



## RESEARCH ARTICLE

### EVALUATION OF SURFACE CHANGES IN DECIDUOUS ENAMEL CAUSED BY COMMONLY USED PEDIATRIC LIQUID MEDICINES, OBSERVED UNDER SCANNING ELECTRON MICROSCOPY (SEM): AN *IN VITRO* STUDY

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#### ABSTRACT

**Background:** The present in-vitro study was a scanning electron microscope (SEM) study conducted in primary teeth in order to evaluate the erosive potential of two commonly used pediatric liquid medications (PLMs), the anti-biotics and the analgesics. The commonly used antibiotic in the study was Mox-redimix, Ranbaxy and Ibugesic Plus, cipla was chosen for the analgesic group.

**Materials and Methods:** Thirty extracted teeth were randomly divided into 2 groups viz. Control group and Test Group. Control group (n=10) samples were immersed in 10 ml of artificial saliva whereas the Test Group was divided into 2 subgroups viz. Antibiotic Group (n=10) and Analgesic Group (n=10). The teeth from the Test Group were maintained in the pediatric liquid medicines for 8 hours at 37 C. After 8 hours, the samples were rinsed with running water and observed under scanning electron microscopy (SEM) under the environmental setting of the microscopy.

**Results:** Deciduous enamel treated with pediatric liquid medicaments at 8 hours was observed under SEM. Surface mapping was done according to Sharma *et al.* Control group samples, which were treated with artificial saliva, did not show any changes on the primary enamel. In the test group, i.e. the antibiotic and analgesic groups the SEM micrographs showed that the surface was smooth, etched and outlines of scales were seen. The enamel rods were clearly opened. In most of the samples of the analgesic group, the surface topography could be related to the Type III etching pattern, which is generally associated with an aprismatic type of enamel. While the samples of the antibiotic group, showed crater like formation.

**Conclusion:** The pediatric liquid medicines are acidogenic in nature and their frequent use should be discouraged, unless absolutely necessary. Preventive protocol should be advised along with the use of pediatric liquid medicines eg., ingestion at mealtime if possible, avoid ingestion at bed time.

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#### INTRODUCTION

Dental caries has been associated with type, concentration and frequency of consumption of sugar in various forms. Many parents are aware that sugars cause tooth decay, they commonly relate this solely to the consumption of sweets and biscuits. They are often unaware of hidden, added sugars in many foods and drinks including pediatric liquid medicines. The active ingredients in these medicines are necessary for improvement or maintenance of health, while some inactive ingredients pose dangers like dental erosion and dental caries (Girish Babu *et al.*, 2008). Many liquid oral pediatric medicines are embedded with carbohydrates, such as sucrose and glucose which directly

influence the cariogenic and acidogenic potential of the solutions. Pharmaceutical firms sweeten liquid preparation to increase the palatability, add bulk, and supposedly increase compliance. Sucrose remains widely used because it is cheap, non hygroscopic, and easy to process (Anne Maguire *et al.*, 1994). High sucrose concentration of 80% in pediatric medicines has also been reported. Thus, sucrose concentration in medicines is higher than in soft drinks (4.3%) and ice-cream (15.1%) (Marqezan *et al.*, 2017). In addition to the sucrose content in the medicines and caries risk in children, these products sometimes have a low pH, which increases the risk of dental erosion. The erosive potential of food, beverages and liquid preparations depends on: pH, total acid level, type of acid (pKa), calcium chelation properties affecting adherence to the enamel surface and stimulation of salivary flow.

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The aim of this study was to observe the erosive potential of the pediatric liquid medicines.

## MATERIALS AND METHODS

This study was performed in the Bharati Vidyapeeth University – Dental College & Hospital, Pune after it was approved by the research committee of the institute. Human deciduous extracted or exfoliated teeth were used as samples which were obtained from the patients visiting Bharati Vidyapeeth University – Dental College & Hospital. The teeth used were extracted for therapeutic reasons.

