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Research / Araştırma Makalesi

Evaluation of Cariogenic and Erosive Potentials of Pediatric Liquid Medicines

Çocuklarda Yaygın Kullanılan Şurup Formundaki İlaçların Karyojenik ve Eroziv Potansiyellerinin Değerlendirilmesi

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ABSTRACT

Background: This study aims to evaluate the cariogenic and erosive effects of pediatric liquid medicines (PLM) on the enamel of primary teeth, which have been increasingly used in children with acute or chronic diseases.

Methods: Five long-term and widely used pediatric drugs (Augmentin, Zimaks, Calpol, Vitabiol, and Ferro Sanol B) were selected for this study. In order to evaluate the erosive and cariogenic potentials of the drugs, the sucrose concentrations, pH values and calcium concentrations they dissolve from the enamel tissue were determined. The samples were subjected to acid incineration with MARS XPress (CEM Brand) Microwave oven. Calcium concentrations were then measured by Inductively Coupled Plasma-Mass Spectroscopy (ICP MS). For the statistical data of the study, it was analyzed using the SPSS Statistics 21 (Statistical Package for Social Sciences, IBM Inc., USA) package program. Mean, standard deviation and percentage statistics are given in the expression of continuous variables. Data are shown as arithmetic mean±standard deviation (AO±SD) values.

Results: Most of the pediatric liquid drugs (80%) have a pH of less than 5.5. It is therefore critical for enamel to be affected. The syrup with the highest acidity value was Ferro sanol B (average pH 2.96 ± 0.01) and the lowest acidity value was Calpol (average pH 6.42 ± 0.03). All of the pediatric syrup samples we used in our study contain sucrose.

Conclusion: As a result, it has been observed that syrups used for various reasons in early childhood may cause erosion on tooth surfaces at different pH and acidity values. All syrups examined have cariogenic effects as they contain sucrose. Calcium transition from enamel to all solutions was observed in all three time intervals for all pediatric liquid drugs. In general, the amount of dissolution increased as the holding time increased. The lowest calcium dissolution rate was observed in the Augmentin syrup sample at the first minute (15.87 mg/L), the highest calcium dissolution rate was observed in the Zimaks syrup sample (609.69 mg/L) at the eighth hour. There is no statistical correlation between the pH values of the syrups and the amount of calcium dissolved from the enamel.

Keywords: Pediatric syrup drugs, ICP-MS, Ph meter

ÖZ

Giriş ve Amaç: Bu çalışma, akut veya kronik hastalığı olan çocuklarda kullanımı giderek artan pediatrik sıvı ilaçların (PLM) süt dişlerinin minesi üzerindeki karyojenik ve aşındırıcı etkilerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Bu çalışma için uzun süreli ve yaygın olarak kullanılan beş pediatrik ilaç (Augmentin, Zimaks, Calpol, Vitabiol ve Ferro Sanol B) seçildi. İlaçların eroziv ve karyojenik potansiyellerini değerlendirmek amacıyla, sükroz konsantrasyonları, pH değerleri ve mine dokusundan çözdükleri kalsiyum konsantrasyonları belirlendi. Numuneler MARS XPress (CEM Marka) Mikrodalga fırın ile asit yakma işlemine tabi tutuldu. Kalsiyum konsantrasyonları daha sonra İndüktif Eşleşmiş Plazma-Kütle Spektroskopisi (ICP MS) ile ölçüldü.

Bulgular: Pediatrik sıvı ilaçların çoğunun (%80) pH'ı 5,5'un altındadır. Bu nedenle minenin etkilenmesi kritik öneme sahiptir. Asitlik değeri en yüksek olan şurup Ferro sanol B (ortalama pH 2,96±0,01), en düşük asitlik değeri ise Calpol (ortalama pH 6,42±0,03) oldu. Çalışmamızda kullandığımız pediatrik şurup örneklerinin tamamı sakkaroz içermektedir.

Sonuç: Sonuç olarak erken çocukluk döneminde çeşitli nedenlerle kullanılan şurupların farklı pH ve asitlik değerlerinde diş yüzeylerinde erozyona neden olabileceği görülmüştür. İncelenen tüm şuruplar sakkaroz içerdikleri için karyojenik etkiye sahiptirler. Tüm pediatrik sıvı ilaçlar için her üç zaman aralığında da mineden tüm solüsyonlara kalsiyum geçişi gözlemlendi. Genel olarak bekletme süresi arttıkça çözünme miktarı da arttı. En düşük kalsiyum çözünme hızı 1. dakikada Augmentin şurup örneğinde (15,87 mg/L), en yüksek kalsiyum çözünme hızı ise sekizinci saatte Zimaks şurup örneğinde (609,69 mg/L) görüldü. Şurupların pH değerleri ile minede çözünen kalsiyum miktarı arasında istatistiksel bir korelasyon yoktur.)

