Pediatric Liquid Medicaments – Do They Erode The Teeth Surface? An *In Vitro* Study: Part I

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The present study was conducted to investigate the endogenous erosive potential of some of the most commonly used pediatric liquid medicaments in our day to day practice. Eight commonly used pediatric liquid medicaments were selected and their endogenous pH was measured using a pH electrode meter. Twenty four exfoliated or extracted primary teeth without any carious lesion/restorations, maintained in selected pediatric liquid medicaments were observed under SEM after 1 min, 10 mins and 8 hours of time intervals. The pH ranged between 6.05 (Salbutamol) to 6.77 (Paracetamol) which were acidic, whereas Theophylline had a basic pH of 7.71. The irregular pattern of pit –like erosion area were seen in all specimens, varying from site to site and probably depending on the prismatic versus aprismatic nature and composition of the affected enamel. In conclusion, all the pediatric liquid medicaments used in this study showed an erosive effect on the primary enamel surface irrespective of their pH when viewed under SEM.
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INTRODUCTION

The use of liquid pharmaceutical preparations is usually for short duration, but for some children it may be a daily occurrence. The active ingredients in these medicines are necessary for improvement or maintenance of health; some inactive ingredients pose dangers like dental caries and dental erosion.

The recent move to remove sugars from medicines to reduce the risk of dental caries has been welcomed by dentists, but concern has been expressed that the replacement sugar-free medicines might themselves damage teeth.[1]

To reformulate medicines without sugars, some products might require addition of weak acids to optimize their palatability and formulation properties. The question is whether this might increase the risk of dental erosion, i.e., have we swapped one problem (dental caries) for another (dental erosion)?[1]

Dental erosion becomes a potential issue when medicines with prolonged oral clearance are taken long term for chronic illness. In healthy children, the risk of medicine-induced erosion is low compared with the risk of erosion from acids in fuzzy soft drinks, but it is important in chronically sick children who may need more complex dental care because of their underlying medical condition.[1]

The erosive potential of food, beverages and liquid preparations depends on; pH, total acid level (titratable acid), type of acid (pKa), calcium chelation properties and physical and chemical properties affecting adherence to the enamel surface and stimulation of salivary flow.[2]

Liquid preparations with the lowest pH have been found to erode enamel mostly *in vitro*.[3] In essence, any medication with a low pH that comes in frequent and /or sustained contact with teeth has the potential to cause dental erosion. As early as 1886 the erosive potential of medicines was demonstrated by Weld GW.[4] More recently achlorhydria sufferers were found to sustain dental erosion as a result of treatment with liquid hydrochloric acid by mouth.[5,6]

Many other western studies have confirmed that these pediatric liquid medicaments are cariogenic and acidogenic in nature.[7,8,9] But, only few studies have been conducted in our environment to research the acidogenic potential of these medicated syrups.

Hence, the aim of the present study was to investigate the endogenous erosive potential of some of the most commonly used pediatric liquid medicaments in our day to day practices. This was studied by measuring the endogenous pH of the medicaments and observing the surface changes of primary enamel upon exposure to these medicaments.

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Table 1. Pediatric Liquid Medicaments used in the study and their pH.

PLM	Generic Name / International Nonproprietary Name(INN)	Brand Name	Pharmaceutical company	pH of the PLM
Analgesics	Nimesulide Paracetomaol	Nise ® Crocin®	Dr. Reddy's Lab Ltd. Smithkline Beecham Asia Pvt. Ltd.	6.2 6.77
Antibiotics	Amoxycillin Erythromycin	Mox® Althrocin®	Ranbaxy Lab Ltd. Alembic Ltd.	6.62 6.73
Antiasthmatics	Salbutamol Theophylline	Salbid® Theopid®	Eros Pharma Ltd. Cipla Ltd.	6.05 7.71
Multivitamin	Multivitamin with zinc Multivitamin	Zevit ® Vi-syneral®	Remidex Pharma Pvt. Ltd. Aviat Chemicals Pvt.Ltd	6.25 6.67

MATERIALS AND METHODS

The eight commonly used pediatric liquid medicaments (PLM) were selected for the study and their endogenous pH was measured (Table 1) using a pH electrode meter.

Twenty seven exfoliated or extracted caries and restoration-free primary teeth were selected for the study. The teeth were stored as per the OSHA regulation until the experiments were performed.

