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Erosive Effects of Pediatric Liquid Medicinal Syrups with Remineralising Agents on Primary Enamel: An *In vitro* Comparative Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The use of liquid medicinal syrups in childhood to the reasons that children suffer from illness quite often. The acidic component in the formulations may cause erosive to the dental tissues.

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Aims: The aim of study was to test the erosivity of common Paedtric medications and to assess the change of the erosive potential of the medications in the presence of commercial Remineralilising agents.
Materials and Methods: A total of 27 extracted/exfoliated non carious Deciduous molars were used. 8 medical syrups were used.
Statistical Analysis Used: ANOVA and post hoc analysis were applied. An Tukey alpha value of 0.05 was employed.
Conclusion: The knowledge of the erosive potential of commonly used syrups is mandatory as erosion in children teeth.

Keywords: Deciduous molars; erosion; liquid medicinal syrups.

1. INTRODUCTION

"Dental erosion is defined as a form of irreversible non carious tooth loss, which results in chemical dissolution of mineral from the tooth when the PH of the oral enviournment falls below 5.5" [1]. "Dental erosion is the dissolution of dental hard tissues caused by acids of a non-bacterial origin. Dietary acids are considered the predominant and most controllable factor" [2,3].

"It has been increasingly recognized as a problem of all ages of particular concern is the weaning of tooth enamel that is caused by dietary erosion, which is usually observed in individual who consume fruit juices and contributed soft drinks and in those on long term acidic medications" [4]. "Dental erosion is increasingly recognized as a condition affecting the younger age groups, and in previous studies on primary dentition a high prevalence of up to 82% has been reported" [5].

"Dental erosion is a common cause of tooth wear and it may be the main contributing factor in severe tooth wear, more than attrition and abrasion" [6]. "Liquid oral medicines are usually prescribed for children to aid compliance" [7]. "Acidic preparations are often necessary for drug dispersion, chemical stability maintenance, to ensuring physiological compatibility and improving flavor" [7,8].

"In addition to the acidic components, other factors such as prolonged and frequent ingestion (i.e., two or more times daily), bedtime and between meals consumption, high viscosity and the collateral effect of reduced salivary flow may contribute to an increase the risk for medication-induced dental erosion" [9].

2. MATERIALS AND METHODS

A total of 27 extracted/non carious deciduous molars were used. Before use, the teeth were hand scaled and cleaned. The teeth were checked for structural abnormality that could possibly interfere with results, and on this basis, the teeth selection was done.

The roots were removed at the Cemento enamel junction. The crowns were fixed in a wax block parallel to the surface. The specimen before immersion cycle was stored at 37^0 C in Artificial saliva for 24 h.

The 8 commonly available liquid medicaments (PLM) were selected for the study and their endogenous PH was measured using a PH electrode meter (Eutech PH 700).

2.1 PH and TA Measurements

The PH of each Pediatrics liquid medicament was measured using a PH electrode meter. "(Microelectrode,Inc,new Hampshire, USA),Which was calibrated at the start of every session using buffer standards of PH 4 and PH 7 (Islab,werthein,Germanay).Every drink was tested with standard volume (20 ml) from a freshly opened bottle. Every experiment was performed in triplicate at room temperature (22^0C) and the mean and standard deviation obtained. phosphate –buffered saline (PBS) was employed as the control" [5].

"The TA of each drink was assayed using a standard protocol of acid-base reaction [10]. In brief, 0.1 M Sodium hydroxide (NaoH) was progressively added to 20 ml of each drink until neutralization (PH7) was attained using the same electrode. The volume of 0.1 M NaoH required was recorded" [5].

2.2 PH and TA Acidity Measurements of Representative Drinks after Addition of Remineralising Agents

Representative items (Table 2) were randomly selected from the each category in (Table 1) and were tested to examine the effects after the addition of various Remineralsing agents.

These remineralising agents were tooth mouses.

