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Evaluation of the pH, titratable acidity and viscosity of various brands of syrups sampled from various pharmacy stores in Benin.

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ABSTRACT

Background: For so long now, medicated syrups have been used in paediatric practice for the treatment of disease conditions, as palliatives and even as food supplements / haematinics. Pharmaceutical firms sweeten liquid preparations with sucrose to aid compliance, and this in turn increases their viscosity. Some of the constituents of these syrups are acidic and are capable causing erosion of the dentiture.

Objectives: This *in vitro* study aims to evaluate the endogenous pH, titratable acidity and viscosity of different syrups sampled from different pharmacy stores in Benin City.

Methods: Sixteen (16) commonly used syrups were evaluated. The pH of each syrup was determined using a digital pH meter. The titratable acidity was assessed by titrating 0.1 N sodium hydroxide solution against 30 ml of each syrup until a pH of 8.2 was reached. The viscosity of the syrups was determined using a suspended level viscometer.

Results: The pH of the syrup brands ranged from 3.25 to 6.18. All the syrups had an acidic pH and 82% of the samples showed pH below the critical value of 5.5 which is capable of causing enamel dissolution. The titratable acidity of the syrups ranged from 0.93-7.50 g/100 ml while the kinematic viscosity of the syrups ranged from 6.51-75.96 mm^2S^{-1}.

Conclusion: The outcome of this study confirms that all syrups investigated had high values of pH, titratable acidity and viscosity.

Key words: Tiratable acidity, syrups, viscosity, pH, enamel dissolution.

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Évaluation du pH, de l'acidité titrable et de la viscosité dans une variété de marques de sirops prélevés dans différentes pharmacies au Bénin.

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RESUME

Contexte: Depuis bien longtemps, les sirops médicamenteux sont utilisés dans la pratique pédiatrique pour le traitement des maladies, comme palliatifs et même comme compléments alimentaires/hématiniques. Les entreprises pharmaceutiques édulcorent les préparations liquides avec du saccharose pour faciliter la conformité, ce qui augmente ainsi leur viscosité. Certains des constituants de ces sirops sont acides et sont capables de provoquer une érosion de la dentition.

Objectifs: Cette étude *in vitro* vise à évaluer le pH endogène, l'acidité titrable et la viscosité des différents sirops échantillonnés dans différentes pharmacies de la ville de Bénin.

Méthodes: Seize (16) sirops couramment utilisés ont été évalués. Le pH de chaque sirop a été déterminé à l'aide d'un pH-mètre numérique. L'acidité titrable a été évaluée en titrant une solution d'hydroxyde de sodium 0,1 N contre 30 ml de chaque sirop jusqu'à ce qu'un pH de 8,2 soit atteint. La viscosité des sirops a été déterminée à l'aide d'un viscosimètre à niveau suspendu.

Résultats: Le pH des marques de sirop variait de 3,25 à 6,18. Tous les sirops avaient un pH acide et 82% des échantillons présentaient un pH inférieur à la valeur critique de 5,5 qui est capable de causer la dissolution de l'émail. L'acidité titrable des sirops variait de 0,93 à 7,50 g/100 ml tandis que la viscosité cinématique des sirops variait de 6,51 à 75,96 mm^2S^{-1}.

Conclusion: Les résultats de cette étude confirment que tous les sirops étudiés avaient des valeurs élevées de pH, d'acidité titrable et de viscosité.

Mots-clés: Acidité tirable, sirops, viscosité, pH, dissolution de l'émail.

INTRODUCTION

Pleasantly tasted syrups have long been used in paediatric practice to aid compliance with medication and children receive a variety of oral liquid medications for the treatment of diseases, improvement and maintenance of health.

