

## Original Research Article

# Erosive potential of three different commonly used pediatric syrups on deciduous teeth enamel: an in vitro study

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## ABSTRACT

**Background:** The aim of the study is to compare the erosive potential of three different commonly used pediatric syrups on deciduous teeth enamel. The objectives of the study were to assess the endogeneous pH and titratable acidity of mefenamic acid syrup (meftal P), cetirizine syrup (alerid) and multivitamin syrup (zincovit) and to evaluate the microhardness of the enamel after successive immersion cycles in each of the syrups.

**Methods:** 40 non carious deciduous teeth were included for the study. The samples were then randomly allocated into 4 groups (10 in each group): Group A- mefenamic acid syrup (meftal P), Group B- cetirizine syrup (alerid), group C- multivitamin syrup (zincovit) and group D- control (distilled water). The samples were then subjected to the immersion cycles in the syrups. Assessment of enamel surface microhardness was done using Vickers hardness tester at 7th day and 14th day. The pH and titratable acidity of the syrups were also assessed. One way analysis of variance (ANOVA) and post hoc tests were used for the statistical analysis.

**Results:** Out of the test groups, group C showed the lowest pH of around 4.2 and exhibited the largest titratable acidity (22.8 ml) compared with 21 ml in group A and 15.5 ml in group B. At the end of 14th day, group A had microhardness of about  $293.43.84 \pm 6.34$ , group B had  $299.930 \pm 6.85$ , group C had  $313.380 \pm 6.23$  and group D had  $334.190 \pm 5.51$ .

**Conclusions:** All the pediatric liquid medications assessed in the study, meftal P, alerid and zincovit showed acidic pH, high titratable acidities and all the syrups showed loss of microhardness after exposure to the syrups for 14 days. Loss of microhardness was highest for meftal P followed by alerid and least for zincovit.

**Keywords:** Enamel, Erosion, Microhardness, Syrups

## INTRODUCTION

Dental erosion can be defined as the irreversible dissolution of the tooth structure caused by intrinsic or extrinsic acids without bacterial involvement.<sup>1-3</sup> It can be caused by intrinsic or extrinsic factors.<sup>1</sup> Intrinsic factors include contact of dental tissues with gastric acids (i.e. regurgitation disorders due to gastrointestinal diseases). Extrinsic factors include consumption of acidic food, sports, drinks, wines and acidic medications.<sup>4,5</sup> Even though dental erosion in children can be controlled by modifying the dietary habits, exposure to long term medication can be a predisposing factor to dental erosion in children especially with chronic illness.<sup>6-8</sup>

Literature shows that liquid oral medications with high sucrose concentrations, high acidity and low endogeneous pH shows cariogenic potential.<sup>9</sup> To mask the bitter taste of most of the drugs caused by their chemical nature, pediatric medications usually contain sugars such as sucrose, fructose and glucose in addition to flavouring agents, preservatives and colouring agents.<sup>10</sup> Sucrose is the most commonly used sweetener for such medications, as it is an easily processed as well as cost-effective substance. These sugars, particularly sucrose, act as a substrate for the oral bacteria, which are responsible for their fermentation, leading to the production of acids and a subsequent drop in intraoral pH.<sup>11</sup> Acids are also added to medicines which acts as a buffering agent, helps to maintain a pH at which

the drug is sufficiently soluble and also chemically stable.<sup>12</sup> Addition of acids also ensures physiological compatibility.<sup>3</sup> As result of these characteristics, various studies have pointed out the possible relationship between dental caries and frequent intake of liquid oral medicines.<sup>6</sup>

Studies have also shown a positive correlation between the count of *Streptococcus mutans* (the main microorganism involved with dental caries) and antibiotic intake in children during the period considered the most critical to acquire these bacteria, which is between 1½ to 3 years of age, as compared to children who did not take antibiotics during the same period.<sup>13</sup>

