INTRODUCTION

Dental caries is a degradation of tooth structure, which eventually leads to tooth breakdown caused by acids produced by bacteria. It is mostly treated surgically, although various strategies have been recently used for its non-invasive management. Fluoride protects the integrity of the tooth structure by reducing bacterial acid production, bacterial tolerance to acidic media, and the equilibrium solubility of hydroxyapatite through the formation of fluorapatite crystals which improve its resistance to solubility. Thus, fluoride plays a major role in the prevention of dental caries through a topical mechanism by inhibiting the demineralization of the crystal surfaces inside or on the tooth, enhancing remineralization at the crystal surfaces, and inhibiting bacterial enzymes. Also, there is convincing evidence that fluoride has a valuable effect on remineralization in both enamel and dentine.

Several materials containing fluoride are available in the market, such as toothpaste or gel (at concentrations ranging from 950 to 1,450 ppm, the highest available in Japan), acidulated phosphate fluoride (APF), at 9,000 ppm, and silver diammine fluoride (SDF), containing more than 50,000 ppm. Dentifrices consumed in Japan, containing sufficient concentrations of fluoride, were shown to prevent and control dental caries. Fluoride concentration in dentifrices is positively associated with their caries-preventing effects.

Treatment with APF, specifically at 1.23% concentration of fluoride, was shown to have a better protective effect against erosive enamel loss compared with tooth mousses casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). Tooth mousse is a water-based, sugar-free dental crème containing casein phosphopeptide and amorphous calcium phosphate. The casein based carrier vehicle delivers calcium and phosphate ions to the tooth surface at the optimal ratio necessary to stimulate remineralization. The caries-inhibiting effect of APF is supported by empirical evidence, but the relevance of the time of clinical application is still under debate.

Recent studies on SDF have shown that it is an effective, safe, and efficient caries control agent that can be used to help achieve the World Health Organization Millennium Goals and fulfill the US Institute of Medicines criteria for 21st century medical care, and it is considered a simple to use, cost-effective, and non-invasive method in caries management. Despite the relative success of SDF in arresting carious lesions, the staining surrounding the tooth structure and the tooth-colored restorations are disagreeable side effects.

Toothpaste, APF, and SDF were used to evaluate the effects of fluoride on the tooth in previous studies. Although some of the solutions used in this study have concentrations similar to those of previously analyzed materials, comparison with such materials was not our goal because of the differences in acidic scale (pH), conditions and preparation of the materials. Walther et al. showed in their in-vitro study the significance of sodium fluoride (NaF) and potassium fluoride (KF), where KF gel (1,450 ppm) blocked further demineralization, whereas NaF toothpaste (5,000 ppm) induced remineralization. The water solubility of...
NaF is low (4.22 g/100 mL) at 18°C, while that of KF is higher (92 g/100 mL) at the same temperature\textsuperscript{19}. Since KF has higher solubility and is relatively free from ion association, it is used as a reference for the standardization of the lanthanum fluoride membrane electrode, and it is considered superior to NaF\textsuperscript{19}. KF is used to provide higher fluoride concentrations than NaF, which is widely used in dental products\textsuperscript{20}.

Therefore abundant evidence is available about the effects of toothpaste, APF, and SDF on dental caries. However, there is no information about the effects of different concentrations of fluoride on the inhibition of demineralization, or about the differences between the effects of NaF and KF on dental tissue at the same pH.

Furthermore, there have been several studies on the behavior of bonding materials used on enamel treated with fluoride; however, to the best of our knowledge, studies comparing the effects of high concentrations of fluoride on the inhibition and performance of enamel bonding were never attempted. The purpose of this study was to assess the effects of different concentrations of KF and NaF on micro-shear bond strength (µSBS) using a two-step self-etching adhesive system, and their protective effect against acidic challenge on bovine enamel.

**MATERIALS AND METHODS**

**Materials used**
The solutions used in this experiment were prepared by mixing deionized water with KF and NaF powder (Wako pure chemical industrial, Osaka, Japan) to produce different concentrations, as shown in Table 1. The materials used are, water (serving as control), a two-step self-etching adhesive system (Clearfil SE Bond 2, Kuraray Noritake Dental, Tokyo, Japan), and a resin composite (Clearfil AP-X, Shade A2, Kuraray Noritake Dental) (Table 2).

