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ORIGINAL RESEARCH

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Prevention of erosion caused by pediatric medications in primary teeth with CPP-ACP and fluoride: an *in vitro* study

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Abstract

Background: Dental erosion is a significant issue in pediatric dental health, often resulting from the long-term use of pediatric liquid medications (PLMs). Preventive strategies are crucial to mitigate the erosive effects caused by these medications on primary teeth. This study aims to evaluate the preventive effects of fluoride varnish (FV) and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) against the erosive effects of common PLMs on primary teeth. **Methods**: Ninety caries-free deciduous molar teeth specimens were prepared and divided into three main experimental groups (artificial saliva (AS), FV and CPP-ACP), each with three subgroups exposed to one of three PLMs (amoxicillin trihydrate/clavulanic acid, multivitamin and salbutamol). The specimens underwent pH cycling to simulate daily oral environmental conditions. The surface microhardness of enamel specimens was measured at baseline and the end of the seventh day using a Vickers hardness testing machine. Statistical analyses were performed using SPSS Statistics for Windows (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY, USA). **Results**: Microhardness values did not differ significantly between groups at baseline. However, they did differ significantly among groups on the seventh day. They decreased significantly after the immersion cycle for all groups except those treated with FV. Microhardness values did not differ significantly between baseline and the seventh day in FV-treated groups. PLMs significantly reduced the microhardness of primary teeth. **Conclusions**: Among the tested preventive agents, 5% FV successfully prevented mineral loss of the enamel against PLMs and acid attacks. In contrast, CPP-ACP did not provide significant protection against dental erosion, failing to protect tooth specimens during erosive challenges. These findings underscore the importance of using FV in pediatric dental care to prevent erosion caused by long-term PLM use.

Keywords

CPP-ACP; Fluoride varnish; Preventive dentistry; Tooth erosion

1. Introduction

Dental erosion is the irreversible and progressive destruction of hard tooth tissues not directly affected by dental caries, mechanical factors or trauma. This type of erosion typically results from exposure to acids without a bacterial relationship, which can be intrinsic (*e.g.*, gastric acid from gastroesophageal reflux) or extrinsic (*e.g.*, dietary acids from soft drinks and fruit juices) [1]. Erosion may cause tooth sensitivity, aesthetic and nutritional problems, pulp exposure, abscesses, early tooth loss and altered occlusion [2].

Children's general health status is essential in developing dental erosion [3]. Oral liquid pharmaceutical formulations, such as suspensions, solutions and syrups, are widely used to treat pediatric patients [4]. Long-term use of commonly prescribed drugs, such as antibiotics, analgesics, cardiovascular and gastrointestinal drugs, antipsychotics, antiemetics, potassium supplements and asthma medications, has been found to have erosive potential in children [5]. Liquid pharmaceutical drugs have erosive properties due to their low endogenous pH levels, high titratable acidity (TA), calcium-chelating abilities, and adherence to dental surfaces [6]. Buffering agents, such as acids, are frequently added to their formulations to preserve chemical stability, control tonicity, ensure physiological compatibility, improve flavor, and increase the palatability of liquid drugs. Citric acid is the principal acid used in oral pharmaceuticals. Despite being classified as a weak acid, citric acid demonstrates potent erosive characteristics due to its capacity to chelate calcium within hydroxyapatite, which reduces saliva supersaturation and accelerates the dissolution rate of hydroxyapatite crystals [3].

Recommendations to minimize the effects of regular pe-

diatric liquid medications (PLMs) include taking them between meals, chewing gum or rinsing the mouth with water after their intake [5]. In addition, various products have been developed and used to prevent the significant effects of tooth erosion by reducing demineralization and increasing remineralization. The anti-erosive properties of fluoride and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) have been extensively examined [7–10]. Topical use of highly concentrated fluorides has been evaluated to prevent enamel dissolution and enhance its defense against erosive attacks. The efficacy of fluorides is based on forming a calcium fluoride (CaF_2)-like layer on the enamel surface, which acts as a physical barrier against acid attack or a mineral reservoir for remineralization [11].

