Acidogenic Evaluation of Pediatric Medications in Saudi Arabia

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Background: To gain patient compliance, pediatric medication preparations are made palatable by adding sugars such as sucrose, glucose, or fructose. These readily fermentable carbohydrates can significantly increase dental caries potential in the young and chronically sick children.

Objectives: To evaluate acidogenic potential of commonly used pediatric liquid medicaments (PLMs).

Materials and Methods: The acidogenic potential is assessed by estimating the endogenous pH of PLM.

Results: The mean endogenous pH was higher in Azomycin (9.16 ± 0.25) and lowest in Lorinase (3.16 ± 0.15).

Conclusion: Of nine, eight PLMs were acidic in nature.

Keywords: Acidic pH, acidogenic potential, hidden sugars, pediatric liquid medicaments

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INTRODUCTION

Oral health is interlinked with general health for children’s growth and development. The most prevalent and common oral disease of the oral cavity is dental caries.[1]

There are many theories to explain the caries onset and the most widely accepted among them is by the action of acids produced by bacterial fermentation of carbohydrates from the diet. This can be further enhanced by some disease or use of medication.[2]

The commonly prescribed pediatric liquid medicaments (PLMs) to improve or maintenance of children health are easily accepted by both parents and children due to the sweetening agents present in it. But these inactive ingredients can be a risk to dental health.

Children with chronic conditions and under medications are said to be at higher risk for dental caries by the American Academy of Pediatric Dentistry (AAPD) after using caries risk assessment tool.[3]

These pharmaceutical preparations have a greater sugar load, with a mean sugar content of 55%,[4] To enhance the taste and acceptance by children, sugars were added in children’s medicines[5] although they may produce unwanted dental side effects in children, who are already medically compromised.[6]

When James and Parfitt[7] described the extensive labial caries developed in children taking iron tonics in 1953, long-term use of medicines to treat rampant caries were kept under observation. The most conclusive evidence was given by Roberts and Roberts[8] and Feigal and Jensen,[9] who showed that long-term consumption of sucrose-based medicines cause dental caries and related gingivitis.

Rekola[10] showed that sweetened syrups either with sucrose, fructose or with a combination of fructose and sorbitol causes a long-term drop in the plaque pH leading to favorable condition for the occurrence dental caries.[11,12]

There is growing concern among dentists about the increased consumption of “hidden sugars” by children, especially those who are chronically ill. It is important to assess the cariogenic potential of commonly used PLM.

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Hence, the purpose of this study was to evaluate the endogenous pH of commonly used PLMs in Saudi Arabia.

**Materials and Methods**

Nine commonly used pediatric syrups were selected for the study. The PLMs included were three most commonly prescribed analgesics, three antibiotics, and three antitussives. This is an *in vitro* study and was carried out in the College of Applied medical sciences, PSAU, Saudi Arabia.

**pH measurements**

The endogenous pH of pediatric syrup was determined at room temperature using pH meter. According to the manufacturer’s instructions, before starting, it was calibrated by using buffer standards of pH 7 and pH 4 to 0.1. The pH meter was immersed in 10 mL of medication and the values were recorded. Three different readings were recorded for each medication and mean pH was considered as final pH.

**Statistical analysis**

Descriptive statistics were computed and data obtained were analyzed using analysis of variance (ANOVA) and Tukey post hoc test.

**Results**

Table 1 shows the list of syrups (analgesics, antibiotics, and antitussives), manufacturing company, and the main ingredients of the syrup.

Table 2 represents the endogenous pH of the study syrups. The mean endogenous pH was higher in Azomycin (9.16 ± 0.25) and lowest in Lorinase (3.16 ± 0.15). The two syrups, namely Sapofen Junior and Amydramine, had a pH nearly or less than the critical pH. This was statistically highly significant (*P* = 0.000).

Table 3 represents multiple group comparisons using Tukey’s post hoc. This showed there is a significant pH difference between Fevadol – SF and Nurofen, Megamox 312, Azomycin, Histop, and Lorinase. Sapofen Junior showed significant difference with Nurofen, Megamox 312, Cefproz 250, Azomycin, Histop, and Lorinase. Nurofen showed significant difference with Azomycin, Amydramine, Histop, and Lorinase. Megamox 312 showed significant difference with Azomycin, Amydramine, Histop, and Lorinase. Cefproz 250 showed significant difference with Azomycin, Histop, and Lorinase. Azomycin showed significant difference Amydramine, Histop, and Lorinase.