Twenty seven teeth were divided into two groups viz control group and the study group consisting of 3 teeth and 24 teeth respectively. The control group samples (3) were immersed in artificial saliva for three different time intervals (1 min, 10 mins and 8 hours). The study group samples (24) were maintained for 1 min, 10 mins and 8 hours in various selected PLM (Table 2).

The primary enamel surface changes were then observed under Scanning Electron Microscope (SEM) (JEOL, JSM-5600LV, Tokyo, Japan)

Table 2. Procedure protocol for observation of primary enamel surface changes under SEM.

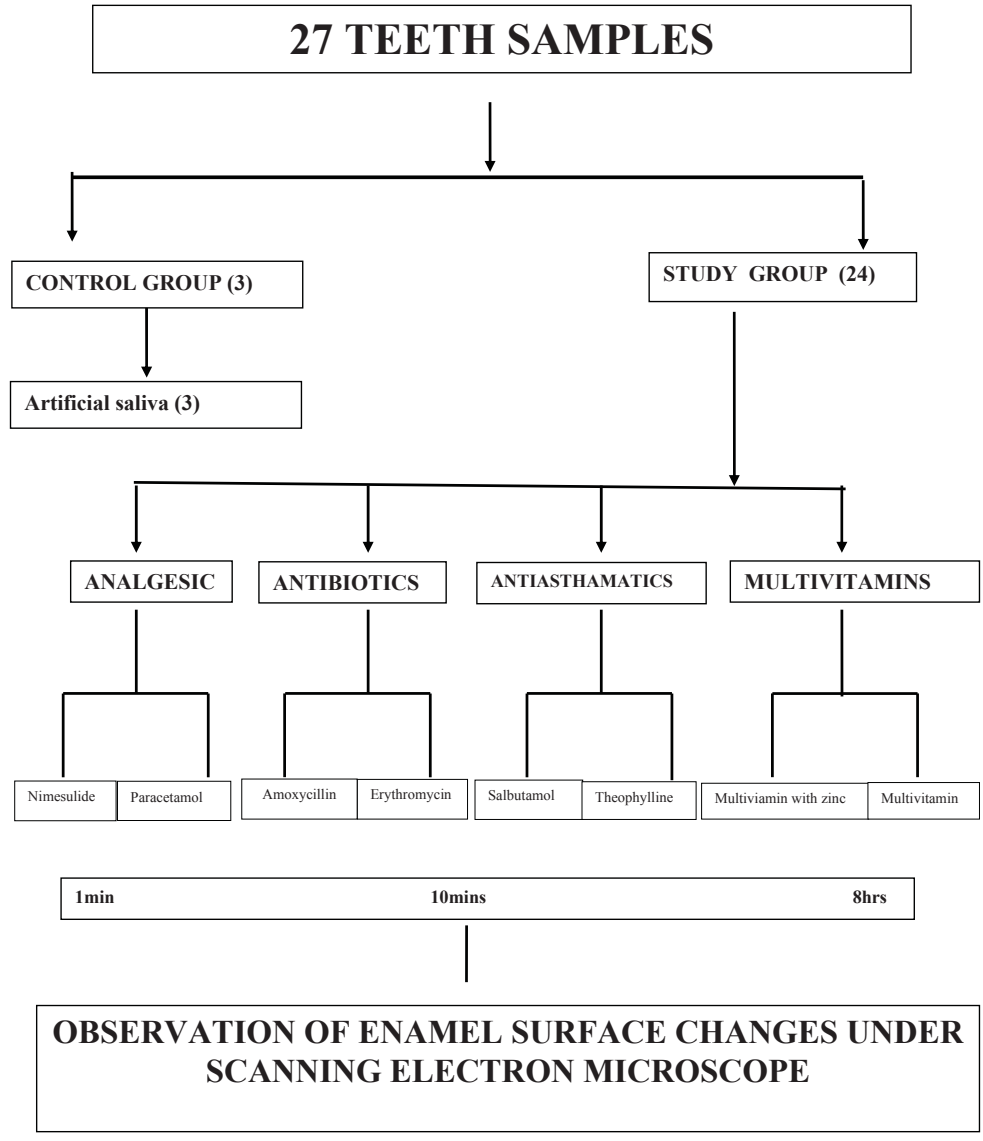

Table 3. Primary enamel surface changes observed under SEM.
(Note: Ж → Type of surface change seen under SEM)