Anahtar Kelimeler: Pediatrik şuruplar, ICP-MS, Ph metre

INTRODUCTION

One of the most common infectious diseases affecting children is dental caries. Acidic by-products formed as a result of fermentation of carbohydrates by bacteria cause a decrease in plaque pH. This causes tooth decay by causing dissolution, destruction and cavitation in the hard tissues of the teeth. [1,2] Dental caries can lead to tooth loss, impaired growth and developmental delay in children. It can also affect the child's speech, aesthetic appearance, self-esteem and school performance. [3] Dental erosion is defined as the irreversible loss of dental hard tissue with acid and/or a chelator without bacterial chemical contamination. [4] Dental erosion can occur due to many factors such as environmental factors, dietary habits, drugs and lifestyle. Among these, the factors that most affect children are stated as drug use and eating habits. [5] Medications in the form of pediatric syrup are the best treatment for young children. The taste of pediatric liquid medicines (PLM) is more acceptable to children than medicines in the form of tablets. [6,7] This is mainly due to sweetened solutions. Sucrose is one of the sweeteners commonly added to pediatric liquid medicines because it is a low-cost and easily processed sweetener. [8] It is also frequently preferred in the pharmaceutical industry because it functions as a preservative, antioxidant, solvent, sedative and bulking agent.[9] Especially long-term use of such liquid medicines can adversely affect the dental structure of children with chronic diseases or allergic rhinitis, sinusitis, otitis media and tonsillitis.[10]

Pediatric liquid medicines contain acids as well as sweeteners. Acids are added to syrups as buffering agents to maintain chemical stability, control tonicity, or provide physiological compatibility. They also improve the aroma to increase patient compliance.[11] In addition to the benefits obtained, such acids also have harmful effects such as dental erosion. Due to their acid content, pediatric liquid medications are cited as one of the main of dental erosion.[12,13]

In similar studies in the literature, there is evidence that the enamel hardness of primary teeth decreases, enamel roughness increases and morphological changes occur in the enamel with the routine use of PLMs.[14,15] In addition, studies are showing that the frequent use of pediatric liquid drugs increases dentin sensitivity and the prevalence of dental caries.[16,17] Therefore, these drugs require a comprehensive

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evaluation to manage both their side effects and corrosive potential.[18,19] Only a few studies are available in the literature measuring the abrasive potential of pediatric liquid drugs on primary teeth.[20,21]

It is thought that the risk of dental caries can be reduced by identifying an alternative harmless therapeutic agent to drugs in syrup form containing sugar.[22]

In this study, since it can be an indicator of the cariogenic and corrosive potential of pediatric liquid drugs; the endogenous pH values of the syrups, their sugar concentrations and their calcium dissolution potential from tooth enamel were evaluated.

MATERIALS AND METHODS

In a survey study conducted with pediatricians in the city of Hatay frequently used and prescribed drugs were determined. In our study, five of the most commonly prescribed and commonly used drugs were selected, and it was aimed to evaluate the erosive and cariogenic effects on primary teeth *in vitro*. Antibiotics, analgesics, multivitamin syrups and iron medications are among these drugs that are frequently prescribed by pediatricians to pediatric patients with acute or chronic diseases. Augmentin, Zimaks, Calpol, Vitabiol and Ferro Sanol B were used as drugs in the form of pediatric syrup. (Drugs used are shown in **Table 1**.)

Table 1. Medicines used in syrup form

Therapeutic Group	Name	Brand Name	Pharmaceutical Form	mg/mL	Manufacturer
Antibiotic	Amoxicillin+ clavulanic acid	Augmentin	Dry powder for preparation of oral suspension	400/70	Glaxo Smith Kline Pharmaceuticals Industry and Trade Inc.
Antibiotic	Cephalosporin	Zimax	Dry powder for preparation of oral suspension	100/5	Science Medicine Industry and Trade Inc.
Analgesic	Paracetamol	Calpol	Syrup	120/5	Glaxo Smith Kline Drugs san. and Trade Inc.
Multivitamin	Multivitamin	Vitabiol	Syrup	100	Ibrahim Etem Ulagay Medicine Industry Turkish Inc.
Antianemic	Iron preparation	Ferro virtual B	Syrup	150	Adeka Pharmaceutical Industry and Trade Inc.

In the determination of the erosive and cariogenic potential in syrups, the sucrose ratios in the contents of the syrups, the pH values of the syrups and the calcium ratios that the syrups dissolve from the enamel of the primary teeth were evaluated.

Calculation of Endogenous pH of Syrups

For endogenous pH determination, 10 mL sample from syrups was made up to 100 mL (10% diluted) and measured with the help of a digital pH meter (Hanna HI desktop pH meter) in Mustafa Kemal University Technology and Research Center. The pH meter, with an accuracy of 0.1, was first calibrated according to the manufacturer's instructions using the pH 7 and pH 4 buffer standards. The temperature was set to 25°C and the electrode was placed on the sample. Before the reading was taken, the screen was allowed to be fixed and the readings were recorded. The electrode of the pH meter was rinsed before each measurement and placed back in the storage solution. The measurement process was repeated three times.

Determination of Endogenous Sugar Concentration

The lane-Eynon copper reduction method was used for endogenous glucose measurement. With this method, glucose concentration percentage and sucrose concentration are measured. While all monosaccharides show reducing properties, sucrose does not. For this reason, in the measurement of sugar by chemical methods, sucrose is first converted to invert form and measured as invert sugar together with glucose and fructose. Since the reducing property of sugar is utilized in the determination of sugar, other substances with reducing **properties in the environment must be removed.**

Evaluation of Endogenous Erosive Potential

In this study, deciduous teeth that were previously extracted for treatment in Hatay Mustafa Kemal University Oral and Dental Health Hospital Pediatric Dentistry Clinic were used for the measurement of endogenous erosive potential. Approval for the use of these teeth was obtained from Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee on 04.10.2021.