**Discussion**

In general, though the use of PLM is for a short duration, it is of concern for chronically ill children. The active ingredients of the medicines are necessary for improvement or maintenance of health, although some inactive ingredients can increase caries.[13] The pediatric medicines used in this study did not specify any information about its pH, the kind of sugar present except the composition with a particular flavor. Therefore, the pH of each PLM was measured.

The pH of the liquid medicines ranged between 3.16 for Lorinase to 9.16 of Azomycin. Eight of the six syrups were acidic and all have a pH <5.5 which is known as the critical pH. The results of this study were contrast to study by Girish Babu *et al.*, where the pH ranged from 6.05 to 7.71 among different syrups evaluated.

| Category       | Syrups         | Manufacturers                                      | Active ingredient                                           |
|----------------|----------------|---------------------------------------------------|------------------------------------------------------------|
| Analgesics     | Fevadol – SF   | SPIMACO, AL-Qassim Pharmaceutical Plant, Saudi Arabia | Paracetamol (120mg/5mL)                                    |
|                | Sapofen Junior | SPIMACO, AL-Qassim Pharmaceutical Plant, Saudi Arabia | Ibuprofen (100mg/5mL)                                     |
|                | Nurofen        | Reckitt Benckiser Healthcare International Limited, Hull, UK | Ibuprofen (100mg/5mL)                                     |
| Antibiotics    | Megamox 312    | Jazeera Pharmaceutical Industries P O BOX 106229 Riyadh 11666, Saudi Arabia | Amoxicillin 250mg and clavulanic acid (as potassium) 62.5 mg |
|                | Cefproz 250    | MEDPHARMA, UAE                                     | Anhydrous cefprozil 250 mg                                 |
|                | Azomycin       | Julphar, Gulf Pharmaceutical Industries, Ras Al Khaimah, UAE | Azithromycin 200 mg                                       |
| Antitussives   | Amydramine     | Julphar, Gulf Pharmaceutical Industries, Ras Al Khaimah, UAE | Diphenhydramine HCL, sodium citrate, and menthol            |
|                | Histop         | SPIMACO, AL-Qassim Pharmaceutical Plant, Saudi Arabia | Chlorpheniramine maleate syrup (2mg/5mL)                   |
|                | Lorinase       | SPIMACO, AL-Qassim Pharmaceutical Plant, Saudi Arabia | Loratadine and pseudoephedrine sulfate                     |
and similar to Cavalcanti et al.,[2] who reported that antitussives had pH below the critical value and had greater cariogenic and erosive potentials.

Many liquid medications have an endogenous low pH[9] that may itself contribute to demineralization or at least inhibit the remineralization process in newly erupted teeth.[15]

The endogenous pH of syrups can be altered by salivary buffers intra orally. At the same time, bacteria-rich plaque adherent to tooth structure show decreased pH due to the metabolization of sugars by bacteria to acid end products, which are not available for salivary buffering. This low pH near the tooth surface causes

| Table 2: Endogenous pH of the studied syrups |
|---------------------------------------------|
| Syrups       | Mean  | SD  | F       | P Value |
|-----------------|-------|-----|---------|---------|
| Fevadol – SF    | 4.96  | 0.15| 493.23  | 0.000***|
| Sapofen Junior | 5.26  | 0.11|         |         |
| Nurofen        | 4.46  | 0.05|         |         |
| Megamox 312    | 4.53  | 0.11|         |         |
| Cefproz 250    | 4.73  | 0.05|         |         |
| Azomycin       | 9.16  | 0.25|         |         |
| Amydramine     | 5.10  | 0.10|         |         |
| Histop         | 3.76  | 0.05|         |         |
| Lorinase       | 3.16  | 0.15|         |         |