PLM	TIME INTERVALS	SEM SURFACE MAPPING		
		SPORADIC ROD ENDS VISIBLE	ETCHED PRISM PATTERN	CRATER FORMATION
Nimesulide	1min		Ж	
	10 mins			Ж
	8hrs		Ж	
Paracetomaol	1 min	Ж		
	10mins	Ж		
	8hrs		Ж	
Amoxycillin	1 min		Ж	
	10 mins			Ж
	8hrs		Ж	
Erythromycin	1min		Ж	
	10 mins	Ж		
	8hrs			Ж
Salbutamol	1 min			Ж
	10 mins	Ж		
	8hrs		Ж	
Theophylline	1 min			Ж
	10 mins		Ж	
	8hrs		Ж	
Multivitamin with zinc	1 min		Ж	
	10 mins		Ж	
	8 hrs		Ж	
Multivitamin	1 min		Ж	
	10 mins		Ж	
	8 hrs	Ж		

RESULTS

pH OF THE PEDIATRIC LIQUID MEDICAMENTS

The pH of each pediatric liquid medicament was measured using a pH electrode meter. The pH ranged between 6.05 (Salbutamol) to 6.77 (Paracetamol) being acidic, whereas Theophylline had a basic pH of 7.71 (Table 1).

SURFACE CHANGES OF PRIMARY ENAMEL

Primary enamel treated with various PLM was observed under the SEM at 1 minute, 10 minutes and 8 hours (Table 3 and Figures 1 to 9) The surface mapping was done according to Sharma *et al.* [10]

This study demonstrated the erosive effect on the primary enamel surface when viewed under the SEM. In most of the medicaments we observed etched prism pattern and crater formation on the enamel immersed in medicaments at 10 minutes and 8 hours and sporadic rod ends were seen at the end of 1minute. But in the case of Multivitamin with zinc (Zevit®) we observed an etched prism pattern in all time intervals. The etched prism pattern was seen on all the primary enamel surfaces irrespective of the immersion time intervals. In the current study irregular patterns of pit-like erosion areas were seen in all specimens, varying from site to site, and probably depending on the prismatic versus aprismatic nature and composition of the affected enamel.

DISCUSSION

Despite the success of preventive dentistry there are a growing number of reports of a decline in the quality of very young children's teeth.[11,12] High intake of acidic drinks, fruits and medications may constitute the possible etiological or aggravating factors for severe dental erosion,[13] the predisposing factor for dental caries. In addition, it would appear that the frequency of sugar intake is more important than the total amount consumed. Thus, an important method of preventing dental caries is to limit the frequency of sugar containing foods and drinks to meal times. Many parents are aware that sugar causes tooth decay but commonly compare this solely with the consumption of sweets and biscuits. They are often unaware of the hidden, added sugar in many foods and drinks, including pediatric liquid medicines.[14]

The deleterious effect of liquid oral medicaments has been studied by Imfeld[7] since 1953. The most conclusive

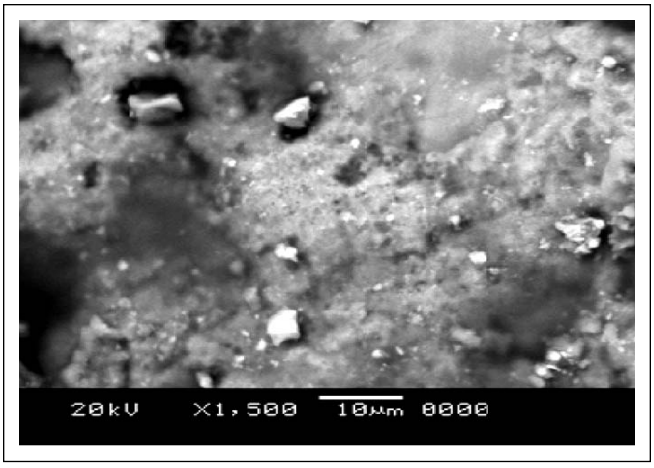

Figure 1. Crater formation seen on primary enamel surface after immersing in Nimesulide for 10 mins.

