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Original Article

Glucose and Added Sugar Contents in Oral Herbal Liquid Medicines

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ABSTRACT

As the population of elderly people has increased,it has become very common to use regular long term medication for chronic medical problems. Chewable tablets and syrup form of medicines are commonly used in elderly. However,in case of Antibiotics and pediatric medicines "Sugars" are added for enhancing the palatability. The objective of this work is to quantify total sugars, added sugar and glucose content in oral liquid medicines. Five different liquid formulations from various drug categories with herbal active ingredients were selected for the study. **Experimental approach** : Quantification of sugar was carried out by Lane and Eynon method and Glucose by iodometry.Total five medicinal syrup samples along with corresponding blank syrups excluding "Food grade sugar" were tested for sugar content. Other possible sources of sugar such as Honey, Food grade Sugar sample and Liquid Glucose were tested for both Sugar and Glucose content. **Findings** : Among all sources of sugar,food grade sugar showed almost 100% sugar content, but did not respond to glucose titration. Honey gave about 35% glucose and almost 65% sugar. Liquid glucose was reported for 30% glucose content.In all the final liquid formulations, glucose content was found in the range of 10%w/v to 15%w/v. Content of actually added sugar was varied from 30%w/v to 50%w/v. **Discussion and Conclusion** :Quantification of added sugar to more than 90% accuracy level of theoretically expected value can help us to determine the safety of administrating the dosage form in diabetic and obese patients.

Keywords: Added sugar, Glucose,Lane and Eynon method, Iodometry, oral liquid medicines.

1. INTRODUCTION

Nowadays people are becoming more and more health conscious. They choose the best fuel for the body to promote dramatic improvement in energy level. Various nutrients like carbohydrates, sugars, fats, proteins, fibres, vitamins and minerals are essential for enhancing the quality of the life we live. All these should be administered in desired proportion, as excess

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of any, may cause adverse effects on our body. Sugar is one of the most important components. It gives us a lot of energy in the form of calories. However, intake of excess sugar may cause diabetes, cardiovascular diseases and even obesity. Hence it is essential to monitor and control the sugar quantity not only in the diet but also in our routine long term medication.

Most fruits and dairy products are high in sugars, and thus naturally occurring sugars are consumed as part of a healthy diet. Sugars are also added to foods during processing or preparation, primarily to enhance taste. "Added sugars" are sugars and syrups that are added to foods or beverages when they are processed or prepared. This does not include naturally occurring sugars such as those in milk and fruits. Also, if you fill up on foods or beverages that contain added sugar, you are less likely to consume healthy foods and beverages that protect your health. Given the rising rates of obesity and heart disease, the American Heart Association recently released guidelines for eating added sugar. The AHA recommends that no more than half of your extra (discretionary) calories come from added sugars. The American Heart Association recently released a statement[1] advising consumers to limit sugar consumption. The macronutrient report for the dietary reference intakes addresses many of these same issues; the expert panel concluded that it was not appropriate to set a tolerable upper intake level for added sugars but suggested a maximal intake level of 25% of energy from added sugars because of concerns about reduced intakes of essential micronutrients. The most likely consequences of sugar consumption beyond the levels described by the food guide pyramid are overconsumption of energy and micronutrient inadequacies.

Naturally occurring sugar is the sugar found in whole, unprocessed foods, such as milk, fruits, vegetables, and some grains. One of the most natural sugars is fructose, which is found in fruits. Another natural sugar is lactose, which is found in milk.

Added sugar is the sugar that is added to processed foods and drinks while they are being made. Food manufacturers may add both natural sugars (for example, fructose) and processed sugars (for example, high-fructose corn syrup) to processed foods and drinks. The sugar you add to your food at home is also added sugar.

Various types of sugars like monosaccharides, disaccharides, trisaccharides, tetrasaccharides and othersweetners are explained in Pearsons text.[2]

On the basis of the 2005 US Dietary Guidelines, intake of added sugars greatly exceeds discretionary calorie allowances, regardless of energy needs.[3]In view of these considerations, the American Heart Association recommends reduction in the intake of added sugars. A prudent upper limit of intake is half of the discretionary calorie allowance, which for most American women is no more than 100 calories per day and for most American men is no more than 150 calories per day from added sugars. (Circulation. 2009; 120: 1011-1020)

Sucralose[4] is used as a sweetening agent in beverages, foods and pharmaceutical applications. It has a sweetening power approximately 300-1000 times that of sucrose. It has no nutritional value and is noncariogenic. Sucralose is not metabolized by the body for energy, and therefore it contains zero calories. It has no effect on blood glucose or insulin levels in people with diabetes, and therefore it is safe for them to consume.

