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ORIGINAL RESEARCH

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The impact of long-term use of pediatric liquid medications on primary tooth enamel: an *in vitro* study

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Abstract

Background: Medication use is common among children, particularly those with chronic medical conditions. This study aimed to evaluate the effects of long-term use of pediatric liquid medications commonly prescribed in Saudi Arabia on extracted primary teeth. **Methods**: Eight medications were included in the study; Ospen, Exjade, Feromin, Predo, Bactrim, Keppra, Risperdal and Pediasure. The medications were analyzed for pH, viscosity and sugar content. Enamel microhardness was assessed at baseline and after a 24-hour immersion period in the tested medications. Samples were further examined using scanning electron microscope (SEM). **Results**: Most tested medications had an acidic pH ranging from 3.1 to 7.3, and viscosities varied from 15 to 925 centipoise. Sugar analysis revealed that all medications, except Keppra, contained one or more types of sugar. Enamel microhardness decreased for all teeth after immersion, indicating enamel surface demineralization. SEM analysis showed that all examined groups, except the Keppra and Predo groups, exhibited erosive effects on the enamel surface of primary teeth. **Conclusions**: The acidic pH, high viscosity, and sugar content of pediatric liquid medications may compromise enamel integrity, increasing the risk of enamel surface loss in children with chronic conditions who frequently consume these medications over extended periods.

Keywords

Tooth erosion; Microhardness; pH; Scanning electron microscope; Children; Medication

1. Introduction

Dental caries is a highly prevalent disease, affecting the primary dentition of over 500 million children [1]. In addition, the incidence of non-carious lesions, such as dental erosion, has increased, leading to irreversible tooth structure loss [2]. This condition is particularly concerning in younger age groups, as primary teeth are more vulnerable to erosion than permanent teeth owing to their softer, thinner, and less mineralized enamel [3].

Medication use is common among children, particularly those with chronic medical conditions. Liquid medications, such as syrups, solutions and suspensions, as well as chewable tablets, are often the most convenient options for young patients [4]. To enhance compliance, pediatric medications are frequently formulated as liquids, especially syrups [5]. Most of these liquid medications are produced with acidic preparations to improve their physiological compatibility and chemical stability. To mask unpleasant tastes, sugars such as fructose, sucrose and glucose are often added to these formulations [6]. Unfortunately, oral bacteria, such as *Streptococcus mutans* and *lactobacilli*, ferment these sugars, producing acids that lower the pH of the mouth and ultimately lead to enamel demineralization [7, 8]. Moreover, factors such as frequent ingestion, nighttime administration, high viscosity, and the acidity of the liquid further increase the risk of medication-induced dental caries and erosion [9–11].

The long-term use of pediatric medications by children with chronic conditions raises concerns about their oral health, particularly when the medications are used frequently and over extended periods [7]. A 2021 study by Jung and Jun revealed that most tested pediatric medications contained sucrose, with the highest concentrations found in analgesics and antipyretics [12]. Several other studies have similarly reported high sugar content in pediatric medications [9, 10]. The acidity of these medications also poses risks to the dental health of children. Previous research has shown that pediatric medications with lower pH values can lead to dental erosion and exhibit the roughest surface textures under scanning electron microscopy (SEM) [13, 14]. Furthermore, a 2017 study in China reported a rapid decline in the microhardness ratios of teeth immersed in tested pediatric medications [15]. Vakil *et al.* [16] observed similar findings, noting a gradual loss of surface microhardness in both tested medications, indicating their erosive potential with prolonged use.

Research on the cariogenic and erosive potential of liquid medications commonly prescribed to pediatric populations in

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Arab countries is limited [14, 17]. Only two studies have examined this issue in Saudi Arabia. The first, conducted in 2017, found that all tested pediatric medications were acidic, with pH levels ranging from 4.22 to 6.10, and contained high sucrose concentrations between 5.38% and 11.41% [18]. The second, conducted in 2020, evaluated the acidogenic potential of commonly used pediatric liquid medications based on their endogenous pH and reported that eight out of nine tested medications were acidic [19]. In view of these findings, understanding how pediatric liquid medications prescribed for chronic conditions in Saudi Arabia affect the enamel of primary teeth is essential to assess their cariogenic and erosive potential. This study aimed to investigate the effects of prolonged use of pediatric liquid medications on primary tooth enamel.

2. Materials and methods

This *in vitro* study was conducted at the Advanced Technology Dental Research Lab of King Abdulaziz University and King Fahad Medical Research Center in Jeddah, Saudi Arabia. The laboratory study protocol (116-07-19) was approved by the Research Ethics Committee of the Faculty of Dentistry at King Abdulaziz University (KAUFD). The study aimed to evaluate the properties of liquid medications commonly prescribed for managing chronic illnesses in children in Saudi Arabia. In addition, primary teeth were immersed in these liquid medications, and their microhardness was assessed before and after immersion. Artificial saliva served as the control.

2.1 Medications

The medications used in the study were selected based on a short survey distributed electronically to a convenience sample of ten pediatricians working in private and public hospitals in Jeddah, Saudi Arabia. The survey was developed following a thorough review of the most prevalent chronic disorders among children in Saudi Arabia, including sickle cell anemia, thalassemia, iron deficiency anemia, leukemia, epilepsy, attention deficit hyperactivity disorder (ADHD), and malnutrition. Pediatricians were asked to identify the most common disorders they managed in their practice and the medications they prescribed most frequently. Based on the survey findings, the most frequently prescribed medications—Ospen, Exjade, Feromin, Predo, Bactrim, Keppra, Risperdal and Pediasure—were selected for inclusion in the study. Table 1 provides a summary of these medications.

2.2 pH

The pH of each pediatric liquid medication was measured using a digital pH meter (Orion Star A214; Thermo Scientific, Waltham, MA, USA). The device was calibrated prior to use with standard buffer solutions at pH 7 and pH 4. The electrode was calibrated then immersed in a 50 mL glass beaker containing 20 mL of each liquid medication. The measurement was performed three times for each medication, and the average pH value was recorded. A pH value below 5.5 was considered critical [20].