Moreover, calcium and phosphate are the most essential building blocks of the remineralization process. CPP-ACP nanocomplexes are peptides derived from casein, which provide an additional source of phosphate and calcium ions in the oral cavity [8]. CPP stabilizes ACP and binds efficiently to the tooth surface under acidic conditions. Casein-derived phosphopeptides serve as buffers for free calcium and phosphate ions, resulting in a high concentration of ACP clusters deposited near the tooth surface. CPP-ACP inhibits the fermentation of small molecule carbohydrates localized on the tooth surface and buffers the decreasing plaque pH [12].

This *in vitro* study aimed to evaluate the preventive effects of a 5% sodium fluoride (NaF) FV and CPP-ACP against the erosive effects of regular use of PLMs by simulating pH changes caused by daily food consumption. It was hypothesized that they would protect against PLMs and acidic attacks during the immersion cycles.

2. Materials and methods

The erosive effects of PLMs containing three active ingredients commonly prescribed to pediatric patients were evaluated: amoxicillin trihydrate/clavulanic acid (ATCA; Augmentin), salbutamol (SB; Ventolin) and multivitamin (MV; Polivit). A 5% NaF FV (Enamelast; BG67V, Ultradent Products Inc., South Jordan, UT, USA) and CPP-ACP (GC Tooth Mousse America Inc., 190903D, Alsip, IL, USA) were used as protective agents to prevent the erosive effects of these PLMs.

G*Power software package (version 3.1.9.4; Heinrich-Heine-Universitaẗ, Dusseldorf, Germany) was used to estimate the required sample size. Ninety tooth specimens were prepared and randomly divided into three main experimental groups (AS, FV and CPP-ACP), each comprising three subgroups treated with one of the PLMs (n = 9): AS-ATCA (AS + ATCA), AS-MV (AS + MV), AS-SB (AS + SB), FV-ATCA (FV + ATCA), FV-MV (FV + MV), FV-SB (FV + SB), CPP-ATCA (CPP-ACP + ATCA), CPP-MV (CPP-ACP + MV) and CPP-SB (CPP-ACP + SB). To simulate the demineralization process following the twice-daily consumption of PLMs and assess the damage caused by low pH levels in the oral cavity after meals, all specimens except those in the AS group were subjected to pH cycling [7, 13]. The enamel specimens' baseline and final microhardness values were recorded and analyzed.

Forty-five newly extracted or exfoliated, caries-free, healthy deciduous molar teeth were used to prepare 90 specimens. Hypoplastic, fractured and malformed teeth were excluded. These teeth were sectioned at the cementoenamel junction to separate the crown and root portions. The crowns were sectioned parallel to the long axis in the mesiodistal direction to create two fragments to obtain 90 specimens, which were embedded in an autopolymerizing acrylic (Integra®; BG-Dental, Turkey) cylinder, exposing the enamel surface. The tooth surfaces were sequentially ground with 600, 900 and 1200 grit aluminum oxide (Al_2O_3) abrasive papers and polished under running water using a Minitech 233 polishing machine (polishing machine, Presi, Grenoble, France) to obtain an equally smoothed enamel surface. The specimens were cleaned with deionized water and cooled by air drying. The specimens were covered with two-layer acid-resistant nail varnish, leaving an exposed enamel window, an approximately 0.5 mm diameter hole, in the center of each tooth surface. The specimens were numbered and randomly divided into nine groups of 10. Before the immersion cycles, the specimens were stored in distilled water for 24 hours at 37 °C [3, 14].