After extraction, the soft tissues surrounding the teeth were removed. These extracted teeth were kept in isotonic serum solution until the study period. 64 deciduous teeth were removed from the solution and dried separately. The teeth are divided mesiodistal by diamond disc. Dentin was removed with the aid of a round diamond bur. (**Figure:1**)

Figure 1. Sample with dentin tissue removed

A fine powder was obtained by grinding the remaining enamel parts using an agate mortar and a pestle. (**Figure:2**) The particle size of the obtained powder was standardized with the help of a 120 mesh sieve. (**Figure: 3**) Approximate 5 g of enamel powder was obtained from 64 primary teeth.

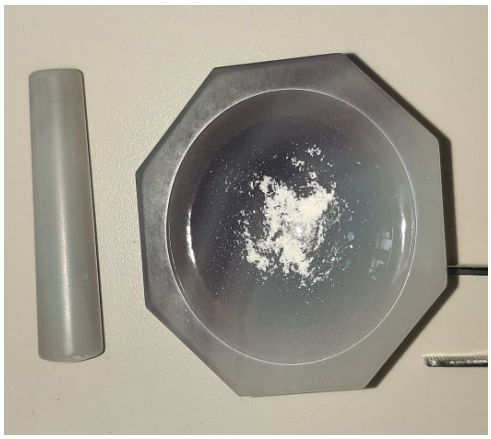

Figure 2. Grinding of enamel samples with agate mortar

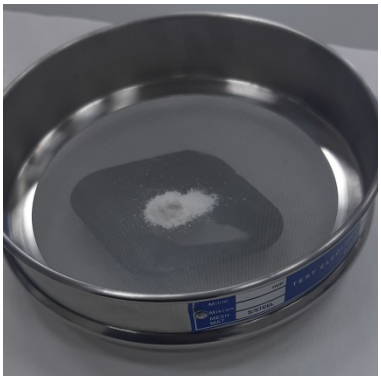

Figure 3. Enamel powder standardized by sieve

Enamel powder weighing 250 mg was added one by one to 5 mL individual pediatric syrup solutions and mixed with the Dlab MX-S Vortex mixer in Hatay Mustafa Kemal University Technology and R&D Application and Research Center for approximately 2-3 minutes until the solutions were homogenized. In parallel with other studies in the literature; it has been maintained for three time intervals of 1 minute, 10 minutes and 8 hours. For each mentioned time interval, the mixtures were centrifuged at 6,000 rpm for 20 minutes with a Weightlab WN-CMV6000 Microcentrifuge device and the pellet and supernatant were separated from each other. The pellets were discarded and the supernatants were stored at +4 °C for further analysis. The samples brought to room conditions were prepared for incineration with a microwave oven. The samples were subjected to

acid incineration with a microwave oven. MARS XPress (CEM Brand) microwave burning system was used in the study. After the acid burning process was completed, the calibration of the Inductively Coupled Plasma Mass Spectrometer (ICP MS) device was made and the Ca concentrations were determined by giving the samples to the device. For the statistical data of the study, it was analyzed using the SPSS Statistics 21 (Statistical Package for Social Sciences, IBM Inc., USA) package program.222 Mean, standard deviation and percentage statistics are given in the expression of continuous variables. Data are shown as arithmetic mean±standard deviation (AO±SD) values. The relationship between pH measurement results and dissolved Calcium ratios in syrups was evaluated with the Spearman correlation coefficient. $p<0.05$ was considered significant.

RESULTS

pH Measurement Results of Drugs in Syrup Form

Table: 2.1. pH values of drugs used

Medicaments used	1. Measurement	2. Measurement	3. Measurement	avg ± SD
Calpol	16589	15858	14397	6.42 ± 0.03
Vitabiol	13575	13940	13940	3.38 ± 0.005
Augmentin	44652	44652	44652	4.22 ± 0.0
Zimax	24532	24898	26359	3.69 ± 0.02
Ferro virtual B	34731	35096	35462	2.96 ± 0.01

Most of the pediatric liquid drugs (80%) have a pH less than 5.5. It is therefore critical for enamel to be affected. The syrup with the highest acidic value was Ferro sanol B (average pH 2.96 ± 0.01) and the lowest acidity value was Calpol (average pH 6.42 ± 0.03). **Table.2.1.**

Sucrose Measurement Results of Syrup Samples

Table 2.2. Sucrose percentages of used syrups

Medicaments used	Percentage of sucrose
Calpol	%17.77
Vitabiol	%35.34
Augmentin	%17.86
Zimax	%19.00
Ferro virtual B	%16.26

Percentages of sucrose in pediatric liquid drugs were; Calpol at a concentration of 17.77%, Vitabiol at a concentration of 35.34%, Augmentin at a concentration of 17.86%, Zimax at a concentration of 19.00% and Ferro Sanol B at a concentration of 16.26%.