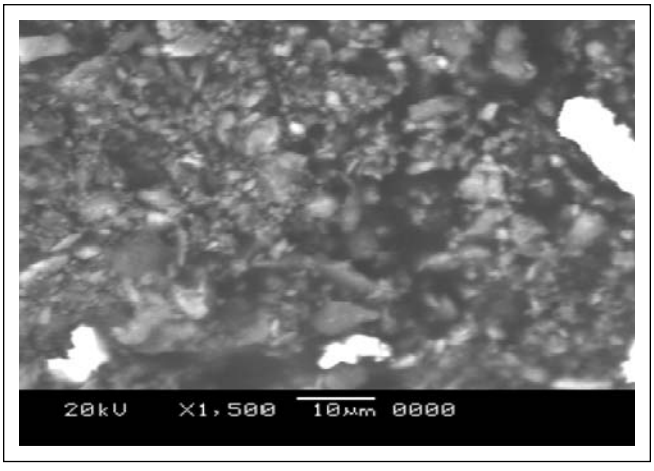

Figure 2. Sporadic rod ends seen on primary enamel surface after immersing Paracetamol for 10 min.

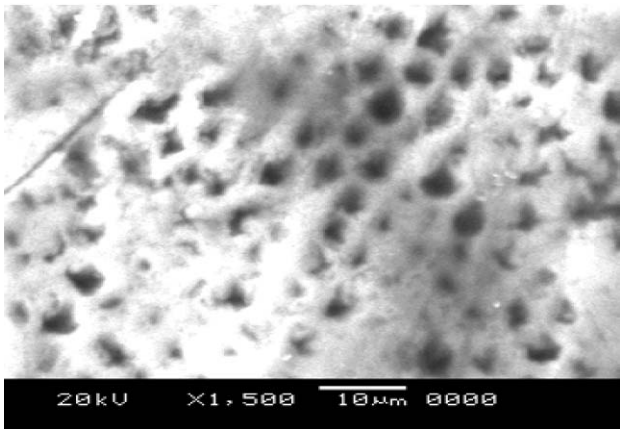

Figure 3. Etched prism pattern seen on primary enamel surface after immersing in Amoxycillin for 1 min.

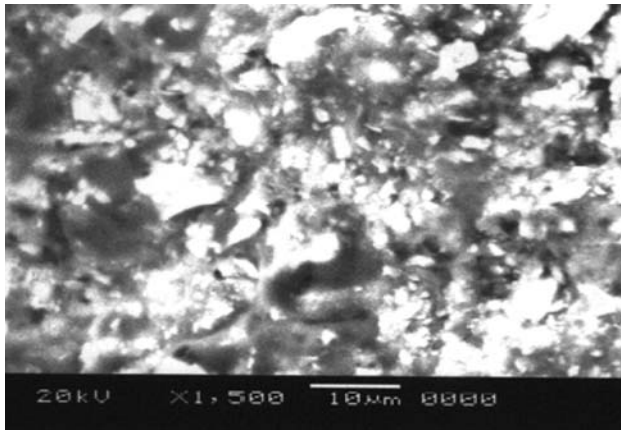

Figure 4. Sporadic rod ends seen on primary enamel surface after immersing in Erythromyocin for 10 min.

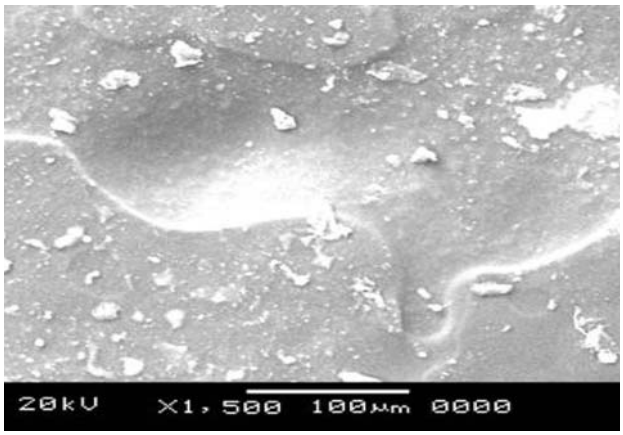

Figure 5. Crater formation seen on primary enamel surface after immersing in Salbutamol for 1 min.