**Table 1** Fluorides used in this study

| Materials                      | Composition          | F ion concentrations       |
|--------------------------------|----------------------|----------------------------|
| Sodium Fluoride (NaF)          | Water, Sodium fluoride | 1,000, 9,000 ppm (pH-7)    |
| (Wako Pure Chemical Industrial, Lot: WEF31463) |                      |                            |
| Potassium Fluoride (KF)        | Water, Potassium fluoride | 1,000, 9,000, 10,000, 20,000, 30,000, 40,000, 55,000 ppm (pH-7) |
| (Wako Pure Chemical Industrial, Lot: PEN6825) |                      |                            |

**Table 2** Adhesive materials used in this study

| Materials              | Composition                                                                 | Manufacturer                                |
|------------------------|-----------------------------------------------------------------------------|---------------------------------------------|
| Clearfil SE Bond 2     | Primer: MDP, HEMA, hydrophilic DMA, CQ, water Bond: MDP, HEMA, Bis-GMA, hydrophobic DMA, CQ, N,N-diethanol p-toluidine, silanated colloidal silica | Kuraray Noritake Dental (Lot:000045)        |
| (Adhesive system)      |                                                                             |                                             |
| CLEARFIL AP-X          | Bis-GMA, TEGDMA, silanated barium glass filler, silanated silica filler, silanated colloidal silica, dl-Camphorquinone | Kuraray Noritake Dental (Lot:B90078)        |
| (Composite resin)      |                                                                             |                                             |

MDP: methacryloxydecyl dihydrogen phosphate, HEMA: 2-hydroxyethyl methacrylate, Bis-GMA: 2,2-bis[4-(2-hydroxy-3-methacryloyloxy-propoxy)phenyl]propane, TEGDMA: triethyleneglycol dimethacrylate

**Specimen preparation**

One hundred seventy fresh bovine incisors were kept frozen until used for the experiment. The remaining tissue on each tooth was removed by a blade and the tooth's crown was dissected from the root. The crowns were free of defects, cracks, and caries. Enamel blocks (6×6×2 mm) were prepared from bovine teeth crowns (labial side) using a low-speed diamond saw (Isomet, Buehker, Lake Bluff, IL, USA) under running water. Enamel surfaces were polished with 600–2000 grit silicon carbide (SiC) paper (Fuji Star, Sankyo Rikagaku, Saitama, Japan) until a flat area was obtained on the surface. The polishing was meant to expose the enamel structure, and also to eliminate any possible superficial defects, so as to create a standard smooth surface. The specimens were treated with each solution according to the experimental design for 1 min, then rinsed with water and dried for 15 s.

**µSBS test**

Enamel specimens (n=30) were treated with 0.3 mL of each solution for 1 min using a dropper (a disposable squeeze pipette). The specimens were bonded using Clearfil SE Bond 2, then a Tygon tube (n=15 each group, 0.79 mm diameter×1 mm height) (Saint-Gobain Performance Plastics, Tokyo, Japan) 5 tubes each for sample was placed on the bonded enamel surface and light-cured for 10 s (Optlux 501, SDS/ Kerr Dental, CA, USA). A resin composite (Clearfil AP-X) was filled into the Tygon tube and light-cured for 40 s. After storage in water for 24 h at 37°C, the Tygon tubes were removed using a scalpel blade. The specimen was fixed to a jig (Bencor- Multi-T, Danville Engineering, San Ramon, CA, USA) using cyanoacrylate glue (Model Repair II Blue, Dentsply-Sankin, Tokyo, Japan) and placed in a
universal testing machine (EZ-Test-500N, Shimadzu, Kyoto, Japan) to measure µSBS. A thin wire with cross-section 0.25 mm was used to form a loop connected to the base of a resin composite cylinder at one end and to the metal rod of the bond strength tester at the other end. The force was increased until failure, at a crosshead speed of 1 mm/min (Fig. 1).

**Failure mode analysis**

After the µSBS test, all the fractured surfaces were inspected to determine the mode of failure using a 3D confocal laser scanning microscope (CLSM) (VK-X150/X160, Keyence, Osaka, Japan) at 10× magnification. Failure modes were classified into three types: type I, adhesive failure at the interface between the bonding resin and the enamel; type II: cohesive failure in the bonding resin; and type III: mixed failure including adhesive failure and cohesive failure in the bonding resin.

**Scanning electron microscopic (SEM) observation**

The morphology of the 30 enamel samples was examined using SEM (JSM-IT100LV, JEOL, Tokyo, Japan). The observation was made both from the top and from a cross-section under the same conditions (solution and time application) as in the previous enamel groups. Examples of observations made at both angles are shown in Figs. 2 and 3.