At the beginning of the study, the baseline microhardness of the specimens was measured using a Vickers HMV-2 microhardness tester (microhardness tester machine, Shimadzu Corporation, Kyoto, Japan) under a 50 g load for 10 s. The measurements were taken at three separate points, and their average was recorded as the Vickers hardness number (VHN; T_0). At the end of the immersion cycles, the final surface microhardness was determined (T_1) and compared to the initial values [3, 14].

An AS solution (pH = 7) was prepared with 0.02 mol/L Tris buffer solution, 150 mmol/L potassium chloride (KCl), 1.5 mmol/L calcium nitrate tetrahydrate ($Ca(NO_3)_2{\cdot}4H_2O$), 0.9 mmol/L disodium hydrogen phosphate dihydrate ($Na_2HPO_4{\cdot}2H_2O$), and 1 L distilled water. A demineralization solution (DS; pH = 4.48) was prepared using 2.0 mmol/L $Ca(NO_3)_2{\cdot}4H_2O$, 2.0 mmol/L $Na_2HPO_4{\cdot}2H_2O$, 75 mmol/L acetate buffer solution, and 1 L distilled water [13, 15].

The pH levels of the solutions used during the immersion cycles and the quantity of the base needed to adjust the pH to 7.0 (TA) were determined using a SevenCompact pH meter (pH meter, Mettler Toledo, Columbus, OH, USA). To measure TA, 20 g of each solution was titrated with 0.5 M sodium hydroxide in 0.02 mL increments at 25 °C. ΔC is the volume of the base added, and ΔpH is the pH change from adding the base. The buffering capacity (BC) was calculated using the following equation [16]:

$$BC = -\Delta C/\Delta pH$$

The AS group (AS-ATCA, AS-MV and AS-SB) was used to determine the erosive effects of the PLMs independently of the preventative treatments. The specimens in the AS group were immersed for five minutes every 12 hours in 10 mL of undiluted PLM solution for five days. After each immersion, the specimens were washed with distilled water and placed in 10 mL of AS at 37 °C until the next immersion.

The FV and CPP-ACP were applied according to their respective manufacturer guidelines. The specimens in the

FV group (FV-ATCA, FV-MV and FV-SB) were treated with 5% NaF FV per the manufacturer's instructions and kept in distilled water for 24 hours. After 24 hours, the FV was removed with a scalpel. A cotton roll was moistened with deionized water and washed with deionized water for one minute [11]. Then, the specimens were immersed in 10 mL of the undiluted PLM for 5 minutes every 12 hours. After each immersion, the specimens were rinsed with deionized water and kept in appropriate solutions during the immersion cycle. They underwent the following immersion cycle for five days to simulate the oral environment [13, 17, 18]: PLM (five minutes) → DS (three hours) → AS (six hours) → DS (three hours) → PLM (five minutes) → AS (12 hours).

Per the manufacturer's instructions, the specimens in the CPP-ACP group (CPP-ATCA, CPP-MV and CPP-SB) were treated with CPP-ACP as a remineralizing agent twice daily for three minutes before and after the immersion cycle. The specimens were carefully cleaned with cotton rolls moistened with deionized water for one minute after the application [8, 10]. The specimens were immersed in 10 mL of the undiluted PLM for five minutes every 12 hours. After the application, the specimens were rinsed with deionized water and kept in appropriate solutions during the immersion cycle [13, 17, 18]: CPP-ACP (three minutes) followed by distilled water (one minute) → PLM (five minutes) → DS (three hours) → AS (six hours) → DS (three hours) → PLM (five minutes) → CPP-ACP (three minutes) followed by distilled water (one minute) → AS (12 hours; Fig. 1).

After all immersion cycles were completed, the specimens were washed with deionized water and stored in AS solution for 48 hours. The temperature of all solutions stabilized at 37 °C. The solutions were refreshed daily, and the PLMs were replaced before each immersion [10, 13].