Total sucrose ratio; the highest Vitabiol (35.34%) and the lowest Ferro Sanol B (16.26%) were measured in the syrup sample. **Table 2.2.**

Calcium Dissolution Rate in Pediatric Liquid Medications

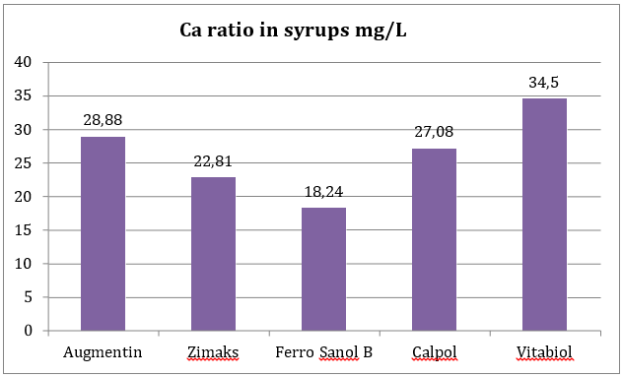

Figure 4. Calcium ratios in syrups

It has been determined that all of pediatric liquid medicines contain certain amounts of calcium element in their content. The distribution of the amount of calcium element in drugs in syrup form is shown in **Figure 4.**

Calcium element transfer from enamel to all sample solutions was observed in all three time intervals for all pediatric liquid drugs. In general, the amount of dissolution increased with increasing residence time. It can be said that as exposure to drugs in syrup form increases, the rate of erosion and dissolution in enamel increases. The total amount of calcium dissolved in syrups and the amount of calcium dissolved from enamel are shown in **Table 2.3.**

Table 2.3. Amounts of dissolved calcium

Medicaments Used	Ca ratio in syrup (mg/L)	Total Ca dissolved in 1 min. amount(mg/L)	The rate of total Ca dissolved in the 10th minute (mg/L)	Total dissolved Ca ratio at the 8th hour (mg/L)	Ca (mg/L) dissolved in 1 min	Ca (mg/L) dissolved in 10 minutes	Dissolved Ca (mg/L) at 8th hour
Augmentin	28.88	44.75	252.6	353.4	15.87	223.72	324.52
Zimax	22.81	227.15	346.95	632.5	204.34	324.14	609.69
Ferro Sanol B	18.24	405.75	426.75	457.6	387.51	408.51	439.36
Calpol	45531	386	369.15	482.95	358.92	342.07	455.87
Vitabiol	34.5	295845	320.15	452.35	261.35	285.65	417.85

DISCUSSION

Despite the advances made in the field of preventive dentistry, the prevention and management of dental caries in children has always been more difficult. [23] Even if the main causes of dental caries are known, caries could not be eliminated. Many parents are aware that sugars cause tooth decay. They associate this situation only with the consumption of sweets and biscuits. Parents are often unaware of the hidden, added sugars found in many foods and beverages, including pediatric liquid medications. [8]

Oral pediatric liquid medicines (PLMs), such as suspensions, syrups, and solutions, are the best treatment for young children. In particular, long-term use of such liquid medicines can adversely affect the dental structure of children suffering from chronic diseases (asthma, respiratory tenderness and convulsions) or frequent acute conditions (allergic rhinitis, sinusitis, otitis media and tonsillitis). [6]

Sugar is often added to oral PLMs as a flavor enhancer. Because it is both easy to process and cost effective, sucrose is the most commonly used sweetener for this type of medicine. Fructose and glucose can also be added to some of these drugs. These sugars act as a substrate for oral bacteria, which are specifically responsible for sucrose fermentation. Thus, it causes acid production and then a decrease in intraoral pH. [8,10,24]

Pediatric liquid medicines contain not only sweeteners but also acids. Acids are added as buffering agents to maintain chemical stability, tonicity, or provide physiological compatibility. They also enhance aroma to increase patient compliance. It is also responsible for increasing shelf life. [25] In addition to the benefits, these acids also have harmful effects such as tooth erosion. Due to their acid content, PLMs can also be cited as one of the main causes of tooth erosion. Erosion in dental tissues is the loss of structure caused by a series of chemical interactions that occur in the absence of bacteria. [4] This process occurs gradually. The critical pH of tooth enamel is 5.5. Depending on the pH of the oral cavity below 5.5 and the frequency and duration of exposure to acids and chelating agents, erosive lesions may occur in the tooth enamel. [26]

According to the study of Linnett and Seow, the prevalence of dental erosion has increased especially among children and adolescents. [27]

The etiology of dental erosion; low endogenous pH, and high acidity has been associated with continued use of drugs that do not contain ions such as calcium, phosphate, and fluoride. [28]

Studies have shown that routine use of PLM can reduce enamel hardness of primary teeth, affect enamel roughness, cause morphological enamel changes, deterioration of composite materials, hypersensitivity of dentin, and an increase in the prevalence of dental caries. Therefore, such drugs need to undergo extensive evaluation to check for their side effects and corrosive potential. [14,29]

Parents are often unaware of the harmful effects of pediatric drugs on teeth. Pediatricians and dentists are in an ideal position to change parents' attitudes towards oral health. [30,31] However, dentists and

physicians are unaware of the sucrose content of commonly prescribed syrups. Even in countries where sugar-free medicines are widely available, many pediatricians continue to prescribe sugar-sweetened medicines. [32]

The reasons for this preference of pediatricians are; the effect of pharmaceutical companies on doctors is thought to be drug costs or patients' preference for sugary drugs. [33,34] However, in a survey conducted by Neves et al., 80.8% of pediatricians thought that pediatric drugs could adversely affect oral health. [32] The risk of dental caries can be reduced by identifying an alternative harmless therapeutic agent to drugs in syrup form containing sugar. [22]

In the literature, there are studies and evidences for the evaluation of the effects of drugs in syrup form on dental caries. However, only a few studies are measuring the corrosive potential of PLM in primary teeth. [25,35] Therefore, this study aimed to evaluate the erosive and cariogenic potential of drugs in the form of syrups that are commonly used.