1. TM; GC Corporation, Tokyo, JAPAN.
2. Tooth mouses plus. (TMP, GC Corporation, Tokyo).
3. Clinpro (3 M, Minnestota, USA).
4. 1.23% NAF and Artificial saliva. (AS).

To stimulate intraoral conditions where there is dilution of the applied paste by saliva, TM, TMP and Clinpro TM were applied as slurries. 1 g of paste to 10 ml distilled water.Neutral NAF solution was applied as a 1.23% wt/vol solution . TM,TMP, Clinpro TM ,NAF and AS were individually added to each representative drink at the following concentration.

The PH and TA were recorded after 5 month to as certain the effects were due to dilution; test with control (PBS) solution was performed.

All experiments were performed in triplicate.

2.3 Statistical Analysis

The students t test (two-tailed), one way ANOVA were performed on instant 3 (Graph pad soft ware, California, USA). A Tukey alpha value of 0.05 was employed.

3. RESULTS

The PH of each Pediatric liquid medicament was measured using a PH electrode meter. The PH ranged between 3.09 to 5.7. The minimum PH value minimum for S1 syrup (3.09) & maximum for S8 (5.7) (Table 1).

After adding the Reminerasing agents the PH value is changed to > 5.5 (Table 2, Graph 1).

The TA of each Pediatric liquid medicament was minimum for S5 and maximum for S4. After adding Remineralising agents the TA value changes **(**Table 3, Graph 2).

Table 1. Summery of PH of pediatric medications in different remineralising agents

Type	Brand name	Generic name	Company name	PH
1.Ironsupplement		Tonoferol.S1	Cipla	3.09
2.Antibiotics	1.Oflox-100	Ofloxocin.S2	Cipla	5.05
	2.Taxim-o	Cefixime.S3	Alkem.	
	3.Pexoclav	Amoxicillin+	Apex	4.6
	4.Bendex.	Clavonic.S4	Cipla.	5.07
		Albendazole.S5		5.46
3.Analgesic	1.Combiflam	Ibuprofen.S6	Sanafi	4.56
	2.P-250	Paracetamol.S7	Apex.	5.35
4.Decongesant (Antihistamine)	Maxtra	Phenylephrine HCL.S8	Zunventus.	5.7

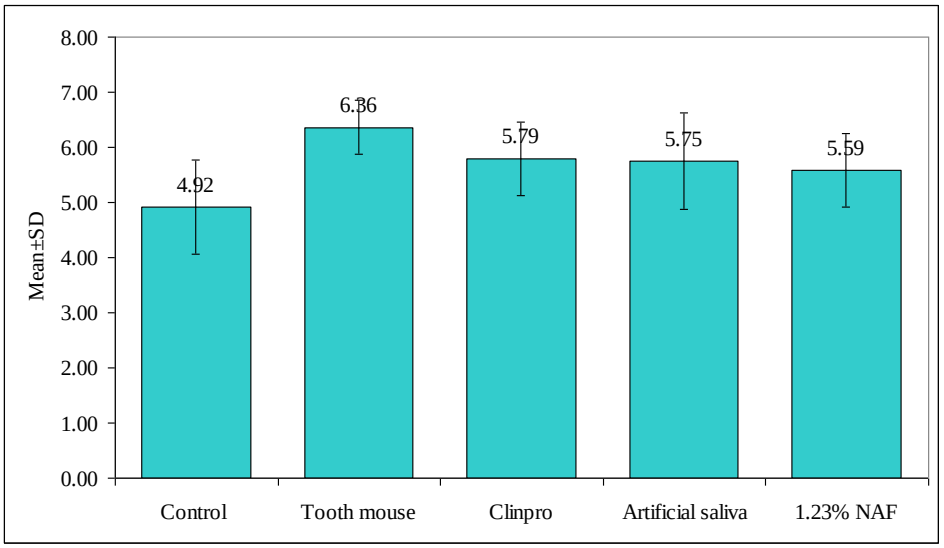
Table 2. Pair wise comparison of PH of Paediatric medications before & after adding Remineralising agents by Tukeys multiple posthoc procedures