The data were analyzed using SPSS Statistics for Windows (version 23.0; IBM Corp., USA). The skewness, kurtosis and conformity of the measured data to the normal distribution were assessed with Shapiro-Wilk tests. Normally distributed variables were compared between groups using analysis of variance and between subgroups within a group using a paired *t*-test. Non-normally distributed variables were compared between groups using Kruskal-Wallis analysis of variance or the Mann-Whitney U test and between subgroups within a group using a Wilcoxon paired-sample test. The data are presented as the median (min–max) or the mean ± standard deviation. A $p < 0.05$ was considered statistically significant.

3. Results

The pH values ranged from 3.94 (SB) to 4.55 (ATCA). The TA was highest in the SB group (1470 mmol/L) and lowest in the ATCA group (190 mmol/L). The BC was highest in the SB group (480.39 mmol/L × pH) and lowest in the ATCA group (77.55 mmol/L × pH; Table 1).

The baseline (T_0) microhardness values did not differ significantly between groups ($p = 0.671$; Table 2). However, the final (T_1) microhardness values did differ significantly between groups ($p < 0.001$).

The within-group comparisons at T_1 (Table 2) showed that, in the AS group, microhardness values did not differ significantly between the AS-MV and AS-ATCA subgroups ($p > 0.05$). In contrast, they were significantly higher in the AS-ATCA subgroup than in the AS-SB subgroup ($p < 0.05$). Similarly, they were significantly higher in the AS-MV subgroup than in the AS-SB subgroup ($p < 0.05$). However, microhardness values did not differ significantly between subgroups in the FV group ($p > 0.05$) or the CPP-ACP group ($p > 0.05$).

The across-group comparisons at T_1 (Table 2) revealed that microhardness values were significantly higher in the FV-ATCA subgroup than in the CPP-ATCA subgroup ($p < 0.05$). Similarly, they were significantly higher in the FV-MV subgroup than in the CPP-MV subgroup ($p < 0.05$). Moreover, they were significantly higher in the FV-SB than in the CPP-SB subgroup ($p < 0.05$).

Microhardness values decreased significantly from T_0 to T_1 in all subgroups except for FV-ATCA, FV-MV and FV-SB. Notably, the change in microhardness differed significantly among the subgroups within each group. In the AS group, the change in microhardness did not differ significantly between the AS-ATCA and AS-MV subgroups. However, the change in microhardness was significantly greater in the AS-SB subgroup than in the AS-ATCA and AS-MV subgroups ($p < 0.05$). In contrast, in the FV group, the change in microhardness did not differ significantly among the subgroups ($p > 0.05$). However, in the CPP-ACP group, while the change in microhardness was significantly smaller in the CPP-ATCA subgroup than in the CPP-SB subgroup ($p < 0.05$), it did not differ significantly between the CPP-ATCA and CPP-MV subgroups or between the CPP-MV and CPP-SB subgroups ($p > 0.05$).

In across-group comparisons, the change in microhardness was significantly smaller in the FV-ATCA subgroup than in the CPP-ATCA subgroup ($p < 0.05$). Similarly, the change in microhardness was significantly smaller in the FV-MV subgroup than in the CPP-MV subgroup ($p < 0.05$). Moreover, the change in microhardness was significantly smaller in the FV-SB subgroup than in the CPP-SB subgroup ($p < 0.05$).

4. Discussion

Continuous demineralization and remineralization in the oral environment affect tooth structure. This imbalance leads to mineral loss and, consequently, to a progressive deterioration of the tooth structure [19]. Dentists must diagnose erosive tooth wear early to determine the main etiological factors and ensure that protective measures are taken [20]. Prescribing PLMs is common to ensure proper compliance with medication intake and avoid swallowing inconveniences in children [4]. However, they have an erosive effect on teeth when consumed by children to treat chronic diseases [21]. This study investigated the effects of PLMs on deciduous teeth. Several *in vitro* studies have investigated the erosive effect of pediatric drugs on primary teeth [7, 22–24]. Deciduous teeth are smaller, have thinner enamel, and differ morphologically from permanent teeth. Therefore, the effects of the erosive process reach the dentine earlier and lead to an advanced lesion after a shorter exposure to acids than permanent teeth [5].