2.3 Viscosity

Viscosity measurements of the medications were performed at 25 °C using a Brookfield Viscometer (Model DV-III Ultra, Middleboro, MA, USA). The viscometer determined the force required to rotate the spindle at a constant speed while submerged in the sample, as torque is directly proportional to fluid viscosity. An integrated stainless teel container with a temperature controller was filled with the medication for measurement. Viscosity, expressed in centipoise (cP), was measured using an S21 spindle at 50 revolutions per minute (RPM) and a constant temperature [20]. The viscosity of each pediatric medication was calculated using the equation: Viscosity (cP) = Dial reading × Spindle Multiplier Factor. For the S21 spindle, the multiplier factor was 5 (Brookfield Engineering Laboratories ICB, Middleboro, MA, USA).

2.4 Sugar content

The fermentable sugar content (sucrose, glucose, fructose, in addition to sorbitol) of each pediatric liquid medication was analyzed using high-performance liquid chromatography with refractive index detection (HPLC-RI). An Agilent Technologies 1100 series liquid chromatograph (Agilent Technologies, Waldbronn, BW, Germany) equipped with an autosampler and a refractive index detector was used for the analysis. One milliliter of each medication was diluted with 50 mL of Milli-Q ultrapure water in a volumetric flask. The mixture was shaken vigorously and further diluted 1:1 (v/v) with pure acetonitrile. After centrifugation, the supernatant was collected for chromatographic analysis. A Shim-pack SCR-101N analytical column was used, with ultrapure water as the mobile phase. Isocratic elution was employed, maintaining a flow rate of 0.7 mL/min for the 20-minute run time. The concentrations of sucrose, glucose, fructose and sorbitol were calculated using compound standards for sugar analysis (Sucrose: S8501, Glucose: G8270, Fructose: F0127, Sorbitol: S1876, Sigma Aldrich, St. Louis, MO, USA) [9] and derived from a calibration curve equation [21].

2.5 Enamel microhardness

Ninety extracted primary posterior teeth with caries-free and defect-free buccal surfaces upon visual examination were collected from pediatric dental clinics at KAUFD and stored in saline solution (0.9% sodium chloride) at room temperature for no longer than three months before the experiment [22]. To minimize bacterial growth, the saline solution was replaced daily throughout the storage period. The teeth were randomly divided into nine groups, with ten teeth assigned to each group. Eight experimental groups corresponded to the investigated medications, and the ninth served as the control group in artificial saliva. The artificial saliva was prepared using the following composition: sodium chloride (0.4 g/L), potassium chloride (0.4 g/L), calcium chloride monohydrate (0.795 g/L), sodium dihydrogen phosphate monohydrate (0.69 g/L), sodium sulfate nonahydrate (0.005 g/L), and 1000 mL of distilled water free of any deposits [23]. Each tooth was mounted on a block of self-curing acrylic, ensuring that the buccal surface was facing upward and remained uncovered by

TABLE 1. Summary of the tested medications.

Medication			Form	Corresponding Medical Condition
Generic Name	Brand Name	Manufacturer		
Phenoxymethyl Penicillin	Ospen	Sandoz Switzerland	Syrup	Sickle cell anemia
Deferasirox	Exjade	Novartis NJ, USA	Oral suspension	Thalassemia
Iron sucrose	Feromin	Riyadh Pharma Saudi Arabia	Syrup	Iron deficiency anemia
Prednisolone	Predo	Jazeera Pharmaceutical Industries Saudi Arabia	Syrup	Leukemia
Sulfamethoxazole and trimethoprim	Bactrim Ds	Saudi Pharmaceutical Industries & Medical Appliances Corporation Saudi Arabia	Syrup	
Levetiracetam	Keppra	Union Chimique Belge Belgium	Syrup	Epilepsy
Risperidone	Risperdal	Janssen Pharmaceuticals Belgium	Syrup	ADHD
Nutritional Supplement	PediaSure	Abbott Nutrition IL USA	Liquid	Malnutrition

ADHD: attention deficit hyperactivity disorder.

acrylic. The teeth were polished and cleaned using fluoride-free pumice and glycerin to remove any deposits.

Ten microhardness readings per group were required to detect statistically significant differences between groups, based on the findings of Cheun *et al*. [13], ensuring a power of 95% at a significance level of 0.05. The baseline surface microhardness was assessed for each group using a Vickers hardness testing device (Buehler, Micromet 6040, Lake Bluff, IL, USA). The diamond indenter applied a force of 25 grams to the enamel surface for 15 seconds at three distinct sites, each 50 μm apart, and the average of these readings was recorded. After baseline measurements, the teeth in the control group were submerged in 20 mL of artificial saliva for 24 hours in a plastic bottle. The teeth in the eight experimental groups were placed in separate plastic bottles, each containing 20 mL of the corresponding undiluted pediatric liquid medication. The 24-hour immersion duration, chosen based on prior *in vitro* studies, simulates approximately one year of twice-daily medication use [20, 23, 24]. All samples were incubated at 37 °C. After 24 hours, the teeth were rinsed with distilled water for 30 seconds, and surface microhardness was reassessed following the same protocol as the baseline measurement [13]. Fig. 1A–C illustrates the steps *involved* in measuring enamel surface microhardness.

2.6 Microstructural analysis using SEM

After immersion, the samples were rinsed with distilled water for 30 seconds to remove residual substances. The following steps were then performed to prepare the samples for SEM analysis. The samples were dried using an ascending series of ethanol concentrations (25%, 50%, 70% and 100%) to eliminate any remaining moisture. Subsequently, the dried samples were mounted on aluminum studs with double-sided tape. A thin layer of gold coating was applied to the entire buccal surface of each sample using a gold sputter coater to enhance the conductivity of the sample and improve image quality.