### Inclusion criteria

Exfoliated or Extracted primary teeth with intact enamel surface

### Exclusion criteria

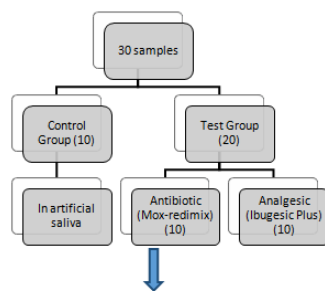
1. carious teeth
2. restored teeth
3. teeth with developmental defects

### Collection of samples and storage

30 deciduous extracted or exfoliated teeth were collected and stored as per OSHA (Guidelines for Infection Control in dental healthcare settings, 2003) (Occupational Safety and Hazard Association) regulations until the experiment was performed. These teeth were cleaned of visible blood and gross debris and maintained in a hydrated state in a well-constructed closed container containing saline. The teeth were heat-sterilized, by autoclaving for 40 minutes.

### Study Design

The extracted teeth were randomly divided into 2 groups viz. Control group and Test Group. The endogenous pH of the test pediatric liquid medicines was assessed using the pH meter (pHEP, Hanna) Control group samples were immersed in 10 ml of artificial saliva whereas the Test Group was divided in to 2 subgroups viz. Antibiotic Group and Analgesic Group. The pediatric liquid medicine from the antibiotic group was Mox-redimix, Ranbaxy and from the analgesic group was Ibugesic Plus,



### To be observed under SEM

The teeth from the Test Group were maintained in the pediatric liquid medicines for 8 hours at 37 C. After 8 hours, the samples were rinsed with running water and observed under scanning electron microscopy (SEM) under the environmental setting of the microscopy.

## RESULTS

The results were tabulated and statistically analyzed using the Non-parametric tests, Mann-Whitney U test for the calculation of p-value and Wilcoxon sign rank tests. Deciduous enamel treated with pediatric liquid medicaments at 8 hours was observed under SEM. Surface mapping was done according to Sharma *et al.* Control group samples, which were treated with artificial saliva, did not show any changes on the primary enamel. Even though the pH was not near the critical pH of the oral cavity, erosion of the primary enamel was evident in the analgesic group and the antibiotic group. This was in agreement with the study of Greenwood (Greenwood *et al.*, 1984), who used SEM to evaluate the erosive potential of liquid syrups on rats' enamel and the study by Girish Babu (Girish Babu *et al.*, 2008) *et al.* Silverstone, Saxton and Dogon, (1975) described three basic types of etching patterns, i.e. Type I, Type II, Type III. In the test group, i.e. the antibiotic and analgesic groups the SEM micrographs showed that the surface was smooth, etched and outlines of scales were seen. The enamel rods were clearly opened. In most of the samples of the analgesic group, the surface topography could be related to the Type III etching pattern, which is generally associated with an aprismatic type of enamel. While the samples of the antibiotic group, showed crater like formation. Mann-Whitney U test was applied and the p-value obtained was less than 0.05 and hence there is significant difference between control group and analgesic group, control group and antibiotic group with respect to grade of change observed under SEM.

## DISCUSSION

Pharmaceutical products often contain agents that have a variety of purposes, including improvement of the appearance, bioavailability, stability and palatability (Beatriz Goncalves Neves, 2007). In the treatment of pediatric patients, physicians often have a difficult task ensuring the compliance of the patient to a particular medication regimen, so the use of pleasant tasting oral liquid medicines has helped in the administration of these drugs (Anne Maguire, 1994). In a study by Beatriz Neves *et al.* 2007, the influence of pharmaceutical industry appears as the least relevant factor for the majority of professionals regarding their prescription patterns' decision. They pointed that even in countries where sugar-free medicines have become widely available; many doctors continue to prescribe sugared medicines. The long-term use of prescribed medicines by chronically sick children is known to cause dental caries (Beatriz Goncalves Neves, 2007; Anne Maguire, 1994; Duward, 1997).