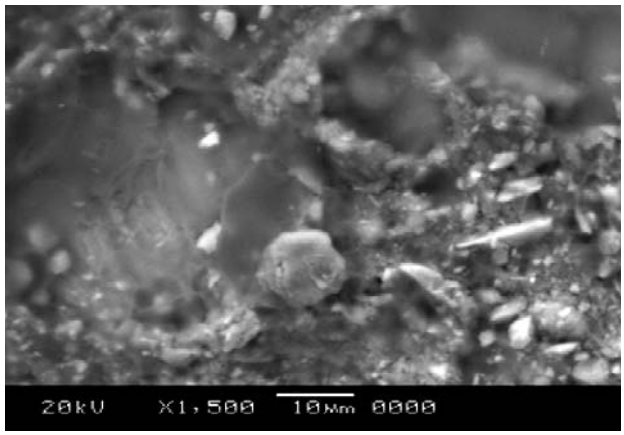

Figure 6. Crater formation seen on primary enamel surface after immersing in Salbutamol for 10 min

evidence was provided by Roberts and Roberts[15,16] showing that, a continuous administration of sucrose based medicines causes dental caries and related gingivitis. Other co-workers have confirmed that these preparations are cariogenic and acidogenic in nature.[3,7,8,9,15] Thus, the present study was conducted to investigate the acidogenic potential of commonly used pediatric liquid medicaments in our day to day practice.

The acidogenicity of liquid preparations depends on pH, tritability, buffering capacity and organic acids present in the medications.[2] Many of the liquid syrups are maintained in acidic pH. In a study conducted by Greenwood, the liquid syrup had an acidic pH of 2.86.[3] The pediatric liquid medicaments data sheet used in the current study did not specify any valuable information about the pH or the specific kind of sucrose present. It read only, along with the specific composition, sweetened with a particular flavor. Therefore, the pH of each pediatric liquid medicament used in the present study was measured using a pH electrode meter. The pH of the each pediatric liquid medicament is shown in table-I ranging between 6.05 (Salbutamol) and 6.77 (Paracetamol) being acidic, whereas, Theophylline had a basic pH of 7.71.

The erosive effects of these pediatric liquid medicaments on the primary enamel surface were studied using the SEM. The teeth specimens were treated with the different pediatric liquid medicaments shown in Table-1 and maintained for three different time intervals (1 minute, 10 minutes and 8 hours). The primary enamel surface changes were observed under the SEM.

Even though the pH of pediatric liquid medicaments was not near the critical pH of that of the oral cavity, erosion of the primary enamel surface was evident when studied under the SEM. This is in agreement with the study of Greenwood who used the SEM to evaluate the erosion potential of liquid syrup on rats' enamel.[3]

We observed an etching pattern on most of the enamel surface. A typical type of prism pattern was observed on the enamel surface treated with Amoxycillin for 1 minute, Theophylline for 1 minute and Multivitamin (Vi-syneral®) for 10 minutes.

Silverstone, Saxton and Dogom[17] described three basic types of etching pattern i.e. type –I, type-II and type-III. The prism pattern on primary enamel surface observed in our study was similar to the type-I etching pattern where the prism core material was preferentially removed leaving the

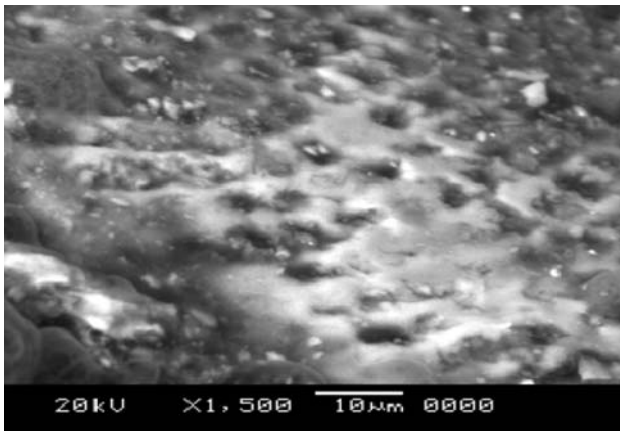

Figure 7. Etched prism pattern seen on primary enamel surface after immersing in Theophylline for 10 min.