The 5% NaF Enamelast varnish and GC Tooth Mousse cream containing 10% CPP-ACP were compared to prevent

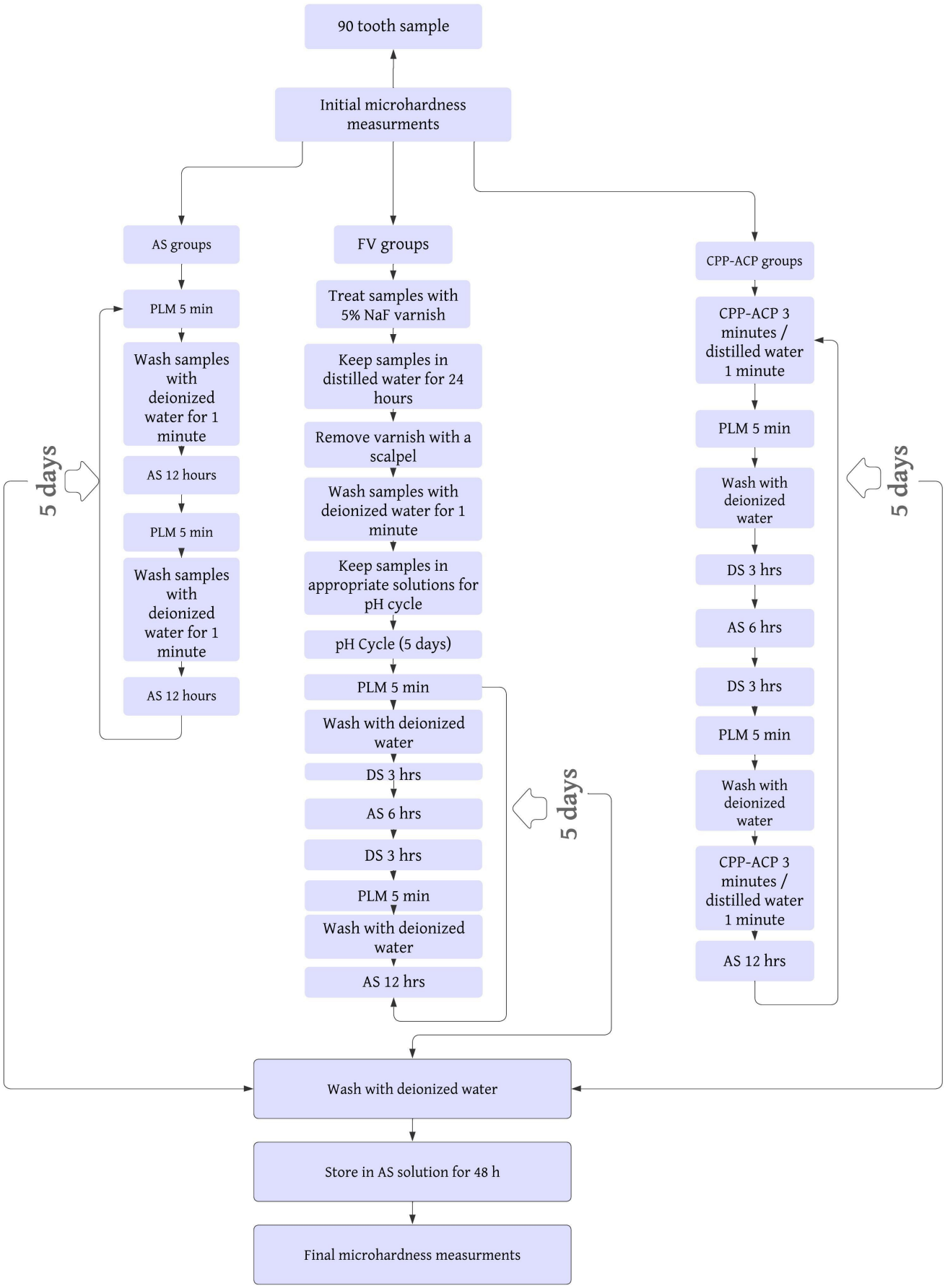

FIGURE 1. Immersion cycle schematic. AS: artificial saliva; PLM: pediatric liquid medications; FV: fluoride varnish; NaF: sodium fluoride; CPP-ACP: casein phosphopeptide-amorphous calcium phosphate; DS: demineralization solution.