Children take medicines on an average three times a day or every eight hours (Ali Menten, 2001). Also, these medicines are often given to children last thing at night. Thus, the samples used in this study (human deciduous extracted teeth) were treated with antibiotic and analgesic syrup for 8 hours. There is a continuous change in salivary pH following consumption of foods and beverages, especially with fermentable carbohydrates. Differences were seen between the caries-free group and caries-active group, with caries-free group having a significantly low pH (Stephan, 1944). As the pH drops from bacterial acid by-products, the level of super saturation of the calcium and phosphate also drops and the risk of demineralization increases. While there is no exact pH at which demineralization begins, a general range of 5.5 – 5.0 is considered critical for tooth mineral to dissolve (Stephan, 1944; Stephan, 1940).

## SEM analysis of the three groups at different magnifications

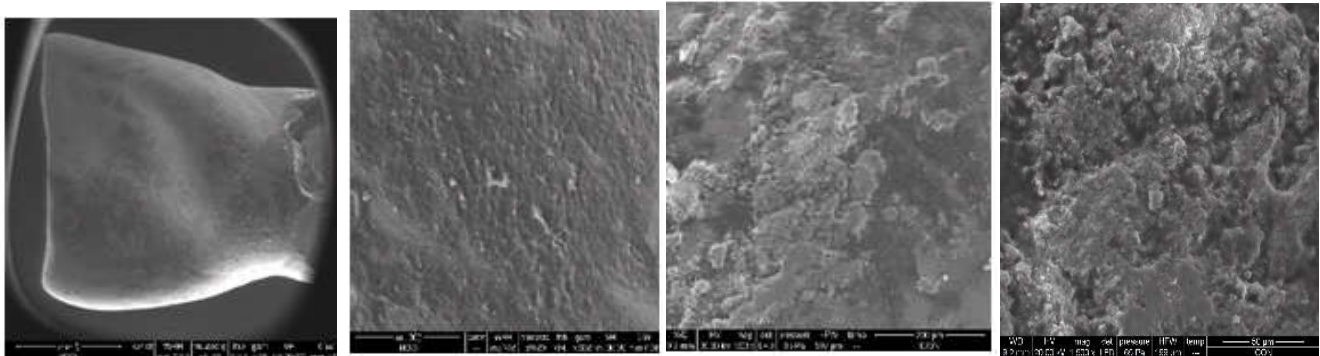


Fig 2. Analgesic Group at 46X, 500X and 1500X magnifications

Fig 3. Anti biotic Group at 42X, 200X, 500X and 1500 X magnification

Table 2. Compilation of Observations

Group	Grade				Total
	No change (0)	Sporadic Rods Visible (1)	Etched Prism Pattern (2)	Crater Formation (3)	
Control	10	0	0	0	10
Analgesic	0	0	6	4	10
Antibiotic	0	0	2	8	10

Table 3. Calculation of p value

	Median Grade	p-value
Control	0	
Analgesic	2	< 0.001
Antibiotic	3	< 0.001

The cariogenic potential of any medicine must take into account not only its sucrose concentration but also its frequency of use, dose, and pattern of use (Ali Mentis, 2001; Pierro *et al.*, 2005). The administration of only one dose at night occurs during a period of significantly decreased salivary flow, which may increase the risk of caries development. It has been postulated that use of sugar containing liquid oral

medicines poses a threat to dental health, especially when taken long-term (Anne Maguire *et al.*, 1994; Aubrey Sheiham, 1984; Duward, 1997). The inclusion of sugars, particularly sucrose, in children's medicines is primarily to mask the less pleasant taste of active ingredients and many studies have related these substances to dental caries (Girish Babu *et al.*, 2008; Pierro *et al.*, 2005).