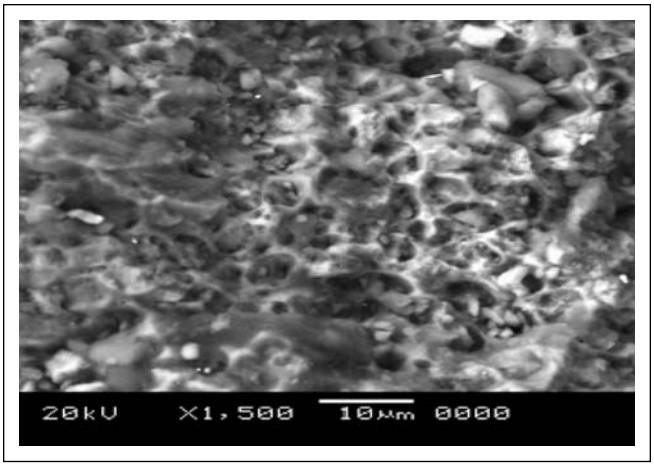

Figure 8. Etched prism pattern seen on primary enamel surface after immersing in Multivitamin with zinc for 10 min.

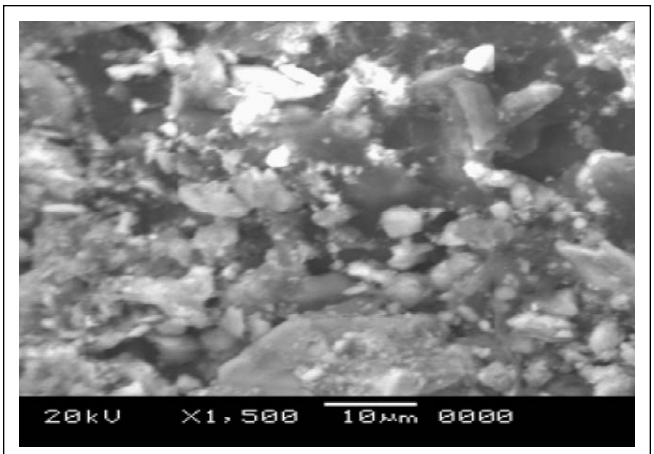

Figure 9. Sporadic rod ends seen on primary enamel surface after immersing in Multivitamin for 8 hrs.

prism periphery relatively intact in a honeycomb prism appearance**.** They also stated that this type I etching pattern can be easily explained by noting that the crystals reach the enamel surfaces at different inclinations in the rods as compared to the inter rod areas. Our SEM micrographs showed that the surface was smooth, slightly etched, revealing faint outlines of scales. The enamel rods were clearly opened. The section edges were deep enough to be visible under the SEM.

The enamel surface was treated with Nimesulide for 1minute and 8 hours, Paracetamol for 8 hours, Amoxycillin for 8 hours, Erythromycin for 1minute, Salbutamol for 8 hours, Theophylline for 8 hours, Multiviamin with zinc (Zevit®) for 1minute and 8 hours and Multivitamin (Vi-syneral®) for 1 minute and 8 hours also presented a prism pattern, but it did not show the classical appearance. This atypical appearance of enamel surface is supported by Grando *et al,* who stated that complexity may be seen in the different patterns of loss of enamel structure in eroded primary teeth.[18] The same has been known with regards to eroded permanent teeth.[19,20]

In some instances, the surface topography could not be related to the type –III etching pattern, generally associated with an aprismatic type of enamel.[17] Some of the enamel surface looked like large craters on a moonscape. This type of appearance was observed on the enamel surface treated with Nimsulide for 10 minutes, Erythromycin for 8 hours, Amoxycillin for 10 minutes, Salbutamol for 1 minute and Theophylline for 1 minute. In this study an irregular pattern of pit-like erosion areas was seen in all specimens, irrespective of their pH, varying from site to site, and probably depending on the prismatic versus aprismatic nature and composition of the affected enamel.

Among the pediatric liquid medicaments, the pH did not appear to contribute to the erosion pattern seen on the primary enamel surface. Therefore, we would relate this to chelation. Chelation is independent of the pH of the medium, so that removal of metallic ions like calcium from a biological calcium-phosphorous system may occur at a neutral or even alkaline pH.[21]

It has been stated that the SEM analyses should be mainly used to visualize the pathology and should not be used in isolation, without quantitative methods.[22] Therefore a step further will be taken in next part of this study where quantification of the erosion caused by the pediatric liquid medicaments will be analyzed.

CONCLUSION

All the pediatric liquid medicaments used in this study showed an erosive effect on the primary enamel surface irrespective of the pH of the pediatric liquid medicaments.

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