The prepared samples were analyzed using a SEM (Quanta™ 250 FEG, FEI Company, Eindhoven, Netherlands). The microscope operated at an accelerating voltage of 20–5 kilovolts (kV) to capture high-resolution images. The buccal surface of each sample was examined at a magnification of 4000× to observe microstructural features.

2.7 Statistical analysis

The data collected from the study were tabulated and analyzed using IBM SPSS Statistics software (version 20.0; IBM Corp., Armonk, NY, USA). The normality of the data was assessed using the Shapiro-Wilk test, along with visual inspections of histograms and normal Quantile-Quantile (Q-Q) plots. Although the Shapiro-Wilk test indicated normal distribution ($p > 0.05$), the visual inspections of histograms and normal Q-Q plots revealed deviations from normality. Considering the small sample size in each group (n = 10), a conservative approach was adopted, treating the data as non-normally distributed. Consequently, nonparametric statistical tests were employed for data analysis. Statistical significance was set at $p < 0.05$. The chemical and physical properties of the medications were presented as percentages for sugar content, mean values with standard deviations (SD) for pH, and numerical values for viscosity.

Measurements of microhardness before immersion in the medications were compared using the independent-samples Kruskal-Wallis test to ensure baseline comparability across

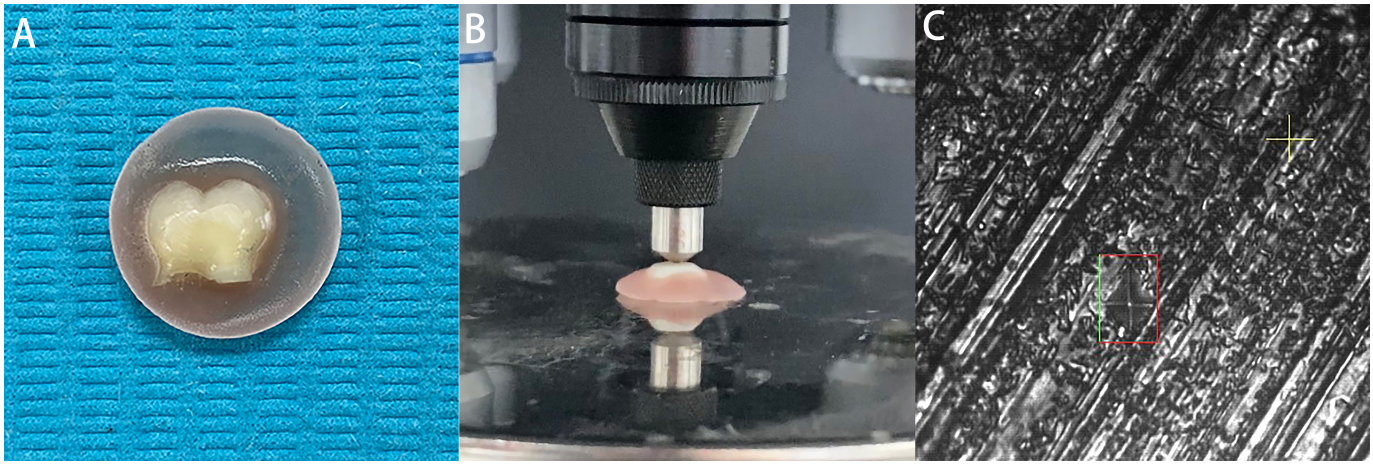

FIGURE 1. Microhardness measurement using Vickers hardness testing machine. (A) Crown fixed in an acrylic mold with its buccal surface exposed. (B) Testing the microhardness of enamel surface. (C) Diamond indenter on the enamel surface.

specimens. For each medication, post-immersion microhardness measurements were compared with baseline values using the Wilcoxon signed-rank test for related samples. The mean change in microhardness was calculated by subtracting the post-immersion measurements from the baseline values for each specimen. The mean change in microhardness for each group was then compared to that of the control group using the independent-samples Mann-Whitney U test. To account for variability in baseline microhardness among the groups, the difference between post-immersion and baseline microhardness was divided by the baseline value to calculate the mean percent change in microhardness. This was expressed using the following formula: Vickers Hardness Number (VHN) percent change = (mean difference/baseline) × 100. The mean percent change in microhardness for each experimental group was compared to that of the control group using the independent-samples Mann-Whitney U test. Furthermore, the mean percent change in microhardness was compared between low-pH (pH $\leq$5.5) and high-pH (pH >5.5) medications using the same statistical test. To evaluate the effects of medication pH and viscosity on microhardness, a simple linear regression analysis was conducted with pH and viscosity as independent variables and microhardness as the dependent variable.

3. Results

Table 2 summarizes the pH, viscosity, and sugar content of the medications included in this study. The average pH of the examined medications was 5.4 ± 1.6, ranging from 3.1 to 7.3. Four of the eight medications had a pH at or below the critical threshold of 5.5. Feromin had the lowest pH (3.1 ± 0.03), whereas Pediasure had the highest (7.3 ± 0.03). The viscosities of the medications ranged from 15 to 925 cP. Exjade had the lowest viscosity (15 cP), whereas Bactrim had the highest (925 cP). Sucrose and sorbitol were detected in five of the eight medications. Ospen contained the highest proportion of sucrose (27.48%), and Bactrim had the highest proportion of sorbitol (37.32%). Risperdal had the lowest concentrations of sucrose (0.008%) and sorbitol (0.004%). Glucose was found in four of the eight medications, albeit at very low concentrations, whereas fructose was not detected in any. Sugar analysis revealed that all medications contained one or more types of sugar (sucrose, glucose or sorbitol), with the exception of Keppra, which did not contain any of the four sugars analyzed.