Agents	Mean Difference	Std. Error	p-value
Control vs Tooth mouse	-1.45	0.36	0.0030*
Control vs Clinpro	-0.87	0.36	0.1380
Control vs Artificial saliva	-0.83	0.36	0.1700
Control vs 1.23% NAF	-0.67	0.36	0.3570
Tooth mouse vs Clinpro	0.58	0.36	0.5150
Tooth mouse vs Artificial saliva	0.61	0.36	0.4510
Tooth mouse vs 1.23% NAF	0.77	0.36	0.2300
Clinpro vs Artificial saliva	0.04	0.36	1.0000
Clinpro vs 1.23% NAF	0.20	0.36	0.9820
Artificial saliva vs 1.23% NAF	0.16	0.36	0.9920

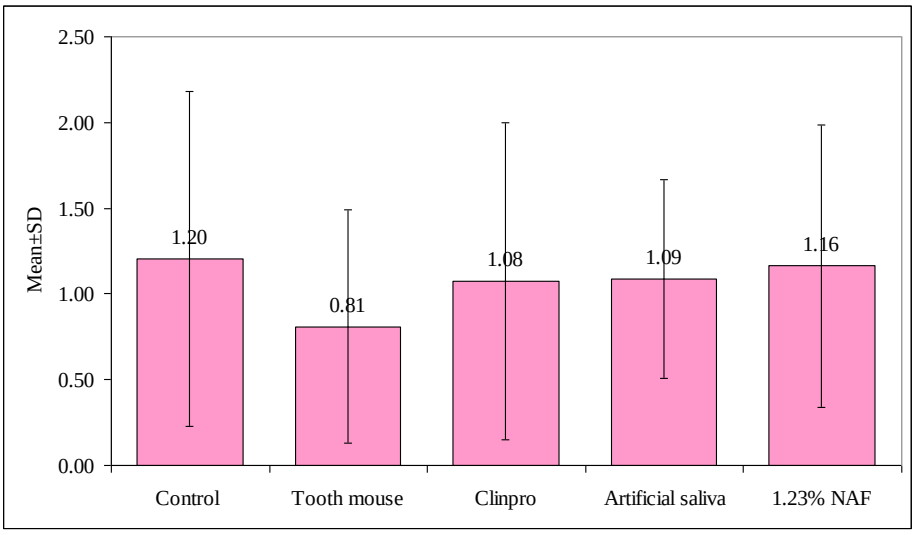
Table 3. Pair wise comparison of TA of Paediatric medications before & after adding

Agents.	Mean Difference	Std. Error	p-value
Control vs Tooth mouse	0.39	0.41	0.8660
Control vs Clinpro	0.13	0.41	0.9980
Control vs Artificial saliva	0.12	0.41	0.9980
Control vs 1.23% NAF	0.04	0.41	1.0000
Tooth mouse vs Clinpro	-0.27	0.41	0.9650
Tooth mouse vs Artificial saliva	-0.28	0.41	0.9590
Tooth mouse vs 1.23% NAF	-0.35	0.41	0.9060
Clinpro vs Artificial saliva	-0.01	0.41	1.0000
Clinpro vs 1.23% NAF	-0.09	0.41	0.9990
Artificial saliva vs 1.23% NAF	-0.08	0.41	1.0000

Remineralising agents by Tukeys multiple posthoc procedures



Graph 1. Comparison of PH of pediatric medications before & after adding remineralising agents



Graph 2. Comparison of TA of paediatric medications before & after adding remineralising agents

3.1 Surface Changes of Primary Enamel

Primary enamel surface treated with various PLMs, and artificial saliva was observed under the SEM at 1 min, 10 min, and 8 h.

In most of the medicaments, etched prism pattern and crater formation were observed on the primary enamel surface immersed in medicaments at 1 min, 10 min, and 8 h time intervals and sporadic rod ends were seen at the end of 1 min time interval at Tonoferol only (Fig. 1). In artificial saliva, no surface changes were observed on primary enamel surface in SEM (Fig. 2).

