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ORIGINAL RESEARCH

Cariogenic Potential of the commonly Prescribed Pediatric Liquid Medicaments in Kingdom of Saudi Arabia: An *in vitro* Study

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ABSTRACT

Aim: The aim of this study was to assess the cariogenic potential of the commonly prescribed pediatric liquid medicaments (PLMs) for dental disease in Jazan region, Kingdom of Saudi Arabia.

Materials and methods: Seven most commonly prescribed PLMs were selected by prior questioning the pediatric dentists as well as general dentists in Jazan region. The endogenous pH and sucrose concentrations of the liquid medicaments were assessed. The endogenous pH was assessed by Hanna pH meter instrument. The sucrose concentration was assessed by anthrone reagent method.

Results: All the PLM were acidic. The pH of the PLM ranged from 4.22 to 6.10. All the PLM contained sucrose and its concentration ranged from 5.38 to 11.41 gm% in the samples.

Conclusion: In this study, all the PLM were acidic and contained sucrose. Hence, they have cariogenic potential.

Clinical significance: Parents and dentists are unaware of the hidden sugars and cariogenicity of these medications. Strict oral hygiene instructions are mandatory for the children taking these medications. The use of PLM should also be minimized and parents should seek early dental treatment to restore child's oral health.

Keywords: Cariogenicity, Pediatric liquid medicaments, pH, Sucrose.

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INTRODUCTION

Liquid medications are generally prescribed to the pediatric population for the commonly occurring ailments. They are widely available and easily accepted by both parents and children. Since it is difficult for children to swallow the tablets/capsules at a younger age, liquid medicament should be an easy way to administer the drugs to the children.

The majority of the pediatric liquid medicaments (PLMs) are made palatable by adding sugars to it.[1] This would mask the taste of its unpleasant active ingredient and hence, help to gain the child's compliance.[2-4] Sucrose is the commonly adjoined sweetener for such medicated formulations as it is an easily processed substance, cost-effective, and nonhygroscopic.[5] Fructose and glucose are also added to the PLM.[4] These added sugars may be fermented by oral bacteria leading to the acid formation and a drop in the intraoral pH. Pediatric liquid medicaments also contain certain acids, which are added as buffering agents to maintain chemical stability, control tonicity, and physiological compatibility of the solution. They also improve the flavor and hence, the medication becomes more acceptable to children.[6]

The added sugars along with the acidic solutions may produce unwanted dental side effects in children. Hence, a high intake of oral medications may result in reduced hardness of primary teeth,[7] morphological enamel alteration,[8] dentinal hypersensitivity,[9] and increased prevalence of dental caries.[10] Many of the authors have expressed their concerns that oral liquid medications contribute to the total sugar load and to the development of dental caries in children.[11-13]

However, in the Middle Eastern countries (especially Kingdom of Saudi Arabia), there have been no studies reported about the cariogenic potential of the commonly prescribed PLM to children. Since the PLM are routinely dispensed at the various hospitals and primary health

care centers in Kingdom of Saudi Arabia, it is very important for us to assess their cariogenic potential. Hence, this study was carried out to evaluate the cariogenic potential of the most commonly prescribed PLM in Jazan region, Kingdom of Saudi Arabia.

MATERIALS AND METHODS

Seven most commonly prescribed PLMs for oral diseases were selected for the study (Table 1). This selection was done after consulting the general dentists as well as the pediatric dentists working in various government and private sectors in Jazan region, Kingdom of Saudi Arabia. These medicaments were from different pharmaceutical companies. These medicaments included antibiotics, analgesics, and a multivitamin. All the samples were coded as RSE1 to RSE 7.

Objectives of the study are as follows:

- To determine the endogenous pH of the seven PLMs
- To assess the concentration of sucrose in these drugs.