Table 3 presents the mean VHN values for all groups before and after medication immersion. The baseline comparison before immersion showed no statistically significant differences in the mean VHN values among the groups ($p = 0.127$). However, after immersion in the medications, significant differences in mean VHN scores were observed between the groups ($p = 0.001$). When baseline and post-immersion VHN scores for each medication were compared using the Wilcoxon signed-rank test for related samples, significant decreases in microhardness were noted in the Ospen ($p = 0.005$), Exjade ($p = 0.017$), Feromin ($p = 0.017$), Predo ($p = 0.013$), Bactrim ($p = 0.017$), Risperdal ($p = 0.007$) and Pediasure ($p = 0.047$) groups. In contrast, no statistically significant differences were observed between baseline and post-immersion VHN values in the Keppra ($p = 0.203$) and artificial saliva ($p = 0.153$) groups.

Table 4 summarizes the comparison of mean percent changes in VHN across the groups after medication immersion. The control group exhibited a mean percent change of −8.97 ± 15.02. Among the teeth submerged in the tested medications, mean percent changes ranged from −8.59 ± 24.22 (Keppra) to −42.12 ± 24.94 (Risperdal). Statistically significant decreases in mean percent changes were observed for teeth immersed in Ospen ($p = 0.004$) and Risperdal ($p = 0.003$) compared with the control group.

A significant difference in the mean percent change in VHN was observed between medications with high pH (mean ± SD: −17.10 ± 21.62) and those with low pH (mean ± SD: −28.33 ± 22.27; $p = 0.025$), indicating greater mineral loss in teeth immersed in low-pH medications (Table 5).

A simple linear regression model was developed to investigate the effects of medication pH and viscosity on microhardness. Table 6 summarizes the unadjusted regression model, with pH and viscosity as independent variables and the mean percent change in microhardness as the dependent variable. The analysis revealed a significant association between microhardness and medication pH ($p = 0.011$). On average, a one-unit increase in pH corresponded to a 3.92% decrease

TABLE 2. pH, viscosity and sugar content values of the tested medications.

Group	pH Mean ± SD	Viscosity (cP)	Sugar Content (%)			
			Sucrose	Glucose	Fructose	Sorbitol
Ospen	5.50 ± 0.01	110	27.484	0.270	ND	ND
Exjade	5.50 ± 0.03	15	25.253	ND	ND	0.015
Feromin	3.10 ± 0.03	50	ND	0.005	ND	23.599
Predo	7.20 ± 0.04	50	11.931	0.270	ND	ND
Bactrim	6.00 ± 0.05	925	ND	ND	ND	37.322
Keppra	5.60 ± 0.02	65	ND	ND	ND	ND
Risperdal	3.20 ± 0.02	20	0.008	ND	ND	0.004
PediaSure	7.30 ± 0.03	30	3.539	0.114	ND	0.064

SD: Standard Deviation; cP: centi Poise; ND: not detected.

TABLE 3. Comparison of enamel surface microhardness between the baseline scores and post-immersion scores in the tested medications.

Group	n	Microhardness (VHN) Mean ± SD (Minimum–Maximum)		*p*-value†
		Baseline	After immersion	
Control	10	208.03 ± 23.94 (190.91–225.16)	190.03 ± 43.04 (159.24–220.82)^{a}	0.153
Ospen	10	249.27 ± 18.10 (236.31–262.21)	169.97 ± 22.63 (153.78–186.15)^{ab}	0.005*
Exjade	10	210.10 ± 39.13 (182.11–238.09)	161.70 ± 21.87 (146.06–177.34)^{ab}	0.017*
Feromin	10	215.50 ± 43.60 (184.31–246.69)	163.83 ± 16.14 (152.28–175.38)^{ab}	0.017*
Predo	10	208.43 ± 35.55 (183.00–233.86)	160.93 ± 16.63 (149.03–172.83)^{ab}	0.013*
Bactrim	10	213.27 ± 52.81 (175.49–251.04)	149.13 ± 26.63 (130.08–168.19)^{bc}	0.017*
Keppra	10	207.63 ± 73.70 (154.91–260.35)	175.10 ± 18.66 (161.75–188.45)^{ab}	0.203
Risperdal	10	206.93 ± 25.85 (188.44–225.42)	115.83 ± 41.28 (86.30–145.37)^{c}	0.007*
PediaSure	10	224.50 ± 30.96 (202.35–246.65)	189.47 ± 28.28 (169.24–209.70)^{a}	0.047*
p-value‡		0.127	0.001*	

SD: Standard Deviation; VHN: Vickers Hardness Number.
†*Related Sample Wilcoxon-Signed Rank test.*
‡*Independent samples Kruskal-Wallis Test.*
**Statistically significant at the 0.05 level.*
^{a}*Microhardness for Control and Pediasure.*
^{ab}*Microhardness for Ospen, Exjade, Feromin, Predo and Keppra.*
^{bc}*Microhardness for Bactrim.*
^{c}*Microhardness for Respirdal.*
Groups sharing similar letters within the column indicate no statistically significant difference between the groups.
Groups with different letters within the column indicate a statistically significant difference between the groups.

in the percent change in microhardness, indicating that the acidity of the medication had a detrimental effect on tooth microhardness. In contrast, viscosity showed no significant impact on microhardness ($p = 0.486$).

Fig. 2A–I presents SEM images of the enamel surfaces for all tested groups.

4. Discussion

This *in vitro* study evaluated the effects of pediatric liquid medications on extracted primary teeth over an extended period. Eight medications were analyzed, most of which had an acidic pH, with four at or below the critical threshold. The viscosities of the medications ranged from 15 to 925 cP. All medications, except Keppra, contained one or more sugars (sucrose, glucose or sorbitol). Significant loss of enamel surface microhardness was observed with all tested medications except Keppra.

Parents and pediatricians may be unaware of the hidden sugars added to foods, beverages, and especially pediatric medications, and may not fully understand their negative effects on the oral health of children [25, 26]. This is particularly crucial during the growth phase, where careful control of dental mineralization is essential, given that this period poses a higher risk for caries [27]. Common chronic medical

TABLE 4. Comparison of the percentage change in microhardness after immersion in the tested medications to the control group as a reference group.