The most conclusive evidence was provided by Roberts and Roberts (Robert *et al.*, 1979) showing that a continuous administration of sucrose-based medicines causes dental caries related gingivitis. The acidogenicity of liquid preparations depends on pH, titrability, buffering capacity and organic acids present in the medication (Addy *et al.*, 2000). Many of the liquid syrups are maintained in acidic pH. In a study by Greenwood (Greenwood, 1984), the liquid syrups had an acidic pH of 2.86. The pediatric liquid medicaments data sheet used in the current study did not specify valuable information about the pH or the specific kind of sucrose present. It read only, along with specific composition, sweetened with a particular flavor. Therefore, the pH of both pediatric liquid medicaments used in the study was measured using a pH electrode meter. The pH values obtained were, 6.4 for Mox-redimix (antibiotic) syrup and 6.1 for Ibugesic Plus (analgesic) syrup. And the value obtained for artificial saliva was 7.0, which is the neutral pH. Both these medicines had slightly acidic pH. The erosive effects in our study were studied on the primary enamel surface using SEM.

In this study, environmental SEM was used which does not require vacuum and renders the samples reusable. Primary enamel treated with the pediatric liquid medicines (antibiotics and analgesics) and the artificial saliva was observed under e-SEM (environmental-SEM). Surface mapping was done according to Sharma *et al.*, (1992) where the observed patterns were classified as sporadic rods visible, etched prism pattern and crater formation. Even though the pH was not near the critical pH of the oral cavity, erosion of the primary enamel surface was evident. This is in agreement with the study by Greenwood (Greenwood, 1984), who used SEM to evaluate the erosive potential of liquid syrup on rats' enamel and the study by Girish Babu *et al.* (2008) In this study, antibiotics were found to be more erosive than the analgesic syrup. Even though, the pH of the analgesic syrup had a lower pH (more acidic) than the antibiotic syrup, antibiotic syrups showed crater formation in 8 out of 10 samples, while etched prism pattern was observed in 2 out of 10. While the samples treated with the analgesic syrup, showed etched prism pattern in most of the cases. These drugs may be erosive because they can possess some characteristics including acid components, low endogenous pH, high acidity, absence or low concentrations of ions such as calcium, fluoride, phosphate in their compositions. People are generally unaware of the damage caused by regular use of these medicines can sometimes cause to children's teeth and pediatricians are in an ideal position to influence parents' attitudes towards oral health (The negative impact of sugar-sweetened beverages on children's health, 2009). A clear policy on the labelling of sugar-containing medicine is needed. All medicines should be labelled with the type of sweetener and concentration, and, if, sugar-containing, with a warning on dangers of tooth (Isabela Albuquerque Passos *et al.*, 2010). This study was conducted simulating a few intraoral conditions under an *in vitro* model to demonstrate demineralization of lesions. The replication of dynamics of the caries and erosion processes, the complexity of the oral environment in these *in vitro* models is very limited. The effect of remineralizing potential of natural saliva, the cyclic changes during demineralization and remineralization and the effect of bacterial assaults in a chemical situation were not determined. However even with the limitations of an *in vitro* study, this study showed significant results in both demineralization with antibiotic syrup and the analgesic syrup. Hence it can be said that:

The commonly used pediatric liquid medicines are acidogenic and cause marked erosion on the deciduous enamel surface. Further *in vivo* studies in the use of pediatric liquid medicines as potential sources for dental caries and dental erosion, and the use of nano-hydroxyapatite containing toothpaste in *in vivo* models is required.

### Summary and Conclusion

Sweeteners added in the pediatric liquid medicines along with low endogenous pH form highly cariogenic formulations. Syrups are routinely prescribed to children because of their increased palatability.

### The conclusions of this study are

**The pediatric liquid medicines used in this study showed an erosive effect on the primary enamel.**

The pediatric liquid medicines are acidogenic in nature and their frequent use should be discouraged, unless absolutely necessary. Preventive protocol should be advised along with the use of pediatric liquid medicines eg., ingestion at mealtime if possible, avoid ingestion at bed time.

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