Pharmaceutical firms sweeten liquid drug preparations with sucrose to increase the palatability; compliance and also to act as a preservative.[1] Additionally, these syrups contain pharmaceutical excipients considered inert, to enhance their bioavailability, stability and appearance without affecting the intended action of the pharmaceutical active ingredient.[2]

However, these excipients tend to cause enamel erosion and dental caries. The effect of long term consumption of sugar containing liquid medications on the teeth is an issue of concern for dental health practitioners. Syrup sweetened with sucrose produced a marked and long term drop in plaque pH, leading to dissolution of the enamel.[3,4,5]

Dental erosion is the chemical dissolution of the dental tissues without bacterial involvement. The underlying etiology of erosion is believed to be a source of acidic action on the susceptible tooth.[6] The erosive effect of dietary acids on dental tissues can be influenced by a number of factors including pH, dissociation constant of acid (Ka), titratable acidity (TA), viscosity, frequency of administration, etc. In addition to the factors listed above, chelation potential, concentration, pellicle layer and variations in tooth structure also contribute to erosion process.[7,8]

The pH of syrup is the measure of the hydrogen ion concentration in the syrup. The pH scale usually ranges from 0 -14. Syrups with pH less than 7 are acidic while those with pH greater than 7 are basic.[9]

Titratable acidity (TA) is measurement of the total acid concentration contained within the solution. It also represents the amount of base required to raise the pH of a solution to 8.2. TA is indeed the buffering capacity which suggests the amount and strength of the available acid.[10]

It has been suggested that TA of dietary substances should be considered more signicant than their pH, since it largely determined hydrogen ion concentration available to interact with the tooth surface.[11]The pH is measured with a universal indicator paper or digital pH meter while the TA is assessed by measuring the weight (in grams) of standard sodium hydroxide necessary for titration to a pre-determined pH level.

The viscosity of a fluid is a measure of its resistance to gradual deformation by shear stress or tensile stress. It is a measure of a fluid's resistance to flow. Viscosity is measured in Pascal second (Pa.s) or Newton second per meters square ($N.s/m^2$) and most medicinal syrups contain a high sugar (sucrose) content, hence an increased viscosity. As the viscosity of the syrup increases, its flowability decreases. Therefore, syrups with a high viscosity tend to have a longer contact time and lower flowability when administered.

Viscosity is measured with various types of viscometers and the type of instrument used depends on the nature of the fluid. The viscosity of syrups can be determined using viscometer which is a special type of rheometer.[13]

This research aims to determine the endogenous pH, TA and viscosity of syrups that are frequently given to Nigerian children and to ascertain the potentials of causing dental cavity erosion.

METHODS

Equipment

Digital pH meter (Search Tech UK), Suspended level viscometer (Ubbelohde viscometer, Technico, England).

Reagents and solvents

Analytical grades of sodium hydroxide (Qualikems, India), concentrated hydrochloric acid(36% w/w), phosphate buffer solutions (at pH 4.0, 7.0 and 10.0) were used for the study.

The syrups used were purchased from various pharmacy stores in Benin City and is shown in Table 1

Table 1: List of syrups and their manufacturing details.

SYRUP	NAFDAC NUMBER	MANUFACTURING DATE	EXPIRY DATE
Analgesics			
Brustan N Ibuprofen	A4-0488	01-2017	12-2018
Emzor paracetamol	04-0289	03-2017	03-2020
M & B paracetamol	04-0247	02-2017	01-2020
Antihistamines			
Allergin (chlorpheniramine)	04-1955	09-2016	09-2017
Flu J syrup	04-6394	03-2017	04-2019
Piriton syrup	04-0437	10-2016	09-2019
Cough syrup			
Benylin cough syrup	04-0820	09-2016	08-2019
Coflin cough syrup	04-0540	01-2017	01-2018
Cofta cough syrup	04-0106	09-2016	08-2018
Emzolyn cough syrup	04-1454	01-2017	01-2020
Multivitamins			
Emvite multivitamin	04-0135	05-2017	05-2020
Kp multivitamin	04-1319	10-2015	09-2017
Supramult syrup	04-7529	10-2016	09-2019
Vitamin C syrups			
Emvit C syrup	04-0262	08-2016	08-2019
Kp vitamin C syrup	04-0879	01-2016	12-2017
Others			
Emgyl metronidazole syrup	04-1452	02-2017	02-2020

Calibration of the digital pH meter

The pH meter was switched on at least 30 minutes before commencing the experiment, to ensure accurate readings. The temperature of the pH meter was maintained at 20^{0}C, and the pH electrode was immersed in a beaker containing 30 ml distilled water, to stabilize the base reading. The pH meter was thereafter calibrated using phophate buffer solutions of pH 4.0, 7.0 and 10.0.

30 ml of each buffer solution was measured into a 50 ml beaker.