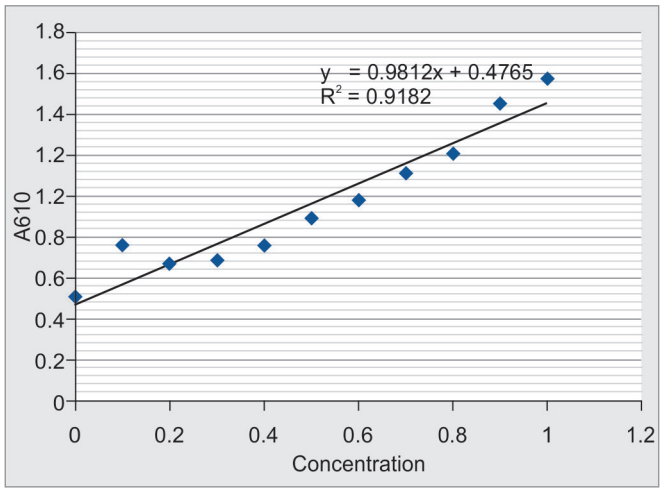
Endogenous pH Estimation

The endogenous pH was measured using HANNA digital pH meter (Fig. 1). The pH meter was set to pH mode and the temperature was adjusted to 25°C. The electrode was placed in the sample to be tested. The pH of the solution appeared in the display. The display was allowed to be stabilized before the reading was taken. The pH electrode was rinsed and placed back in the storage solution.

Endogenous Sucrose Assessment

The sucrose estimation in the sample was done by anthrone reagent method. The anthrone method is an example of a colorimetric method of determining the concentration of the total sugars in a sample. It is nonstoichiometric, and therefore, it is necessary to prepare a calibration curve using a series of standards of known carbohydrate concentration (Graph 1). All the experiments were done in triplicates (Figs 2A and B). Sugars reacted with the anthrone reagent under acidic conditions to yield a blue – green color. The sample was mixed with sulfuric acid and the anthrone reagent, and then boiled until the reaction was completed (Figs 3A and B). The solution was then allowed to cool and

Fig. 1: Hanna digital pH meter



Graph 1: Standard graph for sucrose

its absorbance was measured at 620 nm. There was a linear relationship between the absorbance and the amount of sugar that was present in the original sample. This method determines both reducing and nonreducing sugars because of the presence of the strongly oxidizing sulfuric acid.

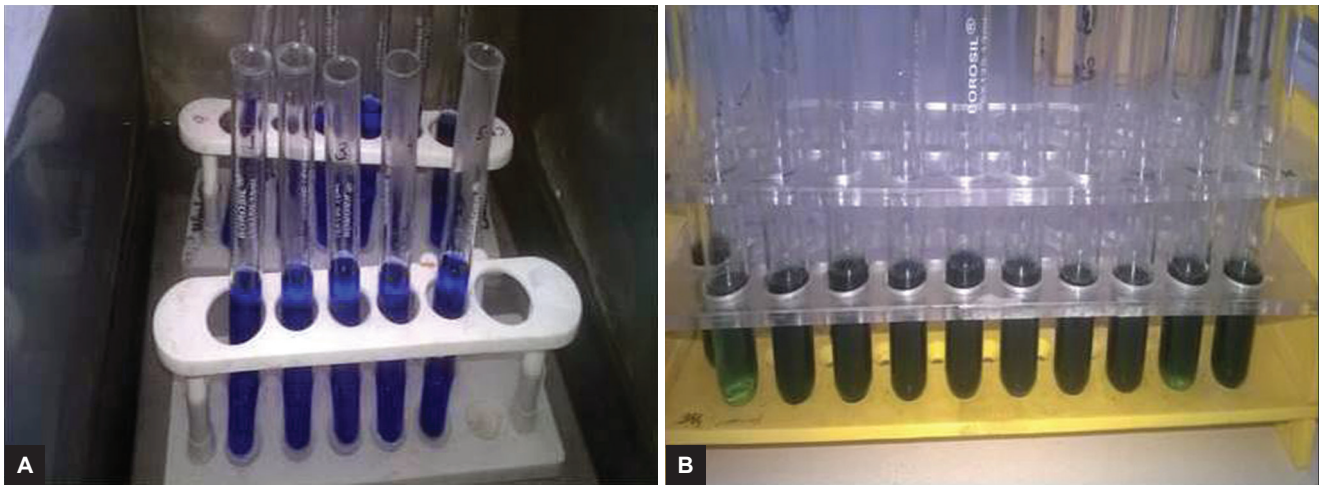
$$\text{Percentage total apparent sucrose} = \frac{A_{sample}}{A_{standard}} \times 15$$