Sucrose syrups are widely used as vehicles in oral liquid – dosage forms to enhance palatability or to increase viscosity.

In the present study, total five herbal oral liquid formulations of different medicinal catagories were selected. The products selected for the study are stress

relieving – Antistresssyrup, fever relieving - antipyretic syrup, syrup used in the management of immunological disorders – Immunomodulator syrup, allergic cough relieving –Antiallergic cough syrup, syrup used as a supportive treatment for symptomatic relief in chronic and respiratory diseases – Antispasmodic cough syrup. These oral medicinal syrup samples along with corresponding blank syrups excluding "Food grade sugar" were tested for sugar content. Other possible sources of sugar such as Honey, Food grade Sugar sample and Liquid Glucose were tested for both Sugar and Glucose content.

2. MATERIALS AND METHODS

Various methods can be applied to determine sucrose or sugar content in the sample such as brix reading, polarimetric[5] method, titration method using Fehling's Reagent[6] and so on. Here in this study the most reliable and simplest "Lane Eynon method" is applied for quantitative determination of sugar and iodometric method is chosen for quantification of glucose content.

2.1 Samples

Two lots of each finished syrup samples along with respective blank samples excluding food grade sugar were manufactured in our own laboratory.Table 1 focuses on various oral liquid formulations under study to facilitate the blank preparation.

Table 1: Formulae of liquid oral medicines (Herbal Syrup formulations)

Sr. No.	Ingredients	Antistress syrup	Antipyretic syrup	Immunomodulatorsyrup	Anti allergic cough syrup	Anti spasmodic cough syrup
A	Active Ingredients					
	Active Ingredients	Shankhapushpi, Jatamansi, Ashwagandha, Sarpagandhaextract	Musta, Guduchi, Chiraita, Kantakari, Pitpada, Sunthi, Ajwainsatwa extracts	Amla, Neem leaves, Guduchi, Tulsi, Haridra extracts	Vasa, Tulsi, Shathi, Pippali,Bahedra, Yashtimadhu, Bharangi, Haridra extracts	Vasa, Kasondi, Baheda, Marshmallow, Pippali extracts
B	Excipients in mg per 10ml					
	Sugar (food grade)	4000	4000	4000	5000	3000
	Sorbitol 70% solution	3000	2500	2500	500	2000
	Liquid glucose	1500	1000	---	1000	1000
	Honey	1000	1000	1000	500	1000
	Sucralose	1	15	---	---	---
	Other excipients	As per the requirement				
	Purified water	q.s.	q.s.	q.s.	q.s.	q.s.

All these samples along with blank preparations were subjected to testing its glucose content and total sugar content by the appropriate valid methods. Even the possible sources of sugar such as "Food grade" sugar, Liquid glucose and Honey were estimated for glucose and sugar content.

2.2 Chemicals and Reagents

All the chemicals and reagents used in different processes were procured fromM/s Merck India and M/s Qualigens. Reagents were standardized as per the standard pharmacopoeia.

2.3 Equipments and Instruments

All the glassware used were well calibrated and were procured from M/s Borosil Glass Works Ltd. Instruments used were weighing balance (M/s Schimadzu Corporation) Electric oven and Water bath (M/s Pathak Electrical Works Ltd.).

2.4 Methods

Content of Glucose

Weigh accurately about 2ml syrup sample in a beaker. Dissolve it in about 50ml distilled water and dilute to 100ml with distilled water. Shake well and pipette out 50ml of this diluted solution in iodine flask. Add 40ml of 0.05N iodine solution and 25ml of 0.1N sodium

hydroxide solution. Keep it in dark for 20 minutes. Similarly perform the blank by taking 50ml distilled water instead of sample solution in another iodine flask.

After 20 minutes, add 5ml concentrated sulphuricacid and immediately titrate against 0.05N Sodium thiosulphate, using starch solution as an indicator.

Record the difference between the blank and the test reading and calculate the percentage of glucose by applying the following formula :

Content of Glucose (%w/w) = (B – A) X 0.00450 X (100 / W) X (100 / 50) X NF

Content of Glucose (%w/v) = (B – A) X 0.00450 X (100 / V) X (100 / 50) XNF

Where,

B → Blank Burette Reading in ml

A → Sample Burette Reading in ml

W → Weight of the sample in g, equivalent to V ml volume

V → Volume of sample in ml

NF → Normality Factor of 0.05N Sodium Thiosulphate.

Content of Sugar

Weigh accurately about 2ml syrup sample in a beaker. Dissolve it in 25ml of 1N sulphuric acid. Boil for 2 minutes on a hot plate. Also weigh 1g of sucrose as standard in another beaker and boil it with 25ml 1N sulphuric acid. Cool to room temperature.