In antibiotic group (Ofloxocin, Cefixime, and Albendazole), In Ofloxocin etched prism pattern was seen after 1 min interval (Fig. 3) and crater formation was seen after 10 min and 8h interval, respectively, (Fig. 4) where as, in Albendazole, nothing significant was found after1 min interval, but etched prism pattern was seen after 10 min and crater formation was seen after 8 h interval (Fig. 5).

In analgesics group (Paracetamol and Ibuprofen), etched prism pattern was observed after 1 min interval and crater formation was seen after 10 min and 8 interval in both the medicaments, (Fig. 6) respectively.

In Nimulide group sporadic rod ends were seen only in this group after1 mininterval. Etched prism pattern was seen after 10 min and crater formation was seen after 8h interval (Fig. 7).

In Anti histamine group (Diphenyl hydramines) no significant changes on primary enamel surface were found after 1 min and 10 min interval, where as crater formation was seen after 8 h interval in both the medicaments (Fig. 8).

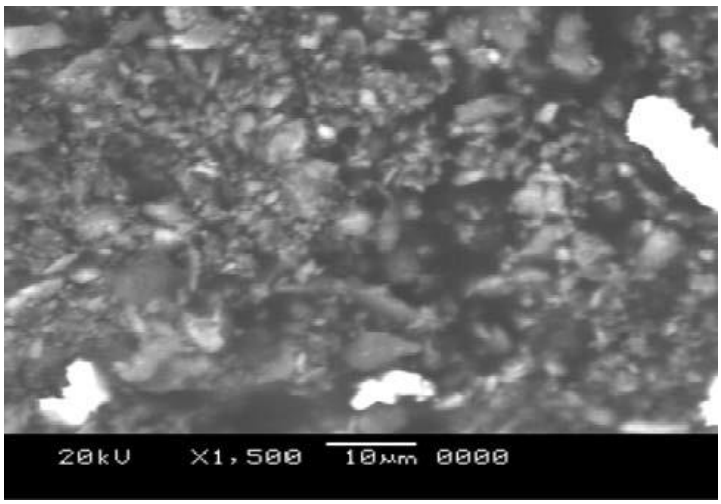


Fig. 1. Sporadic rod ends seen on primary enamel surface after immersing Tonoferol for 10 min

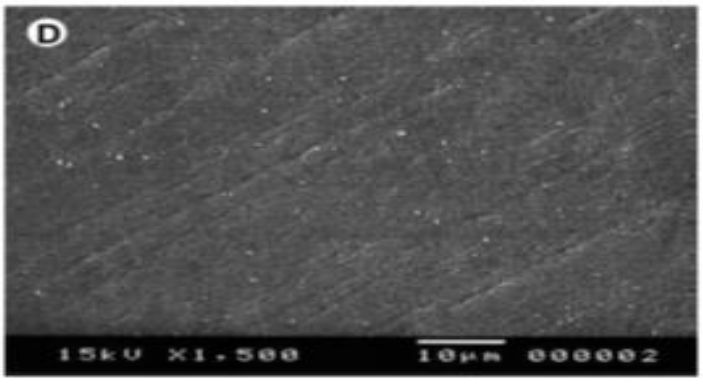


Fig. 2. In artificial saliva, no surface changes were observed on primary enamel surface in SEM

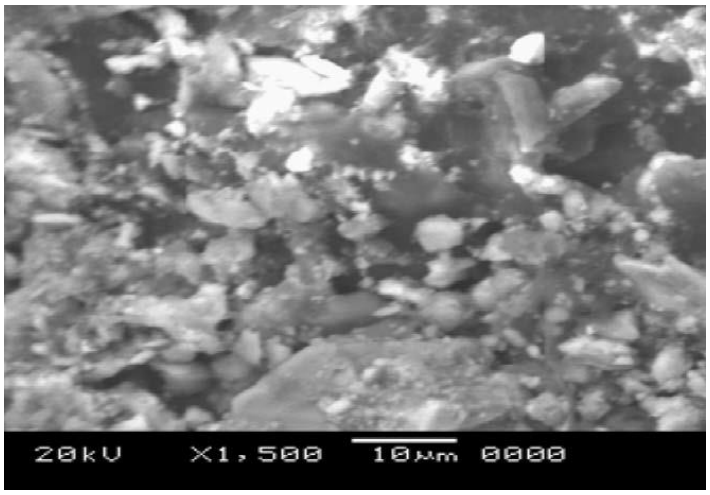


Fig. 3. Etched prism pattern seen on primary enamel surface after immersing in Ofloxocin with zinc for 1 min