RESULTS

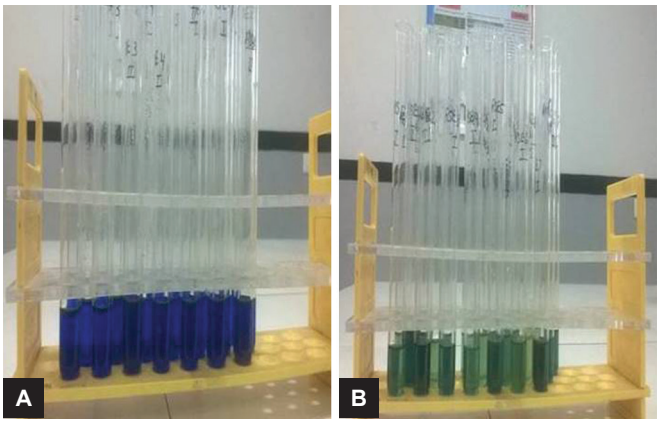
The pH measurements in the provided samples are given in Table 2. It ranged from 4.22 for the nutritional supplement

Table 1: Pediatric Liquid Medicaments selected for the study

PLM	*Generic name*	*Trade name*	*Code*
Analgesic, antipyretic	Paracetamol	Adol	RSE 1
Non-steroidal anti-inflammatory drug	Ibubrufen	Medafen	RSE 2
Antibiotic	Amoxicillin trihydrate	Julphamox	RSE 3
Antibiotic	Amoxicillin trihydrate	Megamox	RSE 4
Antibiotic	Metronidazole benzoate	Riazole	RSE 5
Antibiotic	Amoxicillin and Potassium Clavulanate	Julmentin	RSE 6
Nutritional supplement	Multivitamin	Life mark	RSE 7



Figs 2A and B: Sucrose standard preparation. (A) Fehling solution added in sucrose solution; and (B) addition of anthrone reagent after Fehling treatment



Figs 3A and B: Assessment of sucrose in the study samples. (A) Study samples after treated with Fehling solution; and (B) study samples after being treated with anthrone

"Life mark" to 6.10 for antibiotic "Julphamox." Hence, all the drugs were acidic.

Sucrose was present in all the samples. The concentration of sucrose in each sample is given in Table 3. Nonsteroidal anti-inflammatory drug "Medafen" contained the highest amount of sucrose, which was 11.41 gm%.

Table 2: pH of the Pediatric Liquid Medicaments

Sl. no.	*Sample code*	*pH*
1	RSE 1	5.78
2	RSE 2	5.66
3	RSE 3	6.10
4	RSE 4	4.87
5	RSE 5	5.69
6	RSE 6	5.39
7	RSE 7	4.22

Table 3: Sucrose concentration in the different samples as determined by Anthrone method

Sl. no.	*Sample code*	*Raw value in triplicates*	*Mean ± Standard deviation*	*Percent total apparent sucrose (gm%)*
1	Standard	1.938, 1.838, 1.765	1.847 ± 0.0868	–
2	RSE 1	0.276, 0.255, 0.110	0.68 ± 0.09	5.56
3	RSE 2	0.643, 1.438, 0.761	1.41 ± 0.42	11.41
4	RSE 3	0.193, 0.601, 0.585	0.93 ± 0.23	7.53
5	RSE 4	0.334, 0.217, 0.221	0.73 ± 0.07	5.92
6	RSE 5	0.941, 0.888, 0.832	1.35 ± 0.05	10.93
7	RSE 6	0.262, 0.167, 0.141	0.66 ± 0.06	5.38
8	RSE 7	0.858, 0.980, 0.997	1.4 ± 0.07	11.4

DISCUSSION

Dental caries is the most chronic disease seen in children and is a major concern worldwide.[14,15] It is a disease of the calcified tissues of the teeth caused by the action of microorganisms on fermentable carbohydrates. Sugars are known to be the principal etiologic agent for dental caries. Sucrose is considered to be the arch criminal and the major etiologic agent for dental caries.[16] Many parents are aware that sugar causes tooth decay, but commonly relate this solely with the consumption of sweets and biscuits. They are often unaware of the hidden, added sugar in many foods and drinks, including pediatric liquid medicines. Not only the parents but also the health care workers are unaware of the hidden sugars in PLM, which can drastically predispose an individual to an increased susceptibility for dental caries.