Group	n	Microhardness (VHN)		*p*-value[§] (Compared to the Control Group)
		Mean ± SD	95% CI	
Control	10	−8.97 ± 15.02	(−19.10–1.78)	Reference
Ospen	10	−31.12 ± 12.76	(−40.24–−21.99)	0.004*
Exjade	10	−19.49 ± 23.20	(−36.08–−2.89)	0.280
Feromin	10	−20.58 ± 21.26	(−35.79–−5.37)	0.052
Predo	10	−20.13 ± 18.74	(−33.54–−6.73)	0.165
Bactrim	10	−25.21 ± 26.31	(−44.03–−6.39)	0.075
Keppra	10	−8.59 ± 24.22	(−25.91–8.75)	0.796
Risperdal	10	−42.12 ± 24.94	(−59.96–−24.28)	0.003*
PediaSure	10	−14.48 ± 14.93	(−25.16–−3.80)	0.353

[§]*Independent samples Mann-Whitney U Test.*
**Statistically significant at the 0.05 level.*
CI: Confidence Interval; SD: Standard Deviation; VHN: Vickers Hardness Number.

TABLE 5. Comparison of the mean percent change in microhardness between highly acidic medications and low acidic medications.

Group	n	Microhardness (VHN)		*p*-value[§]
		Mean ± SD	95% CI	
High pH	40	−17.10 ± 21.62	−24.01–−10.19	0.025*
Low pH	40	−28.33 ± 22.27	−35.45–−21.20	

High pH medications included Predo, Bactrim, Keppra and Pediasure.
Low pH medications included Fermoin, Risperdal, Ospen and Exjade.
[§]*Independent samples Mann-Whitney U Test.*
**Statistically significant at the 0.05 level.*
CI: Confidence Interval; SD: Standard Deviation; VHN: Vickers Hardness Number.

TABLE 6. Simple linear regression of mean percent change in microhardness with pH and viscosity.

Variable	Microhardness (VHN)		R^2	*p*-value
	$\beta \pm$ SE	95% CI		
pH	3.92 ± 1.52	0.90–6.93	0.071	0.011*
Viscosity	−0.01 ± 0.01	−0.02–0.01	0.005	0.486

**Statistically significant at the 0.05 level.*
CI: Confidence Interval; SE: Standard Error; VHN: Vickers Hardness Number.

conditions in Saudi Arabia managed with long-term medications include iron deficiency anemia, leukemia, ADHD, sickle cell disease, β-thalassemia, epilepsy, and malnutrition [28]. Pediatric liquid medications are often preferred for younger children owing to their ease of administration. However, their high viscosity and prolonged oral clearance time increase the risk of erosion, particularly with frequent and extended use. The slow clearance rate results in sustained exposure of teeth to potentially harmful substances. This study analyzed the sugars commonly found in pediatric medications. Sucrose was detected in five of the eight medications, with concentrations ranging from 0.008% to 27.484%, and sorbitol was present in five medications, with concentrations ranging from 0.004% to 37.322%. Glucose was identified in only four medications and at lower concentrations. These findings align with previous studies reporting substantial sugar content in pediatric liquid medications [9, 14, 18].

Pediatric liquid medications may have high erosive potential owing to their acidic formulations, making pH analysis crucial when assessing their potential for dental erosion [20]. The current study found that the pH of the examined medications ranged from 3.1 to 7.3. Notably, most of the medications had acidic pH levels, with four of the eight (50%) exhibiting pH values at or below the critical threshold of 5.5 for enamel demineralization [15]. The SEM analysis highlighted the impact of low-pH medications on the primary enamel surface, revealing morphological changes characterized by irregular, porous, and rough enamel surfaces, along with structural