Factors like low endogenous pH and high titratable acidity of these drugs favor dental erosion especially when there is a longer duration of contact with the tooth surface.<sup>1</sup> Liquid formulations that are used for a minimum of three months period are considered as a risk factor for increased incidence of caries.<sup>14</sup> Therefore, children who take vitamin C supplements have 4.7 times higher chance for developing dental erosion lesions.<sup>15</sup> A few studies have also shown that acidic medicines reduces enamel hardness of the deciduous teeth and can lead to morphological alterations of the enamel surface.<sup>16-18</sup> Factors such as high viscosity of liquid oral medication, lack of oral hygiene after the intake of medicine, bedtime and between meals consumption, its frequency of intake (i.e. two or more times daily) and the collateral effects of reduced salivary flow influences the potential for dental erosion and caries.<sup>19</sup> Bedtime intake of these medications can cause harm to the teeth as the reduced salivary flow during sleep will limit the salivary cleansing action.<sup>20</sup>

The trivial illness such as fever, allergy and vitamin deficiencies are very common in childhood and often receive medications such as antipyretic, antihistaminic, and multivitamin syrups for these conditions.<sup>3</sup> A high intake of these syrups may form possible etiological or aggravating factors for severe dental erosion in childhood especially among children under the age of 2 years.<sup>3</sup>

The vulnerability of deciduous teeth to acidic and cariogenic environment is found to be more than permanent teeth mainly because of variations in enamel thickness, its mineralization levels, and structural arrangement.<sup>3</sup> The enamel and dentin thickness of deciduous teeth is lesser than that of permanent teeth while its dental pulp is bigger which triggers fast caries.<sup>21</sup> However, some controversy remains regarding the difference in susceptibility to caries and erosion in both dentitions.<sup>4</sup>

In recent times, there has been an increase in self-medication with over-the-counter drugs which could lead to detrimental effects to the dental hard tissues and most of the parents are not aware about the presence of sugar in pediatric liquid medications.<sup>20</sup> Nowadays, various sugar free pediatric oral liquid formulations are available in the market which does not contain fructose, glucose or

sucrose.<sup>1</sup> Even though sugar substitutes have been introduced, its use in the preparation of pediatric syrups is still very minimal.<sup>2</sup>

The consumption of 'hidden sugars' by children has led to an increased concern among pediatric dentists.<sup>22</sup> However, data about enamel softening of commonly used over-the-counter (OTC) pediatric liquid medications is lacking.<sup>1</sup> Considering that some of these commonly used medicines by children may be a threat to oral health causing dental caries and erosion, the aim of this study is to assess in vitro on deciduous teeth enamel, the erosive potential of commonly used liquid oral pediatric medicines.

The aim of the study is to compare the erosive potential of three different commonly used pediatric syrups on deciduous teeth enamel.

Objectives of the study were to assess the endogeneous pH and titratable acidity of mefenamic acid syrup (mefal P), cetirizine syrup (alerid) and multivitamin syrup (zincovit); and also to evaluate the microhardness of the enamel after successive immersion cycles in each of the syrups.

## METHODS

The present study is an in vitro study which compares the erosive potential of three commonly used pediatric syrups, mefenamic acid syrup (mefal P), cetirizine syrup (alerid) and multivitamin syrup (zincovit). The pH and titratable acidity of the syrups are also compared. Ethical clearance was obtained from Institutional Ethical Review Board of Yenepoya Dental College, Mangalore, Karnataka, India.

### Sample preparation

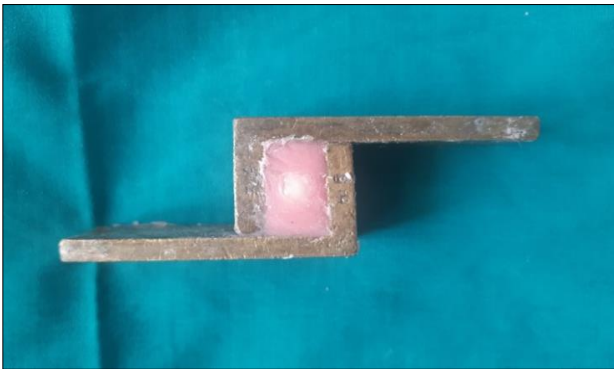
A total 40 non-carious extracted or exfoliated deciduous teeth including both anterior and posterior teeth were used for the study. The teeth which had pre-shedding mobility and which were indicated for extraction were collected from patients who visited Department of Pedodontics and Preventive Dentistry, Yenepoya Dental College, Mangalore. Teeth were hand scaled prior to the study in order to remove any debris on the teeth. Teeth were mounted on an acrylic base using L block such that the buccal surface of the teeth faces upwards and is in the same plane as the acrylic. The samples were polished using 1000-2000 grit abrasive papers and with pumice.