Cavalcanti et al. investigated the erosive effects of different antitussive syrups in their study. The pH, acidity and total amount of soluble particles of the syrups in this study were investigated. According to the results of the research, it was determined that the pH of many of the antitussive syrups was lower than the critical pH, as well as high acidity and sugar content. These data show that these drugs used in children have high cariogenic and erosive potential. [36,2]

Syrups with high pH can cause erosive lesions on teeth when used for a long time or frequently. Oral acid production from refined carbohydrates or sugars in drugs or beverages is defined as acidogenicity. It has been understood that the ratio of refined carbohydrates and additives, which differentiate the properties of the test environments in which the experiment is performed, contribute to pH and titratable acidity. [37-39] On the other hand, there are studies reporting that all pediatric drugs cause erosion and calcium dissolution on the tooth surface. [6,20] In this study, all syrups caused calcium dissolution too.

Considering the precipitation of iron at high pH, buffering agents are often added while preparing iron preparations. These buffering agents also prevent the increase of the pH of the drug. Thus, the pH of iron preparations decreases and their acidity increases. It is known that after a food or beverage with high acidity is taken into the oral cavity, the pH of the environment rises above the critical pH of 5.5 within 2 minutes. An iron preparation with low pH but high acidity taken into the oral cavity requires a much longer time to reach neutral pH. This situation also shows its effect on the enamel surface and increases the formation of acid erosion. [40] In this study, we found that Ferro Sanol B, which is an iron drug, has the lowest pH. We also observed the highest calcium dissolution in this drug at the first and tenth minutes.

According to Maguire et al. examined a total of 97 drugs used by children in terms of pH, sugar content and measurable acidity in their in vitro study.[11] The pH of 57% of the drugs was found below the critical pH. As a result, they found that there was no significant difference between pediatric sugar-free and sugar-free drugs in terms of erosive properties, and the dose forms of the drugs were the more important determinants of the erosive potential of drugs. [11]

In the study of Arora et al., it was aimed to evaluate the erosive potential of 94 drugs used in children. In this study, pH values and acidity of drugs were evaluated. As a result, it was concluded that the relationship between the sugar content, pH and acidity of the drugs was not statistically significant and that the most important thing was the form of the drug. [41] In our study, calcium dissolution from the enamel was also observed regardless of the sugar content in the syrups. We think that the auxiliary chelating agents in the content of the drugs affect the dissolution of calcium. In this study, it was determined that the effect of pH values on calcium dissolution was less.

There are in vitro studies showing that drugs in the form of acidic syrup increase the erosive effect on teeth. [22,42,43] There are also studies showing that these drugs can reduce enamel hardness and affect the surface roughness of enamel. [11,28,41] The pH values of the drugs used in our study vary between 2.96 and 6.42.

It has been determined that all of the syrups with low and relatively higher pH included in our study dissolve calcium ions from the enamel of the primary teeth. It was observed that the pH of the examined pediatric liquid drugs mainly did not contribute to calcium dissolution from the enamel. This situation has been associated with chelating agents used in pediatric liquid drugs.

In our study, the percentage of sucrose in pediatric liquid drugs were; for Calpol at a concentration of 17.76%, Vitabiol at a concentration of 35.34%, Augmentin at a concentration of 17.86%, Zimax at a concentration of 19.00% and Ferro Sanol B at a concentration of 16.22%.

These findings are consistent with those of Lima et al., Kenny-Somaya and Santos Pinto et al. [44,45,46] Lima et al. noted that 58.3% of the drugs examined contained sucrose as a sweetening agent. [45] Pomorico et al. reported the presence of 5-54 g sucrose in 7 of 10 samples used in their study. [47] The most common other sweetener added to pediatric liquid medicines is glucose. In a similar study by Subramaniam and Nandan, it was stated that the sugar content in PLMs ranged from 0.84% to 5.49% g. [23,48]

Sunitha et al., on the other hand, estimated that sucrose levels ranged from 7.2% to 77% w/v in commonly used PLMs. [23,49]

According to Passos et al. measured sucrose levels in PLMs based on frequency and duration of use, and the sucrose values were recorded as 47.15% ± 9.57%, 24.42% ± 18.03%, and 34.43±14.83% for drugs prescribed once a day, twice a day, and 3 -4 times a day, respectively. [49]

In the study of Singana and Suma, it was stated that the sucrose content of the syrups used ranged from 0% to 48.25%. [42]

By the studies mentioned above, the sucrose content in the current study ranges from 16.26% to 35.34%, confirming the fact that pharmaceutical companies use sucrose indiscriminately.

In this study, all of the PLMs tested contained sucrose. The syrups used in our study were the most frequently prescribed preparations by the pediatricians in the region, and it is thought that such results may be because the number of drugs included in the study was less than in other studies.