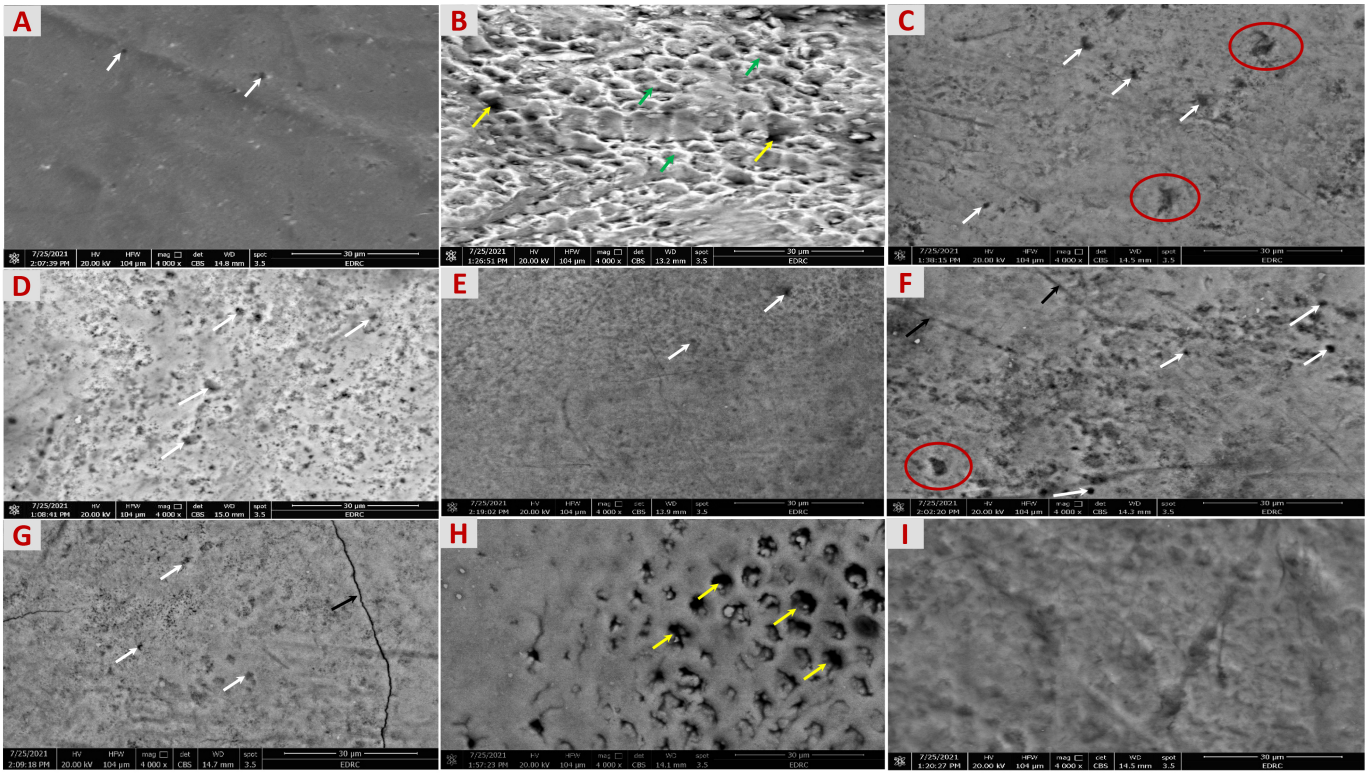

FIGURE 2. SEM micrographs of the enamel surfaces after immersion in different pediatric medications for 24 hours at magnification ×4000. (A) Artificial Saliva (control group) revealed a relatively smooth enamel surface with minimal porosity (white arrows) with no obvious evidence of erosion. (B) Ospen group demonstrated noticeable focal areas with a fish-scale appearance on the enamel surface (green arrows), along with exposed dentin where dentinal tubules were visible (yellow arrows), indicating enamel demineralization. (C) Exjade group displayed a rough, multipored enamel surface (white arrows) with structural enamel loss (red circles) but no dentin exposure. (D) Feromin group displayed a multipored (white arrows), irregular, and rough enamel surface, denoting structural enamel loss. (E) Predo group revealed an almost uniformly smooth enamel microstructure with few pores (white arrows) and no signs of erosion. (F) Bactrim group displayed a pitted and cracked enamel surface (black arrows) with numerous pores of varying diameters (white arrows), indicating structural enamel loss (red circles). (G) Keppra group revealed a relatively smooth enamel surface with some porosity (white arrows) and minimal cracks (black arrow). (H) Risperdal group displayed a rough and pitted enamel surface with exposed dentin and visible dentinal tubules of varying diameters (yellow arrows), indicating structural enamel loss and signs of erosion. (I) PediaSure group revealed irregularities and roughness on the enamel surface. HFW: Horizontal Field Width; WD: Working Distance; EDRC: Electron Detector Rotation Control; CBS: Chamber Back-Scattered.

enamel loss indicative of demineralization. These findings align with previous studies reporting low pH levels in many pediatric liquid medications, emphasizing their potential to erode primary tooth enamel with chronic use [9, 10, 15, 20]. Conversely, SEM analysis of enamel surfaces exposed to medications with pH values ≥7 showed minor surface changes and no erosion-related damage. These results are consistent with those of Seredin *et al.* [29], who reported that exposure to alkaline solutions produces significantly different effects compared with the degradation and erosion caused by acidic solutions.

In addition to pH, the viscosity of medications plays a significant role in dental erosion. The risk of erosion is closely linked to medication viscosity, as higher viscosity increases adherence to tooth surfaces, prolonging contact duration [30]. This study analyzed the viscosities of several medications and observed significant variations, with Bactrim exhibiting the highest viscosity and Exjade the lowest. Despite these substantial differences, both Bactrim and Exjade resulted in moderate loss of enamel microhardness. SEM analysis supported these findings, showing pitted and rough enamel surfaces with numerous pores of varying sizes in both groups. The observed loss of enamel microhardness may be attributed more to the type of sugar used in the medications than to viscosity alone. Bactrim contains sorbitol, a non-cariogenic sweetener that inhibits the formation of cariogenic biofilms. In contrast, sucrose, considered the most cariogenic dietary carbohydrate, is fermentable and serves as a substrate for synthesizing extracellular and intracellular polysaccharides in dental plaque [31]. The minimal loss of enamel microhardness in the Bactrim group could therefore be attributed to its lower content of cariogenic sugars rather than its high viscosity [32].

Measuring the microhardness of the enamel surface is widely regarded as one of the most reliable methods for assessing potential tooth erosion. In this study, enamel surface microhardness decreased across all groups after

exposure to the tested medications, reflecting varying degrees of enamel erosion. The Keppra group exhibited the lowest mean percent change in VHN, whereas the Risperdal group showed the highest. Compared with the control group, teeth immersed in Ospen and Risperdal showed statistically significant differences in the mean percent change in VHN. These findings were corroborated by SEM analysis, which revealed distinct differences in enamel surface characteristics among the medication groups. The Keppra group displayed a relatively smooth enamel surface with minimal porosity, whereas the Risperdal group exhibited an irregular pattern characterized by a rough and pitted enamel surface, indicating structural enamel loss and erosion. These results align with previous studies that identified medications as a potential contributor to gradual tooth structure loss [16, 33].

In this study, liquid medications with acidic pH, high viscosity, and elevated sugar content had a greater impact on reducing enamel microhardness. Among the medications tested, Risperdal, with a highly acidic pH of 3.2, caused the greatest loss of enamel microhardness. Ospen, characterized by a high viscosity of 110 cP, an acidic pH of 5.5, and a high sucrose content of 27.48%, also induced a significant reduction in enamel microhardness (mean ± SD percent change: −31.32 ± 25.36). Bactrim, despite its high viscosity of 925 cP, caused a comparatively lower reduction in enamel microhardness (mean ± SD percent change: −25.21 ± 26.31), likely because of its higher pH (6.00) and the use of sorbitol as a sweetener instead of sucrose. Conversely, despite having an acidic pH of 5.5 and a high sucrose content of 25.25%, caused less reduction in enamel microhardness, likely because of its low viscosity of 15 cP. Keppra, with an acidic pH of 5.6, exhibited the smallest reduction in enamel microhardness, possibly because none of the sugars examined were present in its formulation. These findings underscore the combined effects of pH, viscosity, sugar type, and sugar content on the extent of loss of enamel microhardness induced by different liquid medications. The results demonstrate that the enamel surface dissolution caused by pediatric liquid medications is multifactorial, with low pH, high viscosity, and specific sugar characteristics collectively exerting a more detrimental impact on the enamel surface.