The most conclusive evidence about the cariogenicity of liquid oral medicaments was provided by Roberts and Roberts[17] and Feigal et al[18] who showed that a continuous administration of sucrose-based medicines causes dental caries and related gingivitis. Various other studies have also confirmed that these preparations are cariogenic and acidogenic in nature.[10-13] Thus, this study was conducted to investigate the cariogenic potential of

the commonly used PLMs in Jazan region, Kingdom of Saudi Arabia.

The cariogenic potential of these medicaments depends on many factors, such as pH, titratable acidity, sugar content, viscosity, frequency of ingestion, and physical and chemical properties affecting adherence to the enamel surface.[19] In our study, we focused only on the inherent characteristics that cause dental caries. Hence, the most important factors responsible for cariogenicity, i.e., endogenous pH and sucrose concentration, were assessed.

Many liquid medications have an endogenous low pH[20] that may itself contribute to demineralization or at least inhibit the demineralization-remineralization process in the newly erupted teeth.[21] The sucrose metabolized by oral bacteria to acid end-products decreases the pH. Low pH near the tooth surface causes ionic dissolution from the hydroxyapatite crystals and eventually carious lesions. In an *in vivo* study, it was concluded that PLM causes a drop in plaque pH sufficient to cause decalcification within 2 to 10 minutes, following its initial exposure to the teeth.[12] Furthermore, high concentrations of fermentable carbohydrates in PLM may facilitate the growth of *Streptococcus mutans* by rapidly metabolizing sugars to acids; thus, initiating enamel demineralization.

The HANNA digital pH meter used in our study is more accurate and efficient than conventional electrode pH meter.[12,22] In our study, three out of seven PLM had pH below the critical pH (5.5) of the oral cavity. The range was from 4.22 to 6.10 showing that all were acidic. This is in accordance with other studies.[11-13,23]

Different studies have concluded that the amount of sucrose in the PLM ranged from 0 to 67 gm%.[24] All the PLM in our study contained sucrose, and it ranged from 5.38 to 11.41 gm%. However, this is less compared with that reported in the other studies. Neves et al[13] concluded that 10 out of 23 PLMs had sucrose in their study and the concentration ranged from 11.36 to 85.99 gm%. Pomarico et al[22] reported the presence of sucrose in 7 of the 10 samples studied, ranging between 5 and 54 gm%.

Primary teeth are less mineralized than the permanent teeth. The primary enamel surface being less mature is more prone to dental caries.[25] The oral clearance process is less effective in children than in adults due to lower salivary flow and less pronounced oral muscular coordination ability.[26]

Most of the syrups are given in divided doses of two to three to children. The night dose, especially, has a deleterious effect on the enamel as the salivary flow rate is diminished at night.[26] Further, the pain from irreversible pulpitis is more at night while sleeping (posture) as there are high chances that children wake up from pain at night. To calm them, the analgesic syrup will be given at night. The last dose of an antibiotic is also given at night. These acidic and sucrose-containing syrups taken at nighttime, when there is decreased salivary clearance, can definitely increase the incidence of dental caries. In a child who is already suffering from dental caries, it will increase the severity of the disease. Though there are a good infrastructure and health care facilities, there are many reasons for the delay in seeking dental treatment in children in Jazan region. The lack of cooperation from the child, unwillingness to miss the school, lack of interest by the general dentist in providing dental treatment to young precooperative children, and ignorance of dental disease by the parents are the few reasons. In all such cases, PLMs are given to children to allay them from pain and discomfort. The increase of prescribed medicine intake and of self-medication in developed countries exposes a growing number of children to medication caries, which can be considered a public health problem.[5]

The patients, as well as dentists, should be aware of the hidden sugars in the medicines. In this study, all the PLM were acidic and contained sucrose. It is recommended that all sugar-containing medicines should be labeled with the concentration of sucrose present in them. An important method of preventing dental caries is patient education through reinforcement of good oral hygiene methods.

CONCLUSION

Pharmaceutical preparations with acidic pH and high sugar content have a potential of increasing the susceptibility to dental caries when used frequently.

All the PLMs in our study were found to be acidic. Nutritional supplement "Lifemark" was the most acidic of the PLM, followed by antibiotic "Megamox" (Amoxicillin).

All the PLMs had sucrose, but the concentration was less compared with other studies.

The dentists should be aware of the high cariogenic potential of the commonly prescribed liquid medicaments. The dental personnel should advise the mothers and caretakers to introduce oral hygiene practices after the consumption of the medications.

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