TABLE 1. Characteristics of drug solutions used in the study: brand names, active ingredients, mg/mL, pH, titratable acidity and buffering capacity.

Brand name	Active ingredients	Mg/mL	pH	Titratable Acidity (ΔC)	Buffering Capacity (β)
Augmentin® (Antibiotic)	Amoxicillin trihydrate/Clavulanic acid	200 mg/28.5 mg per 5 mL	4.55	190 mmol/L	77.55 mmol/L × pH
Polivit® (Multivitamin)	1500 IU A Vit., 1 mg B Vit., 1.2 mg B2 Vit., 2 mg B6 Vit., 7 mg Nicotinamide (PP), 3 mg D-Pantenol, 25 mg C Vit., 400 IU D3 Vit., 5 mg E Vit.	per 5 mL	4.05	750 mmol/L	254.24 mmol/L × pH
Ventolin® (Bronchodilator)	Salbutamol	2 mg per 5 mL	3.94	1470 mmol/L	480.39 mmol/L × pH

TABLE 2. Initial and final microhardness measurements of enamel samples.

Groups	Subgroups	T_0 (initial)	T_1 (final)	*p*	Difference of Microhardness
Artificial Saliva					
	AS-ATCA (AS + Amoxicillin trihydrate/clavulanic acid)	320.96 ± 23.37	293.56 ± 30.38	0.001‡*	−27.40
	AS-MV (AS + Multivitamin)	326.53 ± 45.08	312.46 ± 44.23	0.001‡*	−14.06
	AS-SB (AS + Salbutamol)	319.26 ± 38.07	210.00 ± 43.08	<0.001‡*	−109.26
Overall AS		322.25 ± 35.28	271.34 ± 63.21	<0.001‡*	−50.91
Fluoride Varnish					
	FV-ATCA (FV + Amoxicillin trihydrate/clavulanic acid)	342.73 ± 47.86	333.06 ± 33.79	0.138‡	−9.67
	FV-MV (FV + Multivitamin)	351.43 ± 40.37	356.20 ± 50.26	0.747‡	4.77
	FV-SB (FV + Salbutamol)	365.40 ± 38.46	359.80 ± 56.35	0.552‡	−5.60
Overall FV		353.19 ± 42.23	349.02 ± 46.13	0.512‡	−40.17
CPP-ACP					
	CPP-ATCA (CPP-ACP + Amoxicillin trihydrate/clavulanic acid)	331.36 ± 44.92	189.23 ± 48.16	<0.001‡*	−142.13
	CPP-MV (CPP-ACP + Multivitamin)	331.90 ± 43.72	206.50 ± 76.08	0.013†*	−125.40
	CPP-SB (CPP-ACP + Salbutamol)	354.13 ± 46.35	161.73 ± 18.55	<0.001‡*	−192.40
Overall CPP-ACP		339.13 ± 44.33	185.15 ± 47.60	<0.001‡*	−1530.98
p		0.671ǂ	<0.001ǂ*		<0.001ǂ*