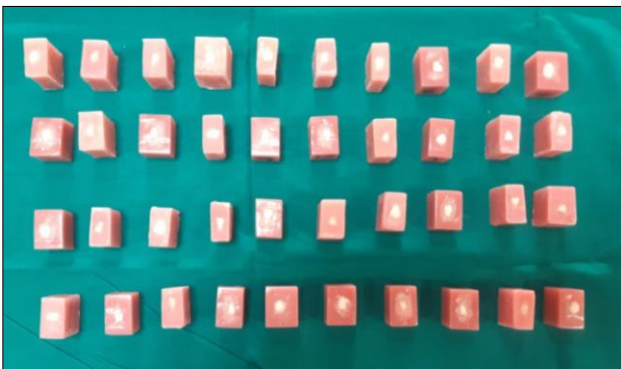
**Figure 1: Samples of deciduous teeth collected for the study.**



**Figure 2: L block used for the preparation of samples.**



**Figure 3: Samples mounted on acrylic using L block.**



**Figure 4: Samples mounted on acrylic mould.**



**Figure 5: Syrups used in the study (zincovit, meftal P, alerid).**



**Figure 6: Digital pH meter (Systronics, pH system 361).**

#### *Measurement of microhardness*

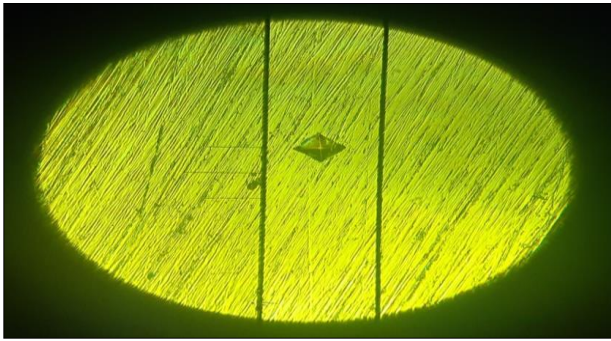
Initial enamel surface microhardness was assessed using Vickers hardness testing machine (Tec sol India) at Yenepoya Dental College, Mangalore (Figure 7). The force of 25 g was applied with the indenter diameter of 45.1 mm on to the enamel surface at three points and the average of the readings was obtained as Vickers hardness number.



**Figure 7: Vickers hardness tester (Tec sol India).**

The samples were then randomly allocated into 4 groups (10 in each group): group A- mefenemic acid (meftal P), group B- cetirizine syrup (alerid), group C- multivitamin syrup (zincovit), and group D- control (distilled water).

The samples were then subjected to the immersion cycles in the syrups which mimics the frequency of intake of each syrup. Each sample was immersed in 10 ml of the respective syrups for 1 minute in each of the test groups. In group A, the samples were dipped twice daily, in group B and C, the samples were dipped once daily for 14 days. Teeth were preserved in commercially available artificial saliva after the immersion cycles. Assessment of enamel surface microhardness was done using Vickers hardness tester (Tec sol India) at 7th day and 14th day.