As a result, it is seen that iron, multivitamin preparations and syrups used for various reasons in early childhood may cause erosion on tooth surfaces at different pH and acidity values. The recommendations that can be made on this subject may become clearer with more in vitro and clinical studies. It is thought that sugars used as flavor enhancers in drugs in the form of syrup and syrups may cause erosive and cariogenic effects due to the active ingredients in them. For this reason, after the use of syrup, the oral cavity should be rinsed with water, drugs should be used close to meal times, and oral hygiene protocols should be observed. It may be recommended to visit the dentist at intervals of 3-6 months, if possible, and to perform preventive fluoride procedures.

Due to the high number of syrups containing sugar, it is thought that the erosive and cariogenic potential is high, especially in the teeth of children with chronic systemic diseases. It may help to raise awareness among pediatricians and parents who prescribe drugs, for drug manufacturers to include labels that report the amount and type of sweetener added to drugs, and possible adverse effects on teeth. In addition, it may be beneficial to increase the number of drugs containing sweeteners with low erosive and cariogenic potential in the market and to express these drugs with "tooth-friendly" symbols. Although the in vivo environment was imitated in our research, since the experiment was carried out under in vitro conditions, it is not possible to fully provide in vivo conditions. In addition, in cases of erosion, early diagnosis is very important to protect teeth. For this reason, it can be recommended to carry out comprehensive studies in which the enamel of the primary teeth is evaluated in vivo, taking into account the chronic diseases, longer-term drugs with different active ingredients are used, and the Ca, F-, $(PO_4)^3$ contents of these drugs are examined in more detail.

CONCLUSION

According to the results of this study in which we evaluated the endogenous pH, sucrose ratio and the amount of calcium According to dissolved by the syrups from the enamel of the drug in five different pediatric syrup forms;

· The lowest endogenous pH values of drugs in the form of pediatric syrup were observed in Ferro Sanol B and the highest pH value was observed in Calpol syrup sample.

· The order of endogenous pH value of pediatric syrup samples is Calpol > Augmentin > Zimaks > Vitabiol > Ferro Sanol B.

· Sucrose was found in all syrup samples.

· Sucrose ratios are listed as Vitabiol > Zimaks > Augmentin > Calpol > Ferro Sanol B.

· A certain amount of calcium dissolution from enamel was observed in all of the syrup samples.

· The highest calcium dissolution rate was observed in Zimaks syrup sample at the 8th hour.

· The lowest calcium dissolution was observed in the Augmentin syrup sample at the 1st minute.

Statistically results were not found when calcium significant dissolutions were compared with the pH values of the syrups.

Değerlendirme / Peer-Review

İki Dış Hakem / Çift Taraflı Körleme

Etik Beyan / Ethical statement

Bu çalışma Prof.Dr. Behiye Bolgül danışmanlığında 19/07/2022 tarihinde sunduğumuz "ÇOCUKLARDA YAYGIN KULLANILAN ŞURUP FORMUNDAKİ İLAÇLARIN KARYOJENİK VE EROZİV POTANSİYELLERİNİN DEĞERLENDİRİLMESİ'' başlıklı yüksek lisans tezi esas alınarak hazırlanmıştır.

Bu çalışmanın hazırlanma sürecinde bilimsel ve etik ilkelere uyulduğu ve yararlanılan tüm çalışmaların kaynakçada belirtildiği beyan olunur.

This study has been prepared on the basis of the master's thesis titled "ÇOCUKLARDA YAYGIN KULLANILAN ŞURUP FORMUNDAKİ İLAÇLARIN KARYOJENİK VE EROZİV POTANSİYELLERİNİN DEĞERLENDİRİLMESİ'' which we submitted on 19/07/2022 under the supervision of Prof.Dr. Behiye Bolgül.

It is declared that during the preparation process of this study, scientific and ethical principles were followed and all the studies benefited are stated in the bibliography.

Benzerlik Taraması / Similarity scan

Yapıldı – ithenticate

Etik Bildirim / Ethical statement

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Çıkar Çatışması / Conflict of Interest

Yazarlar çıkar çatışması bildirmemiştir. | The authors have no conflict of interest to declare.

Yazar Katkıları / Author Contributions

Çalışmanın Tasarlanması | Design of Study: BB(%80),RA(%20)
Veri Toplanması | Data Acquisition: RA(%70),OP(%30)
Veri Analizi | Data Analysis: RA(%50),OP(%25),BB(%25)
Makalenin Yazımı | Writing up: OP(%80),RA(%20)
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REFERENCES