SD = standard deviation

$P < 0.05$

*** Highly significant

| Table 3: Multiple comparisons using Tukey honestly significant difference |
|------------------------------------------------------------------------|
| Syrup                      | Compared with | Mean difference (I–J) | Sig.  |
|-----------------|---------------|----------------------|-------|
| Fevadol – SF    | Sapofen Junior| -0.30                | 0.187 |
|                 | Nurofen       | 0.50*                | 0.005 |
|                 | Megamox 312   | 0.43*                | 0.018 |
|                 | Cefproz 250   | 0.23                 | 0.464 |
|                 | Azomycin      | -4.20*               | 0.000 |
|                 | Amydramine    | -0.13                | 0.937 |
|                 | Histop        | 1.20*                | 0.000 |
|                 | Lorinase      | 1.80*                | 0.000 |
| Sapofen Junior  | Nurofen       | 0.80*                | 0.000 |
|                 | Megamox 312   | 0.73*                | 0.000 |
|                 | Cefproz 250   | 0.53333*             | 0.003 |
|                 | Azomycin      | -3.00*               | 0.000 |
|                 | Amydramine    | 0.16                 | 0.820 |
|                 | Histop        | 1.50*                | 0.000 |
|                 | Lorinase      | 2.10*                | 0.000 |
| Nurofen         | Megamox 312   | -0.06                | 0.999 |
|                 | Cefproz 250   | -0.26                | 0.305 |
|                 | Azomycin      | -4.70*               | 0.000 |
|                 | Amydramine    | -0.63*               | 0.000 |
|                 | Histop        | 0.70*                | 0.000 |
|                 | Lorinase      | 1.30*                | 0.000 |
| Megamox 312     | Cefproz 250   | -0.20                | 0.648 |
|                 | Azomycin      | -4.63*               | 0.000 |
|                 | Amydramine    | -0.56*               | 0.001 |
|                 | Histop        | 0.76*                | 0.000 |
|                 | Lorinase      | 1.36*                | 0.000 |
| Cefproz 250     | Azomycin      | -4.43*               | 0.000 |
|                 | Amydramine    | -0.36                | 0.061 |
|                 | Histop        | 0.96*                | 0.000 |
|                 | Lorinase      | 1.56*                | 0.000 |
| Azomycin        | Amydramine    | 4.06*                | 0.000 |
|                 | Histop        | 5.40*                | 0.000 |
|                 | Lorinase      | 6.00*                | 0.000 |
| Amydramine     | Histop        | 1.33*                | 0.000 |
|                 | Lorinase      | 1.93*                | 0.000 |
| Histop         | Lorinase      | 0.60*                | 0.001 |

*The mean difference is significant at the 0.05 level
Ionic dissolution from the hydroxyapatite crystals and eventually carious lesions.[16]

Hence, initial exposure to the teeth with PLM is sufficient to cause decalcification within 2–10 min.[17]

Along with that, to maintain the chemical stability, physiological compatibility, and to improve the flavor, certain acids are commonly used in medicines as buffering agents. Citric acid is the most commonly used in prolonged oral clearance of medicines. And as a weak acid, it dissociates in solutions of a higher pH and acts as a buffer over a range of pH.[18]

Masters[19] observed reduction in dental caries in children taking antibiotics for long time, but after 4 years of age, this effect was disappeared. Some researchers observed a significant decline in dental caries with the use of antibacterial syrup.[20] Although antibiotics are antimicrobial in nature, their use in children who are on long-term medication should not be ignored, as these preparations have an enamel-erosive potential.[21,22]

Studies have shown that other medicaments did not promote or inhibit Streptococcus mutans growth compared to antibiotics.[13] However, their endogenous pH has been seen to have an acidogenic potential,[21,22] hence, caution must be taken during prescribing these PLM.

As this study is in vitro, the results cannot be compared completely to the in vivo situation. The presence of the pellicle in in vivo situation will protect the teeth from acidic challenges. The amount and quality of saliva, its buffering capacity, are also important in the occurrence of dental caries along with other factors such as retention, bacterial activity, sugar formation, oral hygiene, and hormone factors, which may have a significant contributory effect for causation of dental caries, along with the prescribed medicaments that are absent in in vitro situation.

**Conclusion**

The mean endogenous pH ranging being highest in Azomycin (9.16 ± 0.25) and lowest in Lorinase (3.16 ± 0.15). Of nine, eight PLMs were acidic in nature. Hence, a care should be taken when prescribing the same for a longer duration and instructions to parents to be given to rinse the mouth after consumption of medication to dilute its acidic effect. To measure the total acid content of a given substance, titratable acidity was considered a more reliable measure than the pH itself. Hence, further studies are recommended to include the same.

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**Conflicts of interest**

There are no conflicts of interest.

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