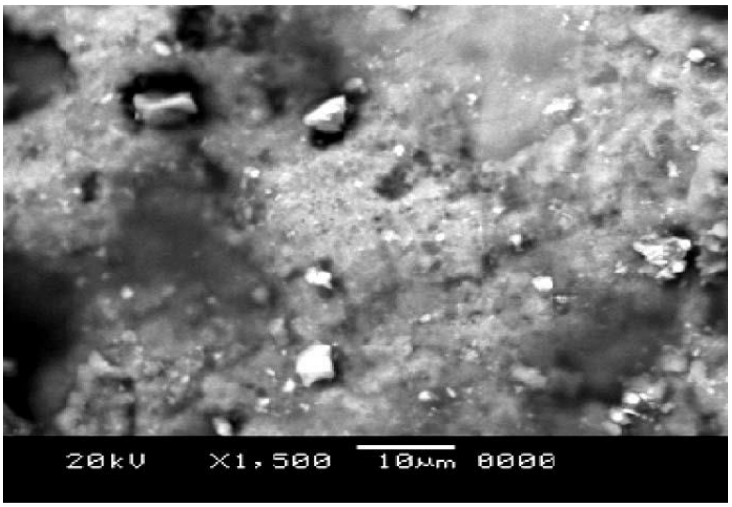


Fig. 4 . Crater formation seen on primary enamel surface after immersing in Albendazole for 10 mins.

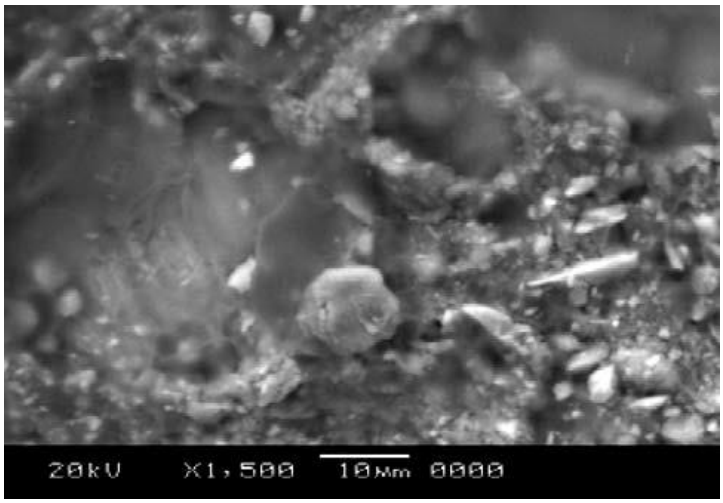


Fig.5. Crater formation seen on primary enamel surface after immersing in Albendazole for 8 h.

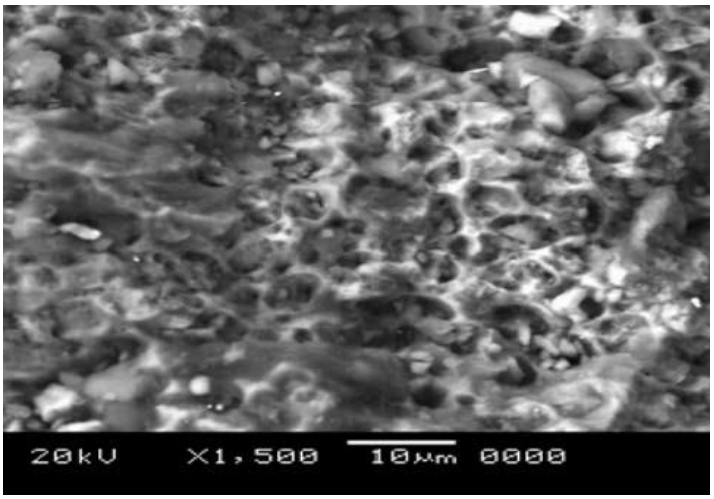


Fig. 6. Etched prism pattern seen on primary enamel surface after immersing in Crocin with Zinc for 1 min