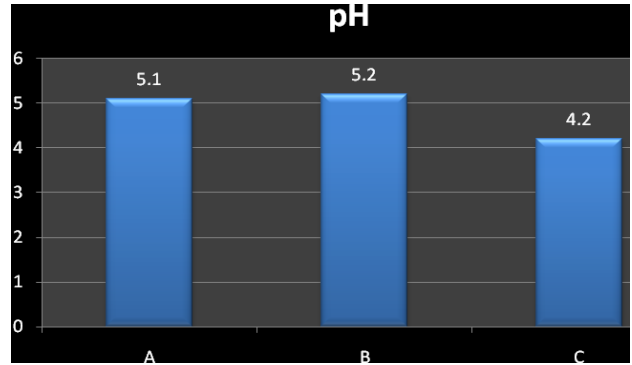
**Figure 8: Indentation seen through Vickers hardness tester.**

**Statistical analysis**

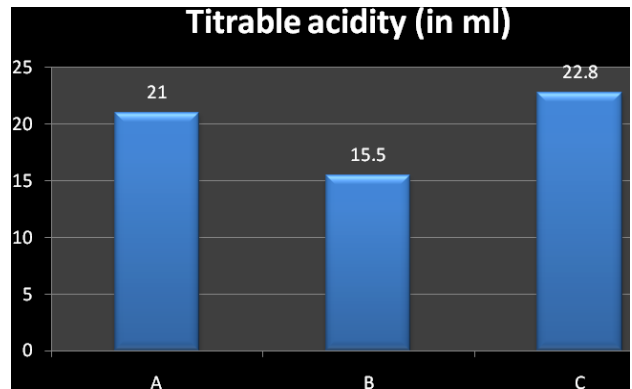
One way analysis of variance (ANOVA) and post hoc tests were used for the statistical analysis. Data analysis was done using Statistical Package for the Social Sciences (SPSS) software.

**RESULTS**

Out of the test groups, group A (meftal P) showed a pH of 5.1, group B (alerid) showed the highest pH which was about 5.2 and group C (zincovit) showed the lowest pH of around 4.2 (Figure 9). Group C (zincovit) exhibited the largest titrable acidity (22.8 ml) compared with 21 ml in group A (meftal P) and 15.5 ml in group B (alerid) (Figure 10).



**Figure 9: Graphical representation of pH of the test groups.**



**Figure 10: Graphical representation of titrable acidity of the test groups.**

At baseline, enamel microhardness values were 332.590±9.38 for group A, 331.2710±6.69 for group B, 331.880±6.49 for group C and 335.110±5.31 for group D. On the 7th day, group A had microhardness of about 312.84±3.83, group B had 316.15±7.3, group C had 322.13±5.39, and group D showed 334.57±5.23. On the 14th day, group A had microhardness of about 293.43.84±6.34, group B had 299.930±6.85, group C had 313.380±6.23 and group D had 334.190±5.51 (Table 1).

**Table 1: Comparison of microhardness using one-way ANOVA.**

	Group	N	Mean	Standard deviation	Standard Error	95% confidence interval for mean		Minimum	Maximum
						Lower bound	Upper bound		
<b>Baseline</b>	Group A	10	332.590	9.3857	2.9680	325.876	339.304	317.1	349.1
	Group B	10	331.270	6.6938	2.1168	326.482	336.058	319.8	339.9
	Group C	10	331.880	6.4937	2.0535	327.235	336.525	318.4	340.2
	Group D	10	335.110	5.3136	1.6803	331.309	338.911	323.5	340.7
	Total	40	332.712	7.0075	1.1080	330.471	334.954	317.1	349.1
<b>Seventh day</b>	Group A	10	312.84	3.836	1.213	310.10	315.58	306	318
	Group B	10	316.15	7.325	2.317	310.91	321.39	302	325
	Group C	10	322.13	5.394	1.706	318.27	325.99	311	331
	Group D	10	334.57	5.236	1.656	330.82	338.32	322	339
	Total	40	321.42	9.964	1.575	318.24	324.61	302	339

Continued.