1. Sharma A. Deshpande S. Effect of Sucrose in Different Commonly Used Pediatric Medicines upon Plaque pH in Human Subjects. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2011, p 144. https://doi.org/10.4103/0970-4388.84688.
2. Lussi A. Ganss C. Erosive Tooth Wear: From Diagnosis to Therapy; Karger Medical and Scientific Publishers, 2014.
3. Moyer VA. US Preventive Services Task Force. Prevention of Dental Caries in Children from Birth through Age 5 Years: US Preventive Services Task Force Recommendation Statement. Pediatrics 2014, 133 (6), 1102–1111.
4. Imfeld T. Dental Erosion. Definition, Classification and Links. EUR. J. Oral Sci. 1996, 104 (2 (Pt 2)), 151–155.
5. Zero DT, Lussi A. Behavioral Factors. monogr. Oral Sci. 2006, 20, 100–105.
6. Girish Babu K, Rai K, Hedge A. Pediatric Liquid Medicaments – Do They Erode The Teeth Surface? An In Vitro Study: Part I. Journal of Clinical 2008.
7. Joshi RR. Editorial [Hot Topic: Protein Peptide Informatics and Drug Designing - Some Computational Techniques for Structural Genomics Based Approaches (Part II) (Guest Editor: Rajani R. Joshi)]. Protein & Peptide Letters. 2007, pp. 625–625. https://doi.org/ 10.2174/092986607781483949.
8. Bigeard L. The Role of Medication and Sugars in Pediatric Dental Patients. Dent. Clin. North Am. 2000, 44 (3), 443–456.
9. Zhao D, Tsoi JK-H, Wong HM, Chu CH, Matinlinna JP. Paediatric Over-the-Counter (OTC) Oral Liquids Can Soften and Erode Enamel. Dent. J. 2017, 5 (2). https://doi.org/ 10.3390/dj5020017.
10. Pierro VS da S, Abdelnur JP, Maia LC, Trugo LC. Free Sugar Concentration and pH of Paediatric Medicines in Brazil. Community Dent. health 2005, 22 (3), 180–183.
11. Maguire A, Baqir W, Nunn JH. Are Sugars-Free Medicines More Erosive than Sugars-Containing Medicines? An in Vitro Study of Paediatric Medicines with Prolonged Oral Clearance Used Regularly and Long-Term by Children. int. J. Paediatr. Dent. 2007, 17 (4), 231–238.
12. Taji S, Seow WK. A Literature Review of Dental Erosion in Children. aust. Dent. J. 2010, 55 (4), 358–367; quiz 475.
13. Bavbek AB, Dogan OM, Yilmaz T, Dogan A. The Role of Saliva in Dental Erosion and a Prosthetic Approach to Treatment: A Case Report. *J. Contemp. Dent. practice* 2009, 10 (3), 74–80.
14. Almeida, ICS; Costa Filho, LC Erosive Effect of an Antihistamine-containing Syrup on Primary Enamel and Its Reduction by Fluoride Dentrifice. *International Journal of* 2006.
15. Opening Ceremonies of the 72nd General Session and Exhibition of the International Association for Dental Research (IADR), the 23rd Annual Meeting and Exhibition of the American Association for Dental Research (a Division of the IADR), and the 18th Annual Meeting of the Canadian Association for Dental Research (a Division of the IADR), March 9,1994, in the Washington State Convention & Trade Center, Seattle, Washington, USA. J Dent. pic. 1994, 73 (7), 1244–1246.
16. Bamise CT, Olusile AO, Oginni AO. An Analysis of the Etiological and Predisposing Factors Related to Dentin Hypersensitivity. J. Contemp. Dent. practice 2008, 9 (5), 52–59.
17. Gillam DG. Dentine Hypersensitivity: Advances in Diagnosis, Management, and Treatment ; Springer, 2015.
18. Sahgal J, Sood PB, Raju OS. A Comparison of Oral Hygiene Status and Dental Caries in Children on Long Term Liquid Oral Medications to Those Not Administered with Such Medications. J. Indian Soc. pedod. Prev. Dent. 2002, 20 (4), 144–151.
19. Babu KLG, Rai K, Hegde A. pH of Medicated Syrups–Does It Really Matter? – An in-Vitro Study: Part-II. J. Clin. Pediatric Dent. 2008, 33 (2), 137–142.
20. McCLURE FJ, Ruzicka SJ. The Destructive Effect of Citrate vs. Lactate Ions on Rats' Molar Tooth Surfaces, in Vivo. J Dent. pic. 1946, 25, 1–12.
21. Nankar M, Walimbe H, Ahmed Bijle MN, Kontham U, Kamath A, Muchandi S. Comparative Evaluation of Cariogenic and Erosive Potential of Commonly Prescribed Pediatric Liquid Medicaments: An in Vitro Study. J. Contemp. Dent. practice 2014, 15 (1), 20–25.
22. Nankar M, Walimbe H, Ahmed Bijle MN, Kontham U, Kamath A, Muchandi S. Comparative Evaluation of Cariogenic and Erosive Potential of Commonly Prescribed Pediatric Liquid Medicaments: An in Vitro Study. J. Contemp. Dent. practice 2014, 15 (1), 20–25.
23. Sunitha S, Prashanth GM, Chandu GN. Subba Reddy, VV An Analysis of Concentration of Sucrose, Endogenous pH, and Alteration in the Plaque pH on Consumption of Commonly Used Liquid Pediatric Medicines. J. Indian Soc. pedod. Prev. Dent. 2009, 27 (1), 44–48.