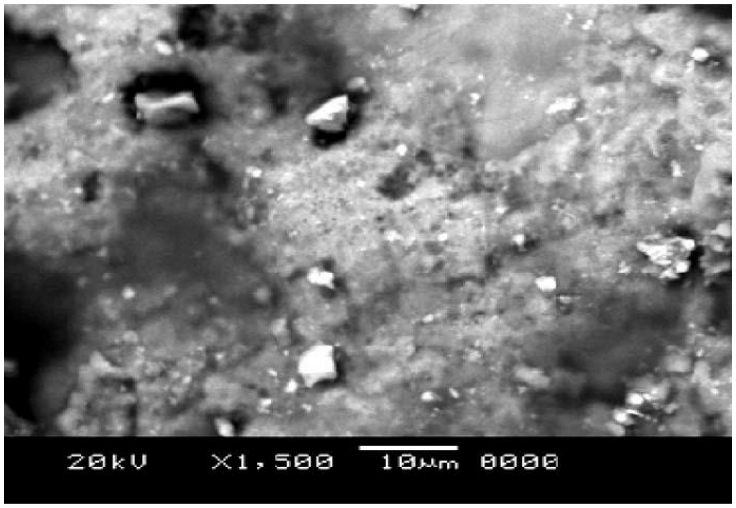


Fig. 7. Crater formation seen on primary enamel surface after immersing in Nimesulide for 10 mins

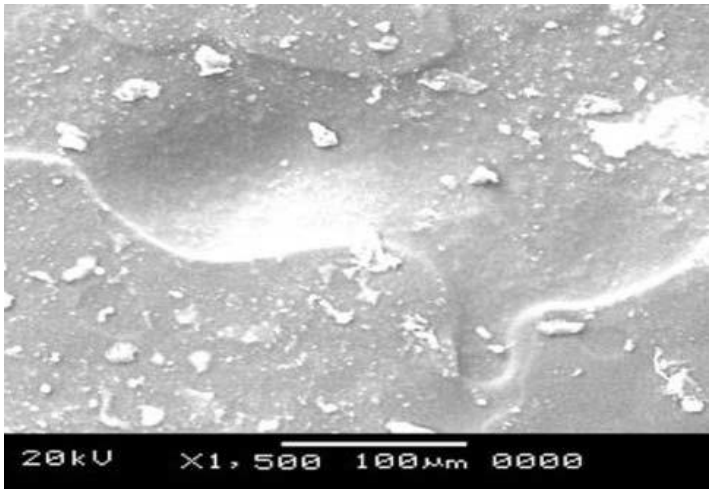


Fig. 8. Crater formation was seen after 8 h interval in antihistamine group

4. DISCUSSION

"Dental erosion is increasingly recognized as common conditions in Pediatric dentistry with complications of dental sensitivity, altered aesthetics and loss of occlusal vertical dimension, eating difficulties, pulp exposure and abscess" [11,12].

"The high levels of consumption of acidic drinks are likely to be associated with the alarming prevalence of erosion among the pre-school children reported" in the studies of Millward et al. [13] and Al-malik et al. [14].

"Interestingly, all Pediatric medications examined in the present study exhibited PH in a similarly range between 3.09 to 5.7. This PH range of the Pediatric medications is in accordance with the handful of previously papers published on prescription medications" [15,16].

Therefore, Paediatric medications have PH values below the critical PH for Demineralization occur.
The findings of present study are similar to those done by Babu KLG et al. [17] which examined the PH of 8 medications ranging from 6.05 to 6.77 and its effects on primary teeth.