The electrodes were dipped into distilled water and wiped dry with cotton wool before the pH of the syrup samples were determined.

Determination of pH of the syrup samples

A volume (30 ml) of each syrup was measured into a pre-cleaned 50 ml beaker. The pH electrode was immersed into the beaker and the reading was allowed to stabilize for about 5 minutes before the final pH value was recorded. Triplicate determinations were done for each syrup sample and the average pH was calculated and recorded.

The pH electrode was rinsed with clean distilled water and wiped dry with tissue paper before successive determinations were carried out.

Determination of titratable acidity

The TA of the samples was determined by titrating aliquot amount of each syrup against 0.1 N sodium hydroxide solution.

Preparation of 0.1 N sodium hydroxide (NaOH) solution

The NaOH (0.1 N) was prepared by weighing 4.00 g of NaOH granules into a beaker and 50 mL of de-ionized water was added. This was stirred until there was complete dissolution and the solution was transferred into a 1000 ml volumetric flask. More distilled water was added to make up to the 1000 ml mark.

Determination of titratable acidity of the syrup samples

A volume (30 ml) of each syrup sample was measured into a 50 ml beaker. The titration apparatus was set up, and the burette was filled with a solution of 0.1 N NaOH. The syrup sample was then titrated against the 0.1 N NaOH from the burette with continuous stirring. A piece of red litmus paper was used as an indicator to monitor the titration. The volume of 0.1 N NaOH needed to bring the pH of the samples to 8.2 was then determined, while monitoring the pH changes using a digital pH meter.

Triplicate determinations was done for each sample.

The titratable acidity of each sample was then evaluated using the formula below,

$$TA\left(\frac{g}{100}\right) = \frac{Volume\ of\ NaOH\ (needed\ to\ raise\ the\ pH\ to\ 8.2)\ x\ 0.1\ N\ x\ 100}{Volume\ of\ sample\ used}$$

Determination of viscosity.

The viscometer was first rinsed with de-ionized water and allowed to dry.

A volume of the syrup sufficient to fill bulb C (of the viscometer), was introduced through the V tube. The viscometer was held vertically at room temperature. The ventilating tube, was then closed and the liquid was drawn into bulb by applying suction pressure at W until the meniscus was just above the mark E. The liquid was held at this level by closing tube W, and Z was opened to ensure the fluid drains away below the capillary. Tube W was finally opened and the time (t), in seconds, taken for the meniscus to fall from mark E to F was observed and recorded.

Triplicate determinations was done for each syrup sample and the average flow time (in seconds), required for each syrup to fall from mark E to F was calculated and recorded.

The flow time is directly proportional to the viscosity of the syrups.

Kinematic viscosity (v) = Kt.

Where, K = Nominal viscometer constant, t =S flow time (in seconds).

The kinematic viscosity of each syrup was then calculated using the equation above.

