups

Group	Frequency			
	0	1	2	3
Control	1 (100.0%)	2 (14.29%)	4 (40.0%)	0 (0.0%)
20%	0 (0.0%)	4 (28.57%)	2 (20.0%)	1 (33.33%)
30%	0 (0.0%)	2 (14.29%)	3 (30.0%)	2 (66.67%)
40%	0 (0.0%)	6 (42.86%)	1 (10.0%)	0 (0.0%)

saliva and blood contamination during the bonding procedure.^{47,48} The present study revealed that SBS decreased as the percentage of nCaF₂ increased (9.50, 10.70, 9.61, and 5.44 MPa, respectively, for the control, 20%, 30%, and 40% nCaF₂ concentrations added to the orthodontic primer). The SBS observed were slightly lower compared to a recent study that reported control and 20%-nCaF₂ values of 13.85 and 15.13 MPa, respectively.²⁸ This difference might be due to variations in the method of preparing the nCaF₂-containing primer. Nevertheless, it was reported that the addition of nCaF₂ to the primer has no apparent effect on the mechanical properties determining SBS and ARI.²⁸ Although orthodontic primer incorporated with 20% of nCaF₂ yielded a mean SBS that was marginally higher (10.70 MPa) than the clinical recommendation (2.8 to 10 MPa)⁴⁶, there were no clinically nor statistically significant differences between the SBS of control and 20% nCaF₂-containing orthodontic primer. Although the orthodontic primer incorporated with 40% nCaF₂ exhibited a significantly reduced SBS (5.44 MPa) compared to the other three groups, the reported SBS fell within the clinically acceptable range to withstand bond failure. In addition, the ARI assessment revealed no significant difference between the four groups. Pickett et al. (2001) notably reported a significant difference between *in vivo* and *in vitro* debonding. By using an intraoral debonding plier and a universal tensile machine, respectively, it was found that *in vivo* debonding strength was 49.6% lower compared to the *in vitro* debonding strength. All the SBS observed in the present study fell within the range reported by Pickett et al. (2001).⁴⁸ Although the 40% nCaF₂ group exhibited clinically acceptable SBS, its values were significantly lower than those of the other groups. This reduction may be attributed to the increased concentration of nCaF₂, which acts as an impurity in the polymer matrix by interfering

with and lowering the level of polymerisation, ultimately weakening the mechanical properties.^{49–51} Therefore, it is crucial to balance remineralisation potential with mechanical stability. To optimise mechanical strength while maintaining therapeutic fluoride levels, future studies could explore alternative strategies to enhance sustained fluoride ion release, such as incorporating drug delivery systems. Encapsulating nCaF₂ within biocompatible drug delivery systems in the form of hydrogels, liposomes, micelles, and dendrimers^{52–54} may reduce the amount of nCaF₂ required in the orthodontic primer, and thereby minimise its detrimental effect on SBS.

ARI is a scoring system that evaluates adhesive residue on a tooth surface after orthodontic bracket removal. It assesses bond strength and debonding effectiveness and indicates whether the adhesive was mainly bonded to the bracket (lower ARI score) or the tooth surface (higher ARI score). This information is valuable for evaluating the risk of enamel damage during bracket removal and for improving bonding techniques.^{30,55,56} According to Mirzakouchaki et al. (2016), obtaining an ARI score of 0 to 1 indicates successful polymerisation in the area just below the bracket, which would be indirectly cured by the light reflected from the enamel surface.⁵⁷ Ahmadi et al. (2020) reported that higher ARI scores were linked to higher SBS values.⁵⁵ It is preferable to obtain a low ARI score, between 0 and 1, as this reduces chair time for cleaning and removing adhesive left on the tooth surface after bracket debonding.⁵⁸ In addition, when there is a need to reposition and rebond a bracket, a low ARI score indicates reduced chair time for the procedure, as there is less adhesive residue on the tooth surface. Conversely, Yang et al. (2002) advocated a high ARI score of 3, considering bond failure at the adhesive-bracket interface advantageous as it diminishes the likelihood of enamel fracture during debonding.⁵⁹