*AS: artificial saliva; ATCA: amoxicillin trihydrate/clavulanic acid; MV: multivitamin; SB: salbutamol; CPP-ACP: casein phosphopeptide-amorphous calcium phosphate; FV: fluoride varnish; ‡: Two-sample paired test; †: Wilcoxon Two-sample paired test; ǂ: Kruskal-Wallis analysis of variance; *p < 0.05.*

erosion caused by PLMs. The protective agent was applied differently in the FV and CPP-ACP groups based on their specific manufacturer guidelines, which aim to optimize their enamel-protective effects. According to the manufacturer's guidelines, FV is recommended to be applied every six months. It should remain on the teeth for 24 hours without brushing to allow for prolonged fluoride release and enhanced enamel protection [25]. In contrast, CPP-ACP should be applied twice daily with a minimum contact time of three minutes to ensure continuous calcium and phosphate ion availability, supporting ongoing remineralization [26].

The erosive potential of PLMs on teeth has been associated with their low pH, TA and frequent or long-term use [27]. TA indicates the total acid content and determines the strength of the erosive potential. BC is the time saliva takes to neutralize the acid in the PLM. In this study, the PLMs' pH, TA and BC were measured before the immersion cycles, and the pH of all the solutions was below the critical value (Table 1). The critical pH of dental enamel plays a significant role in enamel erosion. When the pH of the oral environment drops below the critical pH of 5.5, demineralization of the enamel occurs, leading to increased susceptibility to erosion and decay [16].

Microhardness is often used to determine the early stages of hard tooth tissue dissolution. This technique involves indenting a diamond end of specific geometrical dimensions for a given duration and load [28]. In this study, the baseline microhardness values of the enamel specimens varied between 319 and 365 VHN.

The AS group was used to determine the erosive effects of PLMs independent of preventative surface treatments. In the AS group, the change in microhardness was greatest with SB. Despite its high BC (480.39 mmol/L × pH), low pH (3.94), high TA (1470 mmol/L), and the presence of citric acid and ethyl alcohol contributed to its erosive effects. Similarly, Scatena *et al.* [3] evaluated the erosive effect of four drugs and concluded that SB sulfate caused the greatest change in microhardness. Samir *et al.* [29] showed that teeth specimens immersed in SB PLM exhibited significant structural loss, showing severely irregular surfaces and indistinct enamel prisms. Babu *et al.* [30] observed the erosive effect of SB and theophylline-containing anti-asthmatic PLMs. All the PLMs showed an erosive effect on the primary enamel surface when viewed under a scanning electron microscope (SEM), irrespective of their pH.

This study observed a significant decrease in microhardness for the specimens immersed in ATCA PLM (pH = 4.55; TA = 190 mmol/L; BC = 77.55 mmol/L × pH). This finding is associated with its low pH and excipients and is consistent with previous studies [31–33]. Radwa *et al.* [20] compared the erosive effects of antibiotic syrups with three ingredients, including ATCA, on deciduous teeth and found a significant decrease in final microhardness in all groups. In this study, the MV PLM (pH = 4.05, TA = 750 mmol/L, BC = 254.24 mmol/L × pH) also caused a significant decrease in microhardness. Babu *et al.* [30] demonstrated the erosive effect of MVs by examining specimens under a SEM.

This study found no significant difference between the baseline and final microhardness of the FV group, consistent with previous studies examining fluoride solutions, gels and varnishes [34]. In an *in vitro* study using human teeth, Carvalho *et al.* [35] compared the protective effects of CPP-amorphous calcium fluoride phosphate (ACFP; MI Paste Plus; GC America Inc., USA), FV (Duraphat; Colgate, Brazil), and calcium nanopaste (Desensitized Nano P; FGM Produtos Odontológicos, Brazil) containing 9000 ppm NaF against enamel erosion in terms of changes in surface microhardness. They reported no significant difference between the untreated control and Duraphat groups. Maurya *et al.* [36] evaluated the remineralizing effect of MI Varnish on primary teeth after the exposition of PLMs, showing that applying MI Varnish to enamel nonsignificantly increased its resistance to erosion.