**Acid resistance test**

For the acid resistance test, 0.1 mL of each solution or the control was administered to the specimens for 1 min using the dropper on a 1.5×1.5 mm window. The enamel surface around the window was covered with acid-resistant nail varnish (red color, waterproof, Revlon, New York, NY, USA). Each specimen was then separately immersed in 10 mL of a demineralizing solution (2.2 mM CaCl₂, KH₂PO₄ and 50 mM acetic acid at pH 4.5 with 10 M KOH) at 37ºC for 72 h. The specimen was then dissected cross-sectionally using a low-speed Isomet diamond saw under running water to observe it under 3D CLSM (Fig. 4).
Fluoride uptakes
For fluoride uptake, 50 samples were used. Each sample was treated with 0.1 mL of the specific solution on the 1.5×1.5 mm window for 1 min using the dropper, then rinsed and dried for 15 s. The enamel surface around the window was covered with acid-resistant nail varnish. The samples were then individually immersed in 2 mL of 0.5 M perchloric acid for 30 min to dissolve the surface followed by 2 mL of NaOH with TISAB II solution\textsuperscript{22}. The obtained fluoride content was evaluated using a fluoride ion selective electrode (F-53, Horiba, Kyoto, Japan).

Roughness test (Sa)
Thirty samples were used to determine the surface roughness using 3D CLSM, using the ISO 25178 surface texture parameters. Three samples for each group measured with scanning areas 273×204 µm before and after applying 0.1 mL of each solution.

Statistical analysis
The data on µSBS, fluoride uptake (ppm) and surface roughness were tested for normality using the Kolmogorov-Smirnov test. For µSBS and fluoride uptake, One-way ANOVA was used to compare the groups, followed by pairwise comparison using Tukey’s HSD test. Chi square test use to compare between tested groups for failure mode analysis. For surface roughness, Sa was tested using paired t-test before and after materials application (α=0.05). All statistical analysis was performed with IBM SPSS Statistics for Windows (Version 23.0 was used for statistical analysis, Armonk, NY, IBM, USA)

RESULTS
The difference in µSBS among the groups was statistically significant (p<0.001), as shown in Table 3.

Table 3  Results of fluoride uptake (F), and micro shear bond strength (µSBS) test

|                | F (ppm)     | µSBS (MPa)  |
|----------------|-------------|-------------|
| Control        | 0.049±0.018 | 22.78±2.56  |
| KF (1,000 ppm) | 0.048±0.006 | 22.46±5.17  |
| KF (9,000 ppm) | 0.169±0.061 | 22.57±4.46  |
| KF (10,000 ppm)| 0.227±0.049 | 22.29±4.7   |
| KF (20,000 ppm)| 0.175±0.01  | 18.36±3.7   |
| KF (30,000 ppm)| 0.257±0.073 | 18.96±5.37  |
| KF (40,000 ppm)| 0.42±0.078  | 19.63±3.93  |
| KF (5,500 ppm)| 0.77±0.059  | 18.61±1.71  |
| NaF (1,000 ppm)| 0.026±0.007 | 16.12±5.29  |
| NaF (9,000 ppm)| 0.071±0.018 | 14.96±3.03  |

\[ p\text{-value} \leq 0.001^* \]

Different superscript letters within each column indicates significant difference at \( p<0.05 \)
The KF groups with lower concentrations (1,000, 9,000 and 10,000 ppm) had higher µSBS values compared with the high KF concentration groups (20,000, 30,000, 40,000, and 55,000 ppm) and the NaF groups (1,000 and

Fig. 5  Failure mode distribution (%). All the fractured surfaces were inspected to determine the mode of failure using a 3D CLSM at 10× magnification. Failure modes were classified into three types: type I, adhesive failure at the interface between the bonding resin and the enamel; type II, cohesive failure in the bonding resin; and type III, mixed failure including adhesive failure and cohesive failure in the bonding resin.