Titrate 25ml 1N sulphuric acid against 1N sodium hydroxide using phenolphthalein as an indicator. Record the end point as “B” ml. Add (B + 0.3) ml1N sodium hydroxide in sample and standard to neutralize the acid. Now dilute both to 100ml with distilled water. Shake well and filter. Use these as sample and standard solutions and fill up the burette.

Titrate 20ml Fehling solution (A + B) against sample solution as well as against standard solution using methylene blue as an indicator in hot boiling condition (on hot plate). End point is blue to red precipitate. Record the sample reading and standard reading in ml and by applying following formula, calculate the Total sugar content

Content of Sugar (%w/w) = (Standard reading in ml / Sample reading in ml) X (100 / W)

Content of Sugar (%w/v) = (Standard reading in ml / Sample reading in ml) X (100 / V)

Where,

W → Weight of the sample in g, equivalent to V ml volume

V → Volume of sample in ml

Same methods were applied for estimation of raw materials that is for food grade sugar, liquid glucose and honey sample. Weight of the sample taken was 0.50g to 1g.

Results were recorded in tabular form.

3. RESULTS AND DISCUSSIONS

Xavier et al[7] analyzed drugs which showed physicochemical characteristics indicative of a cariogenic and erosive potential on dental tissues and recommended for the implementation of competent bodies’ strategies in order to broaden the knowledge of health professionals, drug manufacturers and general consuming public about the risks from the consumption of medicines potentially harmful to dental tissues.

Brisboiset al [8] also estimated total and added sugars in the Canadian Diet. As per their study report, analysis of both survey and availability data suggested that added sugars average about 11% - 13% of total energy intake.

Practical evaluation of glucose and sugar content in different raw materials was carried out by above mentioned methods and results are recorded in Table 2.

Table 2: Practical approach - Sources of Sugar

Sr.No.	Sources of glucose /sugar	Content of Glucose (by Iodometry)	Content of Sugar (by Lane and Eynon method)

		Specifications	Findings	Specifications	Findings
1	Sucrose (Food grade sugar)	Nil	Nil	Almost 100%	100%
2	Liquid Glucose	Not less than 30%	35.97%	NA	36.35%
3	Honey	Not less than 35%	35%	Not less than 65%	70%

From the Table 2, it can be seen that sugar sample is not responding to iodometric titration meant for glucose estimation. Food grade sugar shows almost 100% sugar content, liquid glucose is reported for 35% glucose content though it may decline upto 30%as per the acceptance criteria in the form of respective specification.Honey shows about 35% glucose and almost 65% sugar. Sucralose is not metabolized by the body for energy, and therefore it contains zero calories. Hence not considered as a source of glucose or sugar.

Theoretical specifications in different formulations were calculated on the basis of the formulae mentioned in Table 1.Theoretical values of total sugar and added sugar in the form of food grade sugar for respective formulation are recorded in the Table 3.

Table 3: Theoretical calculation of added sugar and total sugar in oral liquid formulations

Sr. No.	Herbal Oral Liquid formulations	Quantity of Sugar + Liquid Glucose + Honey	Quantity of Food grade (added) sugar	Quantity of Total Sugar (%w/v)
1	Antistress syrup	40% + 15% + 10%	40%	40g + 4.5g + 6.5g = 51 %
2	Antipyretic syrup	40% + 10% + 10%	40%	40g + 3g + 6.5g = 49.50 %
3	Immunomodulator syrup	40% + 0% + 10%	40%	40g + 6.5g = 46.50%
4	Antiallergiccough syrup	50% + 10% +5%	50%	50g+ 3g + 3.25g = 56.25%
5	Anti spasmodiccough syrup	30% + 10% + 10%	30%	30g+ 3g + 6.50g = 39.50%

Practical findings of total glucose content in two lots of each final syrup formulations are recorded in Table 4, along with actual results of total sugar content, sugar content excluding food grade sugar in blank preparations and actual values of added sugar in the form of food grade sugar.

Table 4: Practical findings of Total glucose content and sugar content

Sr. No.	Herbal Oral Liquid formulations	Total glucose content (%w/v)		Total Sugar content (%w/v)		Sugar content in Blank	Concentration of food grade (Added) Sugar (%w/v)	
		Lot 1	Lot 2	Lot1	Lot 2		Lot1	Lot 2
1	Antistress syrup	14.67	11.42	52.63	52.77	13	39.631	39.77
2	Antipyretic syrup	14.574	10.58	53.19	51.54	11	42.191	40.54
3	Immunomodulator syrup	13.787	14.25	47.97	48.96	9	38.979	39.96
4	Antiallergic cough syrup	13.321	13.36	55.12	55.23	10	45.120	45.23
5	Anti spasmodiccough syrup	14.783	13.52	43.18	42.41	13	30.182	29.41

