

Awareness of Pharmacists towards Aspartame Side Effects in Khartoum City, 2014

Abstract

Introduction: Aspartame (or APM) is the name for an artificial, non-saccharide sweetener used as a sugar substitute in many foods and beverages. Aspartame is the methyl ester of a phenylalanine/aspartic acid dipeptide. Aspartame is an artificial sweetener. It is 200 times sweeter than sugar in typical concentrations, without the high-energy value of sugar. **Objective:** To study the awareness of pharmacists about aspartame side effects. **Materials and methods:** This study was carried in greater Khartoum, questionnaire for pharmacists to see the consumption and the awareness of them to these interactions during the period from September 2014 to November 2014. Study was conducted among practicing pharmacists. A pre designed and tested questionnaire were used for each category to collect the data. From the hospitals manager. **Result:** 32% were aware of the number of aspartame products. Pharmacists when asked how many patients purchase aspartame products per day, answers showed that 74.5% ranged between 1-10 patients per day, About pharmacist's expectations to develop side effects due to aspartame, use regularly showed that 75% agreed that it would. pharmacists claimed that aspartame can or worsen a certain list of some diseases in which that diabetes represented 30%, Alzheimer's 28% , attention deficit disorder 17.3% , psychological disorders. **Conclusion:** The majority of community pharmacists expect side effects can be developed due to aspartame regular use by patients but majority didn't know what are the exact side effects and the exact diseases that can be worsened when using aspartame.

Introduction

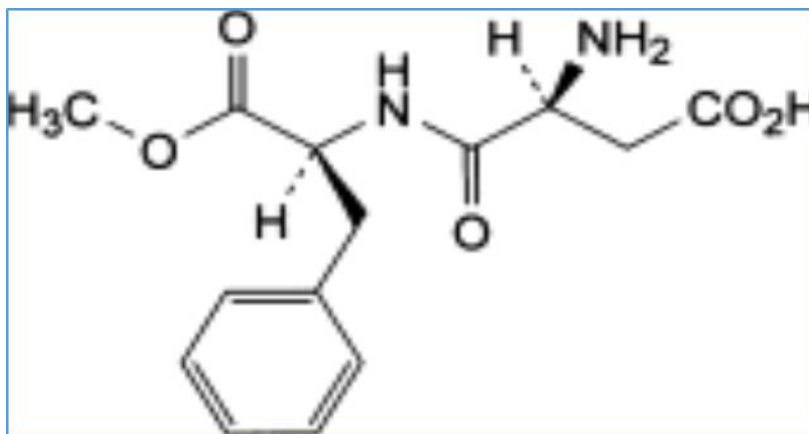
Aspartame (or APM) is the name for an artificial, non-saccharide sweetener used as a sugar substitute in many foods and beverages. Aspartame is the methyl ester of a phenylalanine/aspartic acid dipeptide. Aspartame was first synthesized in 1965. The United States Food and Drug Administration approved its use in food products in 1980. Because its breakdown products include phenylalanine, aspartame is among the many substances that must be avoided by people with phenylketonuria (PKU), a rare genetic condition. The safety of aspartame has been the subject of several political and medical controversies since its initial approval by the U.S. Food and Drug Administration (FDA) in 1974.

Chemistry:

Aspartame is the methyl ester of the dipeptide of the natural amino acids L-aspartic acid and L-phenylalanine. Under strongly acidic or alkaline conditions, aspartame may generate methanol by hydrolysis. Under more severe conditions, the peptide bonds are also hydrolysed, resulting in the free amino acids. In certain markets, aspartame is manufactured using a genetically modified variation of *E. coli*.^(1, 2)

General Notices (PhEur monograph 0973)⁽¹¹⁾

Structural Formula



General Formula and Molecular Weight

C₁₄H₁₈N₂O₅

294.3 53906-69-7

Action And Use

Sweetening agent.

Definition

(3S)-3-Amino-4-[[[(1S)-1-benzyl-2-methoxy-2-oxoethyl] amino]-4-oxobutanoic acid.

Content

98.0 per cent to 102.0 per cent (dried substance).

Toxicity

Fingernail polish (dry), Rust.