	Group	N	Mean	Standard deviation	Standard Error	95% confidence interval for mean		Minimum	Maximum
						Lower bound	Upper bound		
Day 14	Group A	10	293.430	6.3477	2.0073	288.889	297.971	284.2	299.5
	Group B	10	299.930	6.8599	2.1693	295.023	304.837	289.2	309.7
	Group C	10	313.380	6.2314	1.9705	308.922	317.838	301.7	325.7
	Group D	10	334.190	5.5101	1.7424	330.248	338.132	321.0	338.9
	Total	40	310.232	16.8950	2.6713	304.829	315.636	284.2	338.9

## DISCUSSION

Erosion is recognized as one of the important causes for the loss of tooth structure in adults as well as in children.<sup>3</sup> The present in vitro study assessed the erosive potential of three commonly used pediatric syrups, meftal P, alerid and zincovit and it was shown that there is a significant reduction in the microhardness of the enamel when subjected to immersion cycles in the test syrups. This could be attributed to the loss of minerals from the enamel surface which is caused by the intake of the tested pediatric syrups. In the study it is also shown that pH and titrable acidities are not the only major factors that could influence the loss of microhardness.

Liquid formulations are most commonly preferred for use in pediatric patients because of the ease of administration and better patient compliance to the treatment. In addition to this, liquid formulations show greater flexibility which allows the adjustment of dosage during the treatment according to the pathology and also the development of the child.<sup>14</sup>

Acids are also added to medicines which acts as a buffering agent, helps to maintain a pH at which the drug is sufficiently soluble and also chemically stable.<sup>12</sup> Addition of acids also ensures physiological compatibility.<sup>3</sup> As result of these characteristics, various studies have pointed out the possible relationship between dental caries and frequent intake of liquid oral medicines.<sup>6</sup> One of the main acids included in the pediatric syrups is citric acid.<sup>4</sup> Even though it is considered as a weak acid, it is found to cause erosion mainly because of its potential to cause calcium chelation in hydroxyapatite which leads to a reduction in the supersaturation and increase in the rate of dissolution of hydroxyapatite crystals.<sup>4</sup> There are studies which have shown that when the pH of the substance decreases, enamel erosion increases.

Studies done by Kiran et al, Cavalcanti et al, Passos et al, Babu et al assessed of pH of pediatric syrups and showed that pediatric liquid medications with pH lower than critical value (5.5) initiates demineralization of enamel and causes dental erosion.<sup>18,20,23,24</sup>

It has been found that pH is not the only factor which influences the erosive potential of enamel. Other factors on which erosion depends include titrable acidity, calcium

chelation properties, mineral content and also adhesion to the dental surface.<sup>4</sup>

In the current study, meftal P exhibited the highest value for pH which is about 5.2 followed by alerid and zincovit which are about 5.1 and 4.2 respectively. All the tested pediatric syrups shows an acidic pH which is below the critical pH of the enamel i.e. 5.5 which is pointing to their subsaturation in relation to the hydroxyapatite of the tooth.

The total titrable acidity gives a measure of the amount of saliva buffer which is required to provide a neutral pH.<sup>14</sup> It determines the availability of hydrogen ion needed for the interaction with the tooth.<sup>20</sup> For the titrimetric analysis, a known standard sodium hydroxide (NaOH) solution was used. In the present study, titrable acidity was the highest for zincovit which was about 22.8 ml followed by meftal P (21 ml) and lowest value was seen in alerid of about 15.5 ml. This means that the amount of NaOH that is needed to neutralize the pH is greater for zincovit and least for alerid. Also the amount of NaOH that is required to neutralize the acidity is mainly dependent on the inherent pH of the test syrups. Maguire et al in his vitro study of measurement of endogenous pH and titratable acidity of the pediatric syrups had similar findings which showed that pediatric sugar containing medicines were more erosive than paediatric sugar free medicines in vitro and a more significant predictor of their erosive potential was their dose form.<sup>12</sup>

The trivial illness such as fever, allergy and vitamin deficiencies are very common in childhood and often receive medications such as antipyretic, antihistaminic, and multivitamin syrups for these conditions.<sup>3</sup> A high intake of these syrups used in the study (Meftal P, Alerid and Zincovit) may form possibly be the etiological or aggravating factors for severe dental erosion in childhood.