Conclusion

The developed nCaF₂-containing orthodontic primers were homogeneous with no significant agglutination. All groups showed the release of higher fluoride ion levels initially, before stabilising at a consistent level. Of the groups, only orthodontic primers containing 40% nCaF₂ consistently released fluoride ions above 0.010 ppm, which exceeded 0.014 ppm on most days. Although the addition of 40% nCaF₂ significantly statistically reduced SBS, this reduction did not translate into a clinically significant difference, as the SBS values remained within an acceptable range to withstand bond failure. Additionally, ARI was unaffected. As the first report on fluoride ion release from nCaF₂-containing orthodontic primers, the present study provides a basis for future research on nCaF₂-based dental materials for WSL prevention. Further studies are recommended to investigate the long-term fluoride ion release of nCaF₂-containing orthodontic primers, including their rechargeability with fluoridated oral care products. Additionally, exploring the incorporation of drug delivery systems

to prolong and enhance fluoride ion release warrants further investigation.

Conflict of interest

The authors declare that there is no conflict of interest.

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Supplementary I. Shapiro–Wilk test results for Group A (Control/0% nCaF₂-containing orthodontic primer)

Day	Statistic	df	<i>p</i>
1	0.840	7	0.099
2	0.664	7	0.001*
3	0.000	7	0.000*
4	0.000	7	0.000*
5	0.000	7	0.000*
6	0.000	7	0.000*
7	0.000	7	0.000*
8	0.000	7	0.000*
9	0.000	7	0.000*
10	0.000	7	0.000*
11	0.000	7	0.000*
12	0.000	7	0.000*
13	0.000	7	0.000*
14	0.000	7	0.000*

* Not normally distributed (*p* < 0.05).

Supplementary II. Shapiro–Wilk test results for Group B (20% nCaF₂-containing orthodontic primer)

Day	Statistic	df	<i>p</i>
1	0.937	7	0.609
2	0.818	7	0.062
3	0.453	7	0.000*
4	0.769	7	0.020*
5	0.453	7	0.000*
6	0.937	7	0.609*
7	0.777	7	0.024*
8	0.777	7	0.024*
9	0.453	7	0.000*
10	0.453	7	0.000*
11	0.453	7	0.000*
12	0.453	7	0.000*
13	0.600	7	0.000*
14	0.833	7	0.086*

* Not normally distributed (*p* < 0.05).

Supplementary III. Shapiro–Wilk test results for Group C (30% nCaF₂-containing orthodontic primer)

Day	Statistic	df	<i>p</i>
1	0.888	7	0.000*
2	0.538	7	0.000*
3	0.955	7	0.772
4	0.902	7	0.346
5	0.833	7	0.086
6	0.664	7	0.001*
7	0.777	7	0.024*
8	0.453	7	0.000*
9	0.453	7	0.000*
10	0.453	7	0.000*
11	0.453	7	0.000*
12	0.453	7	0.000*
13	0.600	7	0.000*
14	0.600	7	0.000*

* Not normally distributed (*p* < 0.05).**Supplementary IV.** Shapiro–Wilk test results for Group D (40% nCaF₂-containing orthodontic primer)

Day	Statistic	df	<i>p</i>
1	0.922	7	0.482
2	0.781	7	0.026*
3	0.978	7	0.949
4	0.928	7	0.533
5	0.916	7	0.443
6	0.909	7	0.391
7	0.816	7	0.590
8	0.769	7	0.200
9	0.833	7	0.086
10	0.646	7	0.010*
11	0.453	7	0.000*
12	0.600	7	0.000*
13	0.818	7	0.062
14	0.840	7	0.099

* Not normally distributed (*p* < 0.05).**Supplementary V.** Shapiro–Wilk test (Normality test) for SBS

Group	Statistic	df	<i>p</i>
Control	0.888	7	0.262
20%	0.901	7	0.340
30%	0.917	7	0.444
40%	0.890	7	0.277

*Significant (*p* < 0.05).**Supplementary VI.** Levene test for SBS

	Levene stat	df1	df2	<i>p</i>
Based on mean	1.962	3	24	0.147

*Significant (*p* < 0.05).

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