In a study conducted by Greenwood ME et al. [18] the liquid syrup Dimetapp (Brompheramine and Phenylephrine) had an acidic PH of 2.86. The PH of the artificial saliva in the present study was 7.1.
"The other difference between deciduous and permanent tissues may also be of importance. For example deciduous teeth demonstatates a higher degree of enamel porosity and lower degree of mineralization than permanent teeth. In addition, deciduous enamel has repeatedly been noted to have a higher content of Co2 and carbonated as well as alower content of phosphorus than the permanent tissue" [19].

"Deciduous teeth are more susceptible to caries like acid attack than permanent teeth invitro according to Feather stone and Melberg" [20].

Even though the PH of PLM was not near the critical PH of the oral cavity, erosion of PES was evident when subjected to study under SEM.This agrees with the studies of Babu KLG et al. [17] and Green wood ME et al. [15] who used SEM to evaluate the Erosion potential of liquid syrup on rats enamel and human extracted primary teeth respectively.

In the present study Etched prism pattern were seen in enamel surface treated with Azithromycin syrup for 10 min and Crocin syrup for 1 minute and Multivitamin syrup for 10 minutes. These findings were in agreement with findings of Babu KLG et al. [17] who reported similar typical prism pattern on enamel surface treated with Amoxicillin for 1 mintes, Theophylline for 1 minutes and Multivitamin for 10 minutes.

Enamel surface treated with crown suspension for 1 minute Ibugesic plus suspension for 1 minute, Mox Red mix suspension for 1 minute, Although suspension for 10 minutes and 8 hours Valparin 200 syrup for 10 minutes and 8 hours Visyneral syrup for 1 minute and 8 hours and delicious syrup for 1 minute and 8 hours all showed the etched prism pattern this was not of the classical appearance. This atypical appearance of enamel surface can be supported by the study done by Grando LJ et al. [21] who stated that complexity can be seen in the different patterns of loss of enamel structure in eroded Deciduous teeth.

"In the present study there seemed to be no direct relationship between the PH of the selected PLMS and the Erosive changes seen on the PES. This findings is in accordance with that of Babu KLG et al" [17].

Morch T et al. [22] and Onose H et al. [23] reported that "the Chelating agents present in PLMS like sodium salt of various aminoacids and lactate at or near neutral PH, increase the uptake of radioactive phosphorus by loss of ca from enamel. This factor may be responsible for the erosive pattern seen in the surface of PES in the present study".

In the present study, demonstrated that the addition of Remineralizing agents like TM, TMP, neutral NAF, Clinpro and AS resulted in significant changes in PH and TA completed to the control group.

This present study was similar to study done by Manton et al. [24] "The addition of 0.2% CPP-ACP to acidic drinks showed that a slight increase in PH (0.5 units) was associated with a significant reduction in erosive potential".

This present a study result is in agreement with study by Dawes et al. [25] which suggests an inverse proportion relationship between PH and Ca and phosphate concentration.

"CPP-ACP consists of biologically active peptide casein phosphor peptides that holds and stabilizes Ca and phosphate that hold and stabilize Ca and Phosphate ions in a bio available form, and prevents precipitation. These ions become available at the tooth surface when the PH drops, so that Demineralization is inhibited" [26].

Maguire et al. [8], Arora et al. [27] Therefore, "PH, TA are not the only parameters in determining the erosive potential. Furthermore, different conc of active ingredients in medicines may indirectly affect the PH, TA due to the different levels of acids added to mask the taste of the active ingredients".

5. CONCLUSION

In conclusion, the present study demonstrates that pediatric over-the counter medications have erosive potential. It also demonstrates that commercially available Remineralising products, Tooth mouses, Tooth mouse plus, 1.23% Neutral sodium fluoride, and Artificial saliva can potentially to reduce the erosivity of pediatric over the counter medications.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study was approved by the Institutional Ethitical Committee (IERB, MDC 8/2020)

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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