Fig. 6  Cross-sectional images of each group after acid challenge observed by 3D CLSM at 5× magnification.

| Table 4   | Surface roughness before and after materials application |
|-----------|---------------------------------------------------------|
| Groups    | Before        | After         | Paired differences | p-value   |
| Control   | 0.1362±0.0479 | 0.1313±0.0494 | −0.0049±0.0031    | 0.107 NS  |
| KF1000    | 0.1209±0.0069 | 0.1206±0.0050 | −0.0003±0.0093    | 0.958 NS  |
| KF9000    | 0.0926±0.0004 | 0.0929±0.0007 | 0.0003±0.0004     | 0.347 NS  |
| KF10000   | 0.1025±0.0086 | 0.1026±0.0085 | 0.0001±0.0001     | 0.187 NS  |
| KF20000   | 0.1022±0.0039 | 0.1017±0.0046 | −0.0005±0.0015    | 0.642 NS  |
| KF30000   | 0.1194±0.0033 | 0.1219±0.0027 | 0.0025±0.0034     | 0.336 NS  |
| KF40000   | 0.1154±0.0024 | 0.1159±0.0033 | 0.0006±0.001      | 0.412 NS  |
| KF55000   | 0.1247±0.0163 | 0.1257±0.0153 | 0.001±0.0012      | 0.278 NS  |
| NaF1000   | 0.1013±0.0091 | 0.0975±0.0066 | −0.0038±0.0036    | 0.215 NS  |
| NaF9000   | 0.1330±0.0056 | 0.1323±0.0062 | −0.0007±0.0008    | 0.268 NS  |

NS=Non-significant
9,000 ppm). µSBS values significantly differed between KF and NaF at equal fluoride concentrations, as shown in Table 3.

In the mode of failure analysis (Fig. 5), mixed failure occurred more than 50% of the times in all KF, NaF, and control groups with the exception of the 9,000 ppm KF group. The NaF groups showed the highest rates of adhesive failure, and high rates of cohesive failure was observed in the control, 1,000 ppm KF, and 9,000 ppm KF groups compared with the other groups. However no significant differences in failure mode rates were found among the groups (p=0.948).

In 3D CSLM after acid dissolution, the cross-sectional view of the samples showed the unprotected window as a dark depression from the protected enamel in the control, KF (1,000 and 9,000 ppm), and NaF (1,000 ppm) groups. On the other hand, only the beginning of surface demineralization, with no loss of surface integrity, appearing as a whitish surface compared to the protected enamel surface, was shown in the KF (10,000, 20,000, 30,000, 40,000, and 55,000 ppm) and NaF (9,000 ppm) groups, which therefore showed higher resistance to acid challenge. Interestingly, the same concentrations of fluoride between KF and NaF resulted in different acid resistance, as shown in Fig. 6.

Fluoride uptake was significantly different among the groups (p<0.001), KF at 55,000 ppm showing the highest uptake, followed by KF at 40,000 ppm, Control, KF at 1,000 ppm, and NaF (1,000 and 9,000 ppm) showed the lowest uptake values, with non-significant differences among them. Regarding the surface roughness evaluation, non-significant differences were observed among all groups after solution application (Table 4).

**DISCUSSION**

Most dental caries are treated topically with compounds containing fluoride. The most significant success of topical treatments is the formation of intra-oral fluoride reservoirs, which can supply ions for a prolonged period. Even at low fluoride concentrations, the treatment is known to induce remineralization by slow or preventing mineral loss. The fluoride ions may react with enamel in several different ways: exchange with CO₂ on the crystal surfaces, direct adsorption, precipitation as MgF₂ of the magnesium released from crystal surfaces, double decomposition at high fluoride levels to form CaF₂ and Na₄HPO₄, and finally formation of fluorapatite by exchange with hydroxyl ions.

The chemistry of fluoride is largely unknown. However, these chemical equations represent possible explanations:

\[
\begin{align*}
\text{Ca}_{10}(PO_4)_6(OH)_2 + \text{NaF} & \rightarrow \text{CaF}_2 \cdot \text{Na}_4\text{PO}_4 + \text{NaOH} \\
\text{Ca}_{10}(PO_4)_6(OH)_2 + \text{KOH} & \rightarrow \text{CaF}_2 \cdot \text{K}_4\text{PO}_4 + \text{KOH} \\
\end{align*}
\]

From the above equations, it follows that there are two potential reactions, depending on fluoride concentration: Fluorapatite (FAp) is produced at low concentration, whereas CaF₂ is produced at high concentration (≥300 ppm). Since 1,000 ppm was used as the lowest concentration in this study, the precipitation occurring on the surface must be only due to the production of CaF₂.