This study found a significant decrease from initial to final microhardness in the CPP-ACP group. Previous studies have revealed that a CPP-ACP product has no protective effect against erosion [37, 38]. Turssi *et al.* [39] compared the post-erosion remineralization potentials of CPP-ACP (MI Paste; GC, USA), CPP-ACFP (MI Plus Paste; GC, USA), toothpaste containing 1100 ppm F (Sensodyne Cool Gel; GSK), and products containing calcium sodium phosphosilicate using human teeth. All agents significantly increased post-erosion enamel hardness. Furthermore, CPP-ACFP and calcium did not significantly affect the remineralization effects of products containing calcium sodium phosphosilicate compared to fluoride mouthwash, which caused mineral deposits on the tooth surface. Samir *et al.* [29] evaluated the remineralizing effect of Tooth Mousse Plus (GC, USA) and Erosion Protection Toothpaste (Elmex) after an erosion cycle with SB-containing syrup. They concluded that Tooth Mousse Plus was more effective than Elmex when used alone. Pushpanjali *et al.* [40] studied the remineralizing effect of CPP-ACP, revealing that CPP-ACP paste considerably reduced the erosive effect of PLMs. The shorter application period of CPP-ACP may have influenced our results. Previous research has demonstrated that long-term application of CPP-ACP is more effective in increasing the mineral content of *in vitro* subsurface caries lesions [41, 42].

Due to the cooperation of pediatric patients, patient follow-up, standardization, and ethical reasons, this study was conducted using an *in vitro* experimental model. Its primary limitation was that the preventive effects of FV and CPP-ACP were evaluated against the combined effects of the PLMs and the DS and not against the PLMs alone. The pH cycle model was used to simulate the oral environment's natural processes and dynamic conditions for extended periods under physiological conditions. While factors such as the pH, composition, and temperature of the solutions were controlled during the experiment, another limitation of this study was its inability to mimic the complexity of *in vivo* conditions. Future studies should consider increasing the frequency of daily meals and including between-meal snacks to better simulate real-life conditions and testing the agents separately to enhance the understanding of their efficacy. *In vivo* studies could also examine variables that can alter the effectiveness of protective agents, such as diet, oral hygiene practices, and individual variations in saliva composition and flow. This study highlights the need for further research into more effective agents or combination therapies that can provide comprehensive protection against dental erosion. Additionally, conducting *in vivo* studies could provide more comprehensive insights by incorporating the natural complexities of the oral environment.

5. Conclusions

Despite these limitations, this study provides valuable insights into the preventive effects of FV and CPP-ACP on dental erosion caused by PLMs. Its results indicate that PLMs significantly reduce the microhardness of primary teeth. Among the tested agents, 5% NaF FV demonstrated the greatest protection against dental erosion, reducing the erosive effects of PLMs and preventing the softening of tooth enamel. According to these findings, CPP-ACP does not provide significant protection against erosive attacks. This study underscores the importance of using preventive agents, such as FV, in pediatric dental care. Given FV's significant protection against enamel erosion, it should be incorporated into routine preventive strategies, especially for children on long-term PLMs. Pediatric dentists can confidently recommend 5% NaF FV for children with chronic illnesses who frequently consume PLMs. Furthermore, dentists and pediatricians should collaborate to educate parents about the risks associated with PLMs and the

benefits of FV. This collaboration could improve adherence to preventive measures, ultimately enhancing pediatric dental health outcomes.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding authors upon reasonable request.

AUTHOR CONTRIBUTIONS

NM—conceptualized the manuscript; carried out data analysis; drafted the manuscript. NM and ŞÖ—carried out the methodology; edited the manuscript. ŞÖ—supervised the project. Both authors subsequently revised the drafts. Both authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics committee approval was obtained from the Ethical Committee of Non-Invasive Clinical Research of Bezmialem Foundation University, Istanbul, Turkey (54022451-050.05.04-sayılı; 17 July 2020). Informed consent was obtained from all parents/caregivers of participants included in the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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