The protocol used for the immersion cycle was based on the frequency of intake of syrup. The samples were dipped in meftal P twice daily, in alerid and zincovit, the samples were dipped once daily for 14 days. The experimental period of 14 days was selected to check for the changes in a longer treatment period. This protocol was used in the study by Mali et al.<sup>2</sup> According to Shellis et al, one of the most preferred method for assessing the softening of enamel is by microhardness testing.<sup>25</sup> Hence this method was used for evaluation of erosive potential of enamel in this study. Studies have observed the erosive potential of

certain medicines like, iron supplements, expectorant, anti-asthmatic medications, expectorant and anti-histamines and showed that these medicines changes in the surface roughness, microhardness and also morphological alterations in the enamel.<sup>3,12,17,26-28</sup>

In our study, meftal P showed the highest erosive potential compared to the other tested syrups inspite of having a high pH than others, even though all are in the acidic range. This is in accordance with the study by Babu et al who showed that all the pediatric liquid medicaments included in their study showed an erosive effect on the primary enamel surface irrespective of their pH when observed under scanning electron microscope (SEM).<sup>18</sup> However it is reported in the literature that as the pH of the substance decreases, the erosive potential increases.<sup>3</sup> The higher erosive potential in meftal P could be attributed to the increased frequency of intake of the syrup when compared to the other two syrups, alerid and zincovit which were exposed to the syrups once daily.

Studies on deciduous teeth are relevant as there are differences in the morphology of permanent and deciduous teeth.<sup>3</sup> The vulnerability of deciduous teeth to acidic and cariogenic environment is found to be more than permanent teeth mainly because of variations in enamel thickness, its mineralization levels, and structural arrangement.<sup>3</sup> The enamel and dentin thickness of deciduous teeth is lesser than that of permanent teeth while its dental pulp is bigger which triggers fast caries.<sup>21</sup> However, some controversy remains regarding the difference in susceptibility to caries and erosion in both dentitions.<sup>4</sup>

From the findings of the present study, we can understand that enamel dissolution can be caused by pediatric liquid medications with different factors coming into role such as low pH, high titrable acidity and also the frequency of intake of the syrups.

As it is an in vitro study, the oral conditions cannot be exactly simulated. Perhaps the degree of loss of enamel could be greater than the clinical situations as in the oral cavity, the enamel surface is covered by a protective pellicle and plaque layer and is also subjected to flushing, buffering and also remineralizing effects of saliva.<sup>20</sup>

It is thus important to advice oral hygiene maintenance like regular tooth brushing and mouth rinsing with water after the intake of pediatric liquid medications and also addition of calcium, fluoride or phosphate to the formulations so that we can avoid the damage to the tooth that is caused by the regular use of these medications.<sup>3</sup>

Further long term studies are required to establish the direct relationship between various components of liquid medications and its effect on enamel surface before establishing any definitive conclusion and formulating any preventive protocols for dental erosion caused by pediatric liquid medicaments.

Considering the results of the study, strategies of competent bodies must be implemented in such a way that we can broaden the knowledge of the health professionals, manufacturers of the drugs and also the general consuming public about the possible risks that could result from the consumption of medicines to the dental hard tissues and the measures to be taken to prevent it.<sup>14</sup>

## CONCLUSION

All the pediatric liquid medications assessed in the present study, mefenemic acid syrup (meftal P), cetrizine syrup (alerid) and multivitamin syrup (zincovit) showed acidic pH, high titrable acidities and all the syrups showed loss of microhardness after exposure to the syrups for 14 days. Loss of microhardness was highest for mefenemic acid (meftal P) attributing to its increased frequency of exposure followed by cetrizine syrup (alerid) and least for multivitamin syrup (zincovit).

Hence, it is important to sensitize the parents of the diseased children, medical and dental professionals and also the drug manufacturers regarding the erosive potential of the pediatric syrups. Also, dental and medical specialists should be cautious while prescribing the syrups. It is important to advice proper oral hygiene maintenance including regular brushing and also to instruct the parents to dilute the prescribed dose with water or to rinse their mouth with water soon after administration if it is not diluted.

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