24. Nunn JH, Ng SK, Sharkey I, Coulthard M. The Dental Implications of Chronic Use of Acidic Medicines in Medically Compromised Children. Pharm. WorldSci. 2001, 23 (3), 118–119.
25. Siddiq H, Pentapathy KC, Shenoy R, Velayutham A, Acharya S. Evaluation of Sugar Content and Erosive Potential of the Commonly Prescribed Liquid Oral Medications. pesquis brass. Odontopediatria Clin. Integr. 2020, 20. https://doi.org/ 10.1590/pboci.2020.023.
26. from Cate, JM Chemistry of Remineralization and Demineralization of Enamel and Dentine. 2000 .
27. Linnett V, Seow WK. Dental Erosion in Children: A Literature Review. Pediatric Dent. 2001 , 23 (1), 37–43.
28. Costa CC, Almeida ICS, Costa Filho LC. Erosive Effect of an Antihistamine-Containing Syrup on Primary Enamel and Its Reduction by Fluoride Dentrifice. int. J. Paediatr. Dent. 2006 , 16 (3), 174–180.
29. Fejerskov O, Kidd E. Dental Caries: The Disease and Its Clinical Management; John Wiley & Sons, 2009.
30. da Silva Pierro VS, Barcelos R, Maia LC, da Silva AN. Pediatricians' Perception about the Use of Antibiotics and Dental Caries--a Preliminary Study. J. Public Health Dent. 2004, 64 (4), 244–248.
31. Lewis CW, Grossman DC, Domoto PK, Deyo RA. The Role of the Pediatrician in the Oral Health of Children: A National Survey. Pediatrics 2000, 106 (6), E84.
32. Neves BG, Pierro VS da S, Maia LC. Pediatricians' Perceptions of the Use of Sweetened Medications Related to Oral Health. J. Clin. Pediatric Dent. 2008, 32 (2), 133–137.
33. Durward C, Thou T. Dental Caries and Sugar-Containing Liquid Medicines for Children in New Zealand. NZ Dent. J. 1997, 93 (414), 124–129.
34. Meyer-Lueckel H, Paris S, Extrand K. Caries Management - Science and Clinical Practice; Thieme, 2013.
35. Fejerskov O, Nyvad B, Kidd E. Dental Caries: The Disease and Its Clinical Management; John Wiley & Sons, 2015.
36. Cavalcanti AL, Sousa RIM, Clementino MA, Vieira FF, Cavalcanti CL, Xavier AFC. In Vitro Analysis of the Cariogenic and Erosive Potential of Pediatric Antitussive Liquid Oral Medications. Tanzania Journal of Health Research. 2012. https://doi.org/ 10.4314/thrb.v14i2.7.
37. Hellwig E, Lussi A. Oral Hygiene Products, Medications and Drugs - Hidden Aetiological Factors for Dental Erosion. monogr. Oral Sci. 2014, 25, 155–162.
38. Trivedi K, Bhaskar V, Ganesh M, Venkataraghavan K, Choudhary P, Shah S, Krishnan R. Erosive Potential of Commonly Used Beverages, Medicated Syrup, and Their Effects on Dental Enamel with and without Restoration: An in Vitro Study. Journal of Pharmacy and Bioallied Sciences. 2015, p 474. https://doi.org/10.4103/0975-7406.163508.
39. Marcdante K, Kliegman RM. Nelson Essentials of Pediatrics E-Book; Elsevier Health Sciences, 2018.
40. Ozbek N, Akman S. A Slurry Sampling Method for the Determination of Iron and Zinc in Baby Food by Flame Atomic Absorption Spectrometry. Food Addit. my seal. Part A Chem. Anal. Control Expo. Risk Assess. 2012, 29 (2), 208–216.
41. Arora R, Mukherjee U, Arora V. Erosive Potential of Sugar Free and Sugar Containing Pediatric Medicines given Regularly and Long Term to Children. Indian J. Pediatr. 2012, 79 (6), 759–763.
42. Singana T, Suma NK. An In Vitro Assessment of Cariogenic and Erosive Potential of Pediatric Liquid Medicaments on Primary Teeth: A Comparative Study. International Journal of Clinical Pediatric Dentistry. 2021, pp. 595–599. https://doi.org/10.5005/jp-journals-10005-1824.
43. Mahmoud EF, Omar OM. Erosive and Cariogenic Potential of Various Pediatric Liquid Medicaments on Primary Tooth Enamel: A SEM Study. Dent Med Proble 2018, 55 (3), 247–254.
44. Lima K, Almeida I, Senna E. [citation needed] Pediatric Medication-Sweetener Agents and pH. J Bras Odontoped Odonto Bebe 2000.
45. Kenny DJ, Somaya P. Sugar Load of Oral Liquid Medications on Chronically Ill Children. J. Can. Dent. Assoc. 1989, 55 (1), 43–46.

46. Santos-Pinto L, Uema AP, Galassi MA, Ciuff NJ. [EXIT] What Do Pregnant Women Know about Oral Health. J Bras Odontoped Odonto Bebe 2001.
47. Pomarico L, Czauski G, Portela MB, de Souza IPR, Kneipp L, de Araújo Soares RM, de Araújo Castro GFB. Cariogenic and Erosive Potential of the Medication Used by HIV-Infected Children: pH and Sugar Concentration. Community Dent. health 2008, 25 (3), 170–172.
48. Subramaniam P, Nandan N. Cariogenic Potential of Pediatric Liquid Medicaments--an in Vitro Study. J. Clin. Pediatric Dent. 2012, 36 (4), 357–362.
49. Passos IA, Sampaio FC, Martinez CR, Freitas CHS de M. Sucrose Concentration and pH in Liquid Oral Pediatric Medicines of Long-Term Use for Children. Rev. Panama. Salud Publica 2010, 27 (2), 132–137.