Total glucose content in all herbal oral liquid formulations is observed to be between 10%w/v to 15%w/v. considering the average value of two lots, the content of added food grade sugar is found to be around 39.70%,41.37%,39.47%,45.18% and 29.80% w/v equivalent to 99.25%, 103.40%, 98.67%, 90.36%, and 99.33% of theoretically calculated actually added food grade sugar in Antistress syrup, Antipyretic syrup, Immunomodulator syrup , Antiallergic, and Antispasmodic cough syrup samples respectively.All these practical findings are more than 90% with respect to the corresponding expected theoretical values.

Total sugar content and content of added sugar in various oral herbal liquid formulations is graphically represented as Figure 1.

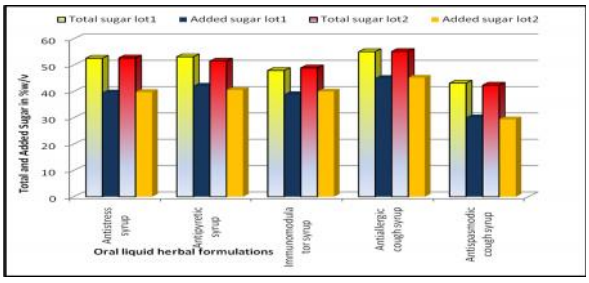

Fig 1: Total sugars and added sugars

Peres K.G. et al [9] estimated sugar in pediatric liquid oral medicines. As per their findings, sugar concentration ranged from 8.59g/100g of drug to 67g/100g of drug.

Chun et al [10] worked on different sources of sugar in various food products and pointed to the need for ongoing research on the specific nutritional contributors to total energy intake, and their potential contribution to increasing prevalence of obesity.

4. CONCLUSION

Iodometric method can be applied to estimate total glucose content in oral liquid formulations. Lane and Eynon method can give proper values for total sugar content.

In case of herbal oral liquid formulations if we consider “food grade sugar” as the only “added sugar”, then we need to subtract the blank reading from the Total sugar where the corresponding blank is to be prepared separately and estimated in the similar manner.

Quantitative awareness of added sugar in the formulations definitely will support to determine the dosage of medicinal syrups for long term treatment in elderly, in diabetic and obese patients, and even in kids.

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6. REFERENCES

1. Suzanne P. Murphy and Rachel K. Johnson, The scientific basis of recent US guidance on sugars intake 1’2’3’4’, The American Journal of Clinical Nutrition 2003, American Society for Clinical Nutrition.
2. Ronald S. Kirk, Ronald Sawyer. Sugars and Preserves, Pearson’s Composition and Analysis of Foods, Ninth edition, Addison – Wesley, London, 1991.
3. Rachel K. Johnson, Lawrence J. Appel, Michael Brands, Barbara V., Michael Lefevre, Robert H. Lusting, Frank Sacks, Lyn M. Steffen, Judith Wylie-Rosett. Dietary sugars intake and cardiovascular health A scientific statement from the American Heart Association, DOI: 10.1161 / circulationaha.109.192627, http://circ.ahajournals.org; December 5, 2014.
4. Sucralose, Sucrose Handbook of Pharmaceutical Excipients, Fourth edition, London, Chicogo: Pharmaceutical Press; 2003: 620, 622.
5. S. Ranganna, Sugar, Handbook of Analysis And Quality Control For Fruit And Vegetable Products, Second edition, Tata McGraw-Hill Publishing Company Limited, New Delhi, 1986 : 185-187.
6. Association of official Analytical Chemists (AOAC). Official methods of analysis : sugar and sugar products. Arlington; 1984.
7. Xavier A.F., Moura E.F., Azevedo W.F., Vieira F.F., Abreu M.H., Cavalcanti A.L. Erosive and cariogenicity potential of pediatric drugs : study of physicochemical parameters. BMC Oral health 2013, http://www.biomedcentral.com/1472-6831/13/71.
8. Brisbois T.D., Marsden S.L., Anderson G.H., Sievenpiper J.L. Estimated Intakes and Sources of Total and Added Sugars in the Canadian Diet, Nutrients 2014; 6: 1899-1912.
9. Peres K.G., Oliveira C.T., Peres M.A., RaymundoMdos S., Fett R. Sugar content in liquid oral medicines for children, Epub 2005; 39 (3) : 486 -9.
10. Chun O.K., Chin C.E.,Wang Y, Padgitt A., Song W.O. Changes in Intakes of Total and Added Sugar and their Contribution to Energy Intake in the U.S., Nutrients 2010; 3 : 834-854.

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