Raw Materials

L-Phenylalanine Methyl Ester HCl

N-Benzyloxycarbonyl-L-aspartic acid-p-nitrophenyl, β benzyl Diester⁽¹²⁾

Hydrogen

Properties and use:

Aspartame is an artificial sweetener. It is 200 times sweeter than sugar in typical concentrations, without the high-energy value of sugar. While aspartame, like other peptides, has a caloric value of 4 kilocalories (17 kilojoules) per gram, the quantity of aspartame needed to produce a sweet taste is so small that its caloric contribution is negligible.⁽³⁾

Discovery and approval:

James M. Schlatter, a chemist working for G.D. Searle & Company, discovered aspartame in 1965. Schlatter had synthesized aspartame in the course of producing an anti-ulcer drug candidate. He accidentally discovered its sweet taste when he licked his finger, which had become contaminated with aspartame.⁽⁴⁾

Metabolism and phenylketonuria:

Upon ingestion, aspartame breaks down into natural residual components, including aspartic acid, phenylalanine, methanol⁽⁵⁾, and further breakdown products including formaldehyde⁽⁶⁾, known to have a number of detrimental effects on the human body⁽⁷⁾, formic acid, and a DKP - Aspartylphenylalaninediketopiperazine⁽⁸⁾. Further studies have shown that a metabolite of aspartame inhibits angiotensin-converting enzyme.⁽⁹⁾

Safety controversy:

A study performed by Northeastern Ohio Universities College of Medicine found that individuals with mood disorders are particularly sensitive to this artificial sweetener, and its use in this population should be discouraged.⁽¹⁰⁾

Materials and methods

This study was carried in greater Khartoum, questionnaire for pharmacists to see the consumption and the awareness of them to these interactions during the period from September 2014 to November 2014.

Study was conducted among practicing pharmacists. A pre designed and tested questionnaire were used for each category to collect the data needed.

A pre designed and tested questionnaire were used for each category to collect the data. The data was collected, entered, cleaned and analyzed using SPSS software version 17. Permission to access the data in the patient records anonymously was obtained from the hospitals manager.

Result

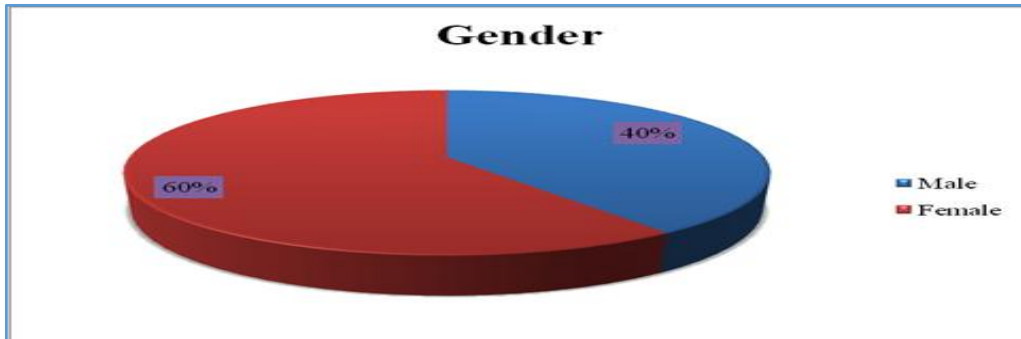


Figure (1): Distribution of study sample according to gender.

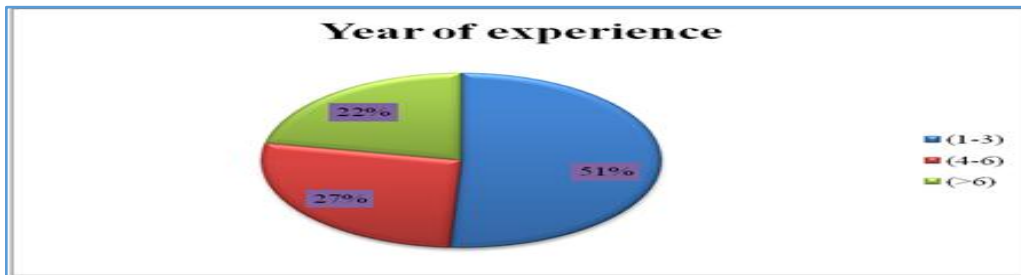


Figure (2): Distribution of study sample according to year of experience.



Figure (3): Distribution of study sample according to qualification.

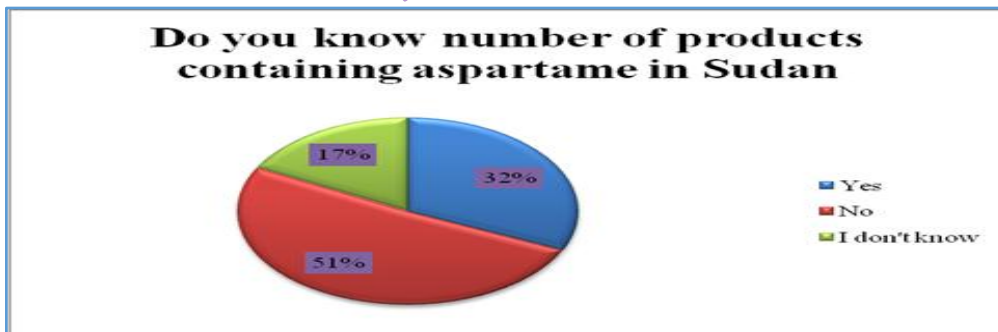


Figure 4: Distribution of study sample according to do you know number of products containing aspartame in Sudan.