The dental impact of liquid medications prescribed to children in Saudi Arabia has only been explored in two previous studies [18, 19]. A notable strength of the current study is its comprehensive approach, addressing each relevant parameter while employing a single operator to conduct the laboratory procedures. This ensured consistency and minimized variability in measurements and analyses. The medications evaluated in this study were selected based on a thorough survey of commonly prescribed liquid drugs for prevalent pediatric conditions in Saudi Arabia. This targeted approach enhanced the clinical relevance of the findings. Furthermore, the methodology of the study was detailed and reproducible, providing a robust framework for future research.

A notable limitation of this study is the simulation of a twice-daily regimen for one year, which may not reflect the actual frequency or duration of medication use. Moreover, only one medication was tested for each chronic medical condition, rather than evaluating all available options. This approach was chosen to avoid extending the study duration and to maintain the clarity of the results. However, the selected medications were those most commonly prescribed by pediatricians for each condition. Another limitation is the *in vitro* nature of the study, which cannot fully replicate the complexity of the oral cavity and may not accurately reflect clinical outcomes. Future studies could improve accuracy by incorporating more dynamic models, such as a cyclic demineralization-remineralization processes. In addition, the investigated medications were those prescribed for disorders prevalent in Saudi Arabia and the Middle East. As these conditions and medications may not be as common in other regions, caution should be exercised when generalizing the findings to different populations.

This study underscores the detrimental effects of prolonged consumption of liquid medications on the enamel of primary teeth in children. Medical professionals should take these effects into account when prescribing or administering medications and, whenever possible, opt for medications that pose less risk to dental health. For cases where prescribing certain medications is unavoidable, healthcare providers should inform parents about potential dental side effects and recommend strategies to mitigate them, such as encouraging children to drink water, rinse their mouths after each dose or use additional home care measures. For example, encouraging using remineralizing tooth pastes for children with medication-controlled chronic diseases has been found helpful in controlling disease and medication dental negative effects [34]. Collaboration between dentists and medical professionals is essential for sharing findings from similar studies and supporting preventive measures. Dentists can contribute by providing oral hygiene instructions to parents and being vigilant for early signs of dental erosion in children, especially those with special healthcare needs. Additional preventive strategies should be implemented for these vulnerable populations. This study highlights the need for further investigation into the effects of commonly prescribed medications on the dental health of the Saudi pediatric population. Clinical research focusing on the dental impacts of medications, particularly for children with special healthcare needs, should be encouraged whenever ethically feasible to develop more effective preventive approaches.

5. Conclusions

Within the limitations of this study, the findings suggest that the examined pediatric medications caused varying degrees of enamel surface loss. Most of these medications exhibited acidic pH levels and high sugar concentrations, which are recognized risk factors for erosion, particularly in children with chronic medical conditions who frequently consume these medications over extended periods.

AVAILABILITY OF DATA AND MATERIALS

The authors may share the data upon reasonable request.

AUTHOR CONTRIBUTIONS

HE, OA and OF—conceptualization; resources. HE, OA, DF, HB, RB and OF—methodology; investigation. OA, HB, RB and OF—data curation. OA and OF—formal analysis. HE and OA—manuscript preparation. HE, DF and OF—project administration. HE—funding acquisition. DF—correspondence. All authors have reviewed and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol (116-07-19) was approved by the Research Ethics Committee at Faculty of Dentistry at King Abdulaziz University. The study *involved* no human subjects and thus consent from participants was not required.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

REFERENCES

[1] World Health Organization. Oral health report (2022). 2024. Available at: https://www.who.int/news-room/fact-sheets/detail/oral-health (Accessed: 27 December 2024).

[2] Pushpanjali M, Sai Sankar AJ, Sridevi E, Sankar KS, Kumar KK, Balaji K. Scanning electron microscopic evaluation of erosive potential of pediatric liquid medicaments on primary teeth. Journal of Orofacial Sciences. 2020; 12: 119–125.

[3] Peker O, Arıkan R. Dental erosion in primary teeth. Journal of Dentistry Faculty of Usak University. 2023; 2: 59–64.

[4] Meyers RS. The past, present, and future of oral dosage forms for children. The Journal of Pediatric Pharmacology and Therapeutics. 2024; 29: 22–31.

[5] Smith L, Leggett C, Borg C. Administration of medicines to children: a practical guide. Australian Prescriber. 2022; 45: 188–192.

[6] Kolling WM, Ghosh TK. Oral liquid dosage forms: solutions, elixirs, syrups, suspensions, and emulsions. In Ghosh TK, Jasti BR (eds.) Theory and practice of contemporary pharmaceutics (pp. 367–385). 1st edn. CRC Press: Boca Raton. 2021.

[7] Al Humaid J. Sweetener content and cariogenic potential of pediatric oral medications: a literature. International Journal of Health Sciences. 2018; 12: 75–82.

[8] Spatafora G, Li Y, He X, Cowan A, Tanner ACR. The evolving microbiome of dental caries. Microorganisms. 2024; 12: 121.

[9] Valinoti AC, da Costa LC III, Farah A, Pereira de Sousa V, Fonseca-Gonçalves A, Maia LC. Are pediatric antibiotic formulations potentials risk factors for dental caries and dental erosion? The Open Dentistry Journal. 2016; 10: 420–430.