In general, there is an inverse proportionality between the concentration of fluoride and the penetration of bonding agents, as a result of the coverage of the treated enamel surface with CaF₂. In this study KF at 1,000, 9,000 and 10,000 ppm did not show differences with the control group in terms of µSBS. The differences between KF and NaF in terms of particle shape, chemical and physical properties, and other factors may influence the bonding between the composite and the enamel. Moreover, other concentrations of KF showed a significant decrease in µSBS compared with the control group, that may be attributed to the formation of thick CaF₂ precipitate which is easily removed from the surface during the 24 h following topical fluoride application. On the other hand, the failure mode results was insignificantly different between tested groups, however adhesive failure tend to increase with the higher concentration solutions. The assumption of the presence of depositions in enamel deep structure (2–6 nm nanochannels) led to this fact because any precipitations could not be detected from SEM observation results and surface roughness test.

Moreover, the application of topical fluoride at 10,000 ppm concentration on the enamel surface did not result in high F levels, since it was easily washed away, thus decreasing the bonding performance to the tooth structure. On the other hand, protections against acid production by the plaque requires higher F-ion concentrations, which are essential to prevent dissolution.

Absorption of fluoride to enamel is possibly quite limited, but can be improved if dissolution reactions occur and the fluoride concentration is high. Etching and fluoride applications on the enamel surface decrease the bond strength of resin components due to several factors, such as the presence of fluoride particles which may completely or partially fill the interprismatic spaces and other spaces, preventing or interfering with tag formation and thus decreasing mechanical retention. Application of fluorides and formation of CaF₂ may alter enamel surface wettability, leading to reduce bonding strength and greater tendency of the bond to be disrupted by water. As a result, a gradual dissolution of the adhesive/enamel interfacial layer results in phase separation by water hydrolysis at the resin/enamel interface. The inhibitory effect of fluoride on adhesion to enamel surfaces has been reported in the literature. Gwinnett et al. used SEM to verify the presence of CaF₂ on the enamel surface as a reaction product of the application of high concentrations of fluoride. Our SEM observation of the enamel surface from top surface and cross-sectional surface did not show any deposition on the enamel surface that may interfere...
with the bond strength.

In our results we observed differences depending on the tested materials and their concentration. In particular, 3D CSLM revealed that the acid resistance test produced surface loss in the outer enamel structures in the control, KF (1,000 and 9,000 ppm), and NaF (1,000 ppm) groups, while the results for the KF (10,000, 20,000, 30,000, 40,000, and 55,000 ppm) and NaF (9,000 ppm) groups showed higher resistance to the acid challenge. Such surface loss in the control and KF (1,000 and 9,000 ppm) and NaF (1,000 ppm) is due to the lower fluoride absorption compared to the higher concentration groups.

Fluoride absorption is affected dramatically by the chemical nature of the teeth, which in turn depends on biological and environmental factors.

Since KF has higher solubility and is relatively free from ion association, it is used as a reference standard for the calibration of fluoride selective electrodes. KF can thus provide higher fluoride concentrations compared with NaF, which is widely used in dental products.

The analysis of fluoride uptake showed that KF at 55,000 ppm resulted in the highest uptake among all groups, followed by KF at 40,000 ppm. The control, KF (1,000 ppm), and NaF (1,000 and 9,000 ppm) groups showed the lowest uptake. Higher KF concentrations lead to higher fluoride uptake, which may give an indication on the prospective remineralization effect of fluoride. Previous studies reported that NaF-gel (12.500 ppm [pH=7.34]) and NaF-TP (5,000 ppm [pH=8.15]) were significantly superior to the NaF-gel (12.500 ppm [pH=6.04]), AmF-gel (12.500 ppm [pH=4.82]), and KF-gel (1,450 ppm [pH=7.65]) in inducing remineralization, while all tested fluoride agents could inhibit future demineralization. Regarding the surface roughness evaluation, the test was performed to show the effect of fluoride solution in different concentrations on the surface topography of the enamel. However, there were no significant differences observed among all tested groups (Table 4). That may be related to the neutral pH of all tested solutions, which may not affect the topography of enamel surface.

Our future studies might need to replicate these results in human teeth. Moreover, the results on the concentration of NaF and KF gave interesting insight for future inquiries. More investigation is required to understand their differences in physical and chemical properties. In this study, the particles seen in SEM for KF and NaF were not similar (Fig. 7), and the significance of this observation for dental tissues requires further investigation.

CONCLUSION

Concentrations lower than 10,000 ppm of KF did not affect µSBS. Nine thousand ppm NaF and 55,000 ppm KF induced resistance to acid challenge, but acid resistance was gradually reduced with decreasing fluoride concentrations.

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Fig. 7 Images obtained by SEM.
P: KF powder particles; S: NaF powder particles.
Both images were obtained at 50× magnification.
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