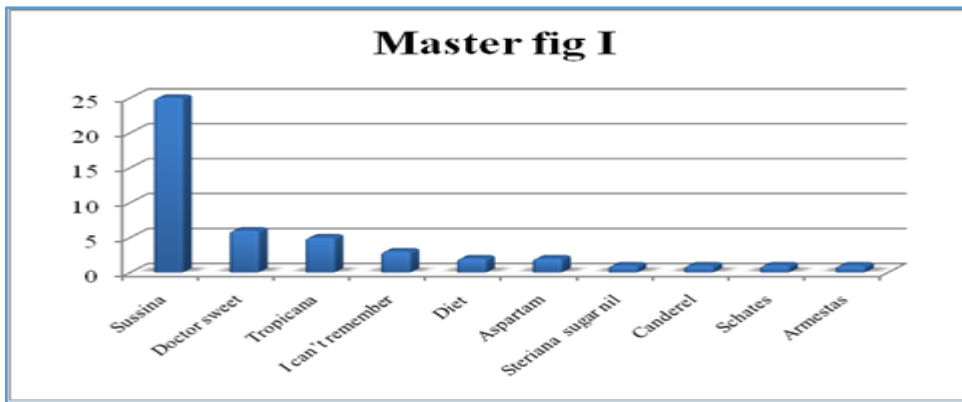


Figure 5: Frequency of do you know number of products containing aspartame in Sudan if yes among study population.

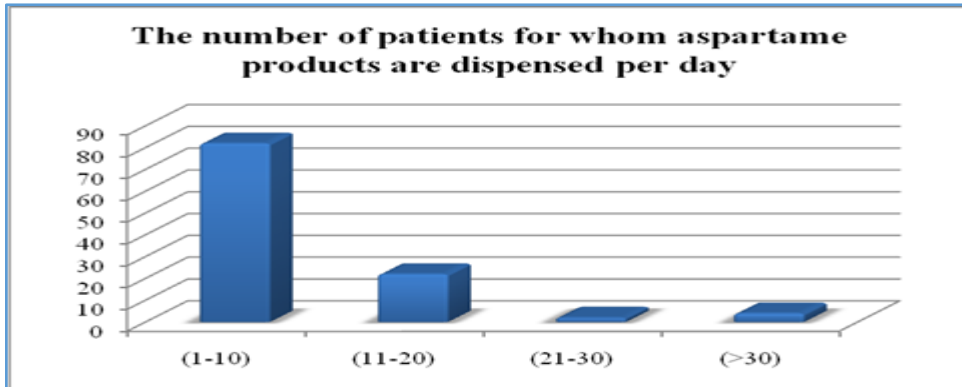


Figure (6): Distribution of study sample according to the number of patients for whom aspartame products are dispensed per day.



Figure (7): Do you expect there will be side effects for aspartame when used regularly.

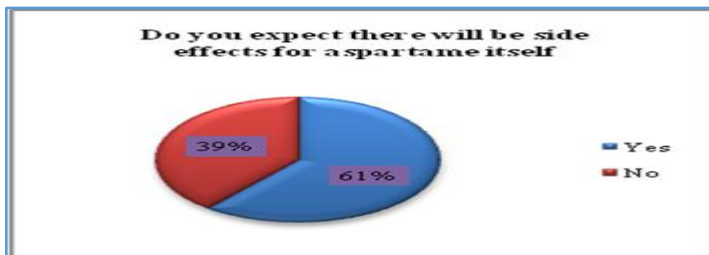


Figure (8): Do you expect there will be side effects for aspartame itself.

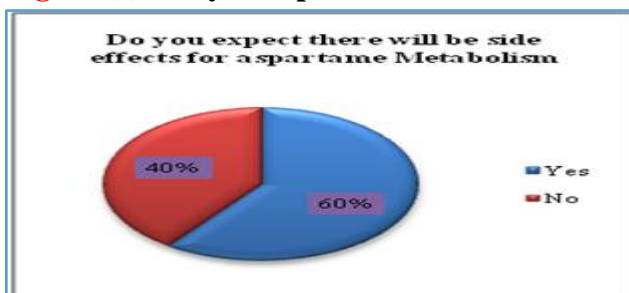


Figure (9): Do you expect there will be side effects for aspartame Metabolisma