[10] Siddiq H, Pentapati KC, Shenoy R, Velayutham A, Acharya S. Evaluation of sugar content and erosive potential of the commonly prescribed liquid oral medications. Brazilian Research in Pediatric Dentistry and Integrated Clinic. 2020; 20: e5025.

[11] Sköld UM, Birkhed D, Xu JZ, Lien KH, Stensson M, Liu JF. Risk factors for and prevention of caries and dental erosion in children and adolescents with asthma. Journal of Dental Sciences. 2022; 17: 1387–1400.

[12] Jung EH, Jun MK. Evaluation of the erosive and cariogenic potential of over-the-counter pediatric liquid analgesics and antipyretics. Children. 2021; 8: 611.

[13] Cheun SK, Jeong MJ, Ahn YS, Lee YJ, Ko MK, Jeong SJ, *et al*. Effects of the enamel erosion caused by certain antipyretic and analgesic medicines for children. Journal of Dental Hygiene Science. 2016; 16: 235–241.

[14] Mahmoud EF, Omar OM. Erosive and cariogenic potential of various pediatric liquid medicaments on primary tooth enamel: a SEM study. Dental and Medical Problems. 2018; 55: 247–254.

[15] Zhao D, Tsoi JKH, Wong HM, Chu CH, Matinlinna JP. Paediatric over-the-counter (OTC) Oral liquids can soften and Erode enamel. Dentistry Journal. 2017; 5: 17.

[16] Vakil N, Kaur K, Sachdeva S. Study of erosive alterations in dental enamel exposed to medicinal syrups. International Journal of Applied Dental Sciences. 2019; 5: 227–229.

[17] Saeed S, Bshara N, Trak J, Mahmoud G. An *in vitro* analysis of the cariogenic and erosive potential of pediatric liquid analgesics. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2015; 33: 143–146.

[18] Gupta M, Panda S. Cariogenic potential of the commonly prescribed pediatric liquid medicaments in Kingdom of Saudi Arabia: an *in vitro* study. The Journal of Contemporary Dental Practice. 2017; 18: 307–311.

[19] Gowdar IM, Aldamigh SA, Alnafisah AM, Wabran MS, Althwaini AS, Alothman TA. Acidogenic evaluation of pediatric medications in Saudi Arabia. Journal of Pharmacy and Bioallied Sciences. 2020; 12: S146–S150.

[20] Kiran KJ, Vinay C, Uloopi K, Sekhar RC, Madhuri V, Alla RK. Erosive potential of medicated syrups on primary teeth: an *in vitro* comparative study. British Journal of Medicine and Medical Research. 2014; 5: 525–532.

[21] Tiwari M, Mhatre S, Vyas T, Bapna A, Raghavan G. A validated HPLC-RID Method for quantification and optimization of total sugars: fructose, glucose, sucrose, and lactose in eggless mayonnaise. Separations. 2023; 10: 199.

[22] Pasdar N, Alaghehmand H, Mottaghi F, Tavassoli M. Experimental study of iron and multivitamin drops on enamel microhardness of primary tooth. Journal of International Society of Preventive and Community Dentistry. 2015; 5: 518–524.

[23] Jamal DY, Farsi NM, El-Housseiny AA, Felemban OM. Effects of pediatric liquid medications on surface properties of dental restorations. Medical Science. 2022; 26: ms57e2000.

[24] Gürgan S, Önen A, Köprülü H. *In vitro* effects of alcohol-containing and alcohol-free mouthrinses on microhardness of some restorative materials. Journal of Oral Rehabilitation. 1997; 24: 244–246.

[25] Boulton J, Hashem KM, Jenner KH, Lloyd-Williams F, Bromley H, Capewell S. How much sugar is hidden in drinks marketed to children? A survey of fruit juices, juice drinks and smoothies. BMJ Open. 2016; 6: e010330.

[26] Mathew MG, Gurunathan D. Evaluation of knowledge, attitude and practice of pediatricians towards long-term liquid medicaments and its association with dental health. Journal for Educators, Teachers and Trainers. 2022; 13: 491–496.

[27] Litsas G, Lucchese A. Dental and chronological ages as determinants of

peak growth period and its relationship with dental calcification stages. The Open Dentistry Journal. 2016; 10: 99–108.

[28] Alharbi SM, Alluheybi AA, AlHarbi AA, Alkaabi LK, Alshahrani KM, Farrash KK, *et al*. Common chronic conditions in pediatric primary care. International Journal of Community Medicine and Public Health. 2022; 9: 3911–3916.

[29] Seredin P, Goloshchapov D, Kashkarov V, Emelyanova A, Buylov N, Barkov K, *et al*. Biomimetic mineralization of tooth enamel using nanocrystalline hydroxyapatite under various dental surface pretreatment conditions. Biomimetics. 2022; 7: 111.

[30] Lussi A, Megert B, Shellis RP. The erosive effect of various drinks, foods, stimulants, medications and mouthwashes on human tooth enamel. Swiss Dental Journal. 2023; 133: 440–455.

[31] Jeong GJ, Khan F, Tabassum N, Kim YM. Alteration of oral microbial biofilms by sweeteners. Biofilm. 2023; 7: 100171.

[32] Yılmaz N, Baygin O, Cakıroglu TN, Tüzüner T, Deger O. *In vitro* evaluation of the effects of frequently prescribed pediatric drugs on the microhardness of permanent tooth enamel. Dental and Medical Problems. 2019; 56: 131–136.

[33] Mukundan D, Vignesh R. Comparative evaluation on the effects of three pediatric syrups on microhardness, roughness and staining of the primary teeth enamel: an *in-vitro* study. Cureus. 2023;15: e42764.

[34] Scribante A, Pascadopoli M, Bergomi P, Licari A, Marseglia GL, Bizzi FM, *et al*. Evaluation of two different remineralising toothpastes in children with drug-controlled asthma and allergic rhinitis: a randomised clinical trial. European Journal of Paediatric Dentistry. 2024; 25: 137–142.

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