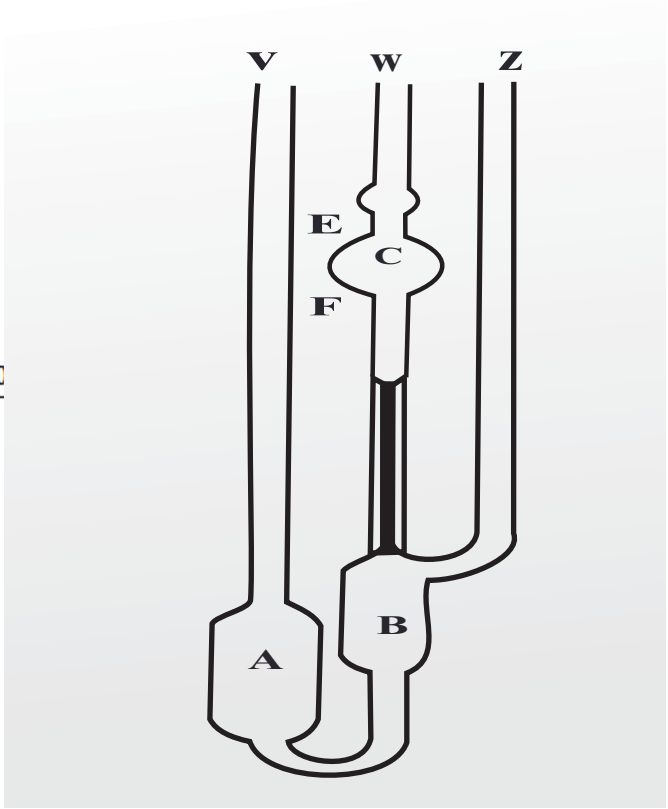

Fig .1 A suspended level viscometer showing tubes V, W and Z, and bulb

RESULTS

Table 2: pH of Syrups

S/N	Syrup (brand name)	Mean pH of the syrup±SD	Titratable acidity (in g/100ml)	Kinematic viscosity (v) (in mm^2S^{-1})
1	Benylin cough syrup	5.34 ± 0.01	4.90	18.54
2	Coflin cough syrup	5.36 ± 0.01	4.13	13.20
3	Emzolyn cough syrup	5.14 ± 0.02	3.90	32.73
4	Cofta cough syrup	4.72 ± 0.01	4.90	22.05
5	Emzor multivitamin	4.12 ± 0.01	3.83	6.51
6	Supramult syrup	3.56 ± 0.01	5.50	16.95
7	Kp multivitamin	4.57 ± 0.01	5.40	3.39
8	Emzor vitamin C	3.25 ± 0.02	7.50	11.25
9	Kp vitamin C	4.03 ± 0.02	5.40	41.16
10	Evans piriton syrup	4.34 ± 0.01	1.17	34.20
11	Allergin chorpheniramine	6.18 ± 0.02	1.07	40.62
12	Flu J syrup	3.79 ± 0.02	3.47	20.10
13	M&B paracetamol	4.65 ± 0.01	1.50	17.64
14	Emzor paracetamol	5.82 ± 0.01	0.93	6.60
15	Emgyl metronidazole	5.92 ± 0.01	3.33	54.99
16	Brustan N Ibuprofen	4.80 ± 0.01	4.73	75.96

SD: Standard deviation

Calculations

(a) Titratable acidity (TA): Using KP vitamin C syrup as an exmple

Volume of 0.1N sodium hydroxide solution required to raise the pH of the sample to 8.2 = 16.20 ml.
Volume of sample used = 30ml

$$TA\left(\frac{g}{100}\right) = \frac{Volume\ of\ NaOH\ (needed\ to\ raise\ the\ pH\ to\ 8.2)\ x\ 0.1\ N\ x\ 100}{Volume\ of\ sample\ used}$$

= 16.20 ml x 0.1 x 100/30 ml. = 5.40 g/100ml

kinematic viscosity (v): Using Kp Vitamin C syrup as an example
Flow time (t) in seconds = 735 seconds,
Nominal viscometer constant (K) = $0.03mm^{2/}S^{-2}$,
Kinematic viscosity (v) = Kt,
= 735 x 0.03 = $22.05mm^2/S^{-1}$

DISCUSSION

The syrups were found to have varied pH values. All the syrups investigated in this study, shows acidic pH values (below 7).

The pH of 5.5 is traditionally considered to be the critical pH of enamel dissolution, though loss of mineral may actually begin at higher pH values.[14] Emzor® vitamin C syrup had the least pH value (3.25), while Allergin® chlorpheniramine syrup had the highest pH value (6.18). Thirteen (13) of the sixteen (16) syrups had pH values lower than the critical pH for enamel dissolution. Liquid medicines with pH < 5.5 is capable of acidifying the dental biofilm by diffusion process, promoting adequate environment for the reproduction of some micro-organisms, thus substantially favouring acid production as a consequence of their intense metabolism leading to the enamel demineralization.[15]

The erosive capacity of these syrups is not only attributable to their low pH. More worrisome is the fact that these syrups are consumed frequently and mainly at night when there is reduced salivary flow.

Reduced salivary flow results in poor oral clearance of the

syrups, leading to increased contact time of these acidic syrups with the enamel. Also, most manufacturers recommend a dosing of at least 4 to 6 hours frequency. This high frequency of daily ingestion of syrups associated with lower levels of mineralization, reduced thickness and maturation of the deciduous teeth, may aggravate their susceptibility to dental erosion.[16]

The commonly used liquid medications included in this study were antitussives, anti-histamines, multivitamins, analgesics, vitamin C and anti-protozoan syrups.
All the syrups showed an acidic pH, and hence have potentials of causing the demineralization of the enamel which will in turn lead to dental erosion. This demineralization is as a result of the liberation of calcium and phosphate ions of the enamel by the action of hydrogen ions in acidic syrups.[17]

The medications with low pH have greater potential for causing erosion. It has been shown that many paediatric syrups with low pH have the ability to initiate the dental demineralization by direct action on the enamel surface without any influenced by the enamel type, temperature and acid exposure time.[18]

The total acid level of the syrup (titratable acidity) is considered to be the primary factor in causing dental erosion rather than the pH, because it determines the actual amount of hydrogen ions available for interaction with the tooth surface.

The TA of the syrup samples was measured by determining the amount of 0.1 N sodium hydroxide required to bring the pH of the acidic syrup to 8.2. The amount of sodium hydroxide required to neutralize the acidity is dependent on the inherent pH of the test syrup. This implies that the higher the volume of sodium hydroxide, the higher the TA, hence the higher the number of hydrogen ions available to cause demineralization of the enamel. . Emzor® vitamin C syrup showed the highest TA of 7.5 g/100 ml, while Emzor® paracetamol syrup showed the least TA of 0.93 g/100 ml. syrups containing ascorbic acid (vitamin C) showed a high TA due to low pH of ascorbic acid while paracetamol syrups and anti-histamines had the least TA with values less than 1.6 g/100 ml. Flu j® syrup which contained both anti-histamine and ascorbic acid had a slightly high TA (3.47).
The erosive potential of the syrups generally tend to increase as their total acid content increases.
The multivitamin syrups, cough syrups and vitamin C syrups showed a higher amount of titratable acidity and pose increased potentials of causing dental erosion, especially with their increased viscosity. Emgyl® metronidazole syrup and ibuprofen syrup also had high total acid content values of 3.33 and 4.73 g/100 ml, respectively.
The flow time of the syrups was used to assess their individual viscosity. The less viscous the syrup, the lower the flow time, while the more viscous syrups had a higher flow time. Emgyl® metronidazole had the highest flow time (2532 seconds) and so the most viscous syrup, while Flu J® syrup had the least flow time (113 seconds). The cough syrups with a flow time >1000 seconds showed high viscosity, while paracetamol and anti-histamine syrups showed lesser viscosity (flow time <600 seconds). The increased viscosity of ibuprofen and metronidazole syrups was due to their formulation as suspensions, making their flowability low.

Liquid preparations are normally sweetened with sucrose to improve their palatability and aid compliance especially in children. However, the sucrose can readily be fermented by oral acidogenic bacteria. Medicines in the form of syrups intended for paediatric use contain about 10-80% sucrose, on an average of 55%.[2]The medicines that have sucrose as sweetening agent possess high viscosity.[19] As a result, these medicines can have slow salivary clearance leading to an increased contact time with the tooth surface which will ultimately result to an increased dissolution of the enamel. Additives such as emulsifiers and thickening agents can also increase the viscosity of liquid preparations.

The higher the viscosity of the syrups, the lower their flowability, hence the longer the time they spend in the oral cavity which increases their potential to cause dental erosion.
The vitamin C and cough syrups which has considerably low flowability and low pH values, pose greater potentials of causing enamel dissolution. This potential of causing dental erosion increases with the frequency of use of these liquid preparations.
It is evident from literature sources that other factors such as type of acid, chelating properties, calcium and phosphate concentrations, temperature, exposure time and frequency of exposure can also contribute to enamel erosion and demineralization.

The protective factors such as saliva also play a role in the dynamism of dental erosion process. Increased saliva outflow can increase the flowability of syrups, enhancing their oral clearance. Saliva is also known to modify dental erosion by causing the formation of an enamel pellicle

which protects the surface from dissolution.[20]
Considering the limitation of laboratory studies, the erosive potentials of the liquid preparations observed in this *in vitro* study should be mild. The study was limited by the unavailability of sophisticated equipment that would been used for further studies.

CONCLUSION

The outcome of this study confirms that all syrups investigated had high values of pH, titratable acidity and viscosity and it is important for health professionals and care givers to be aware of the risk associated with continuous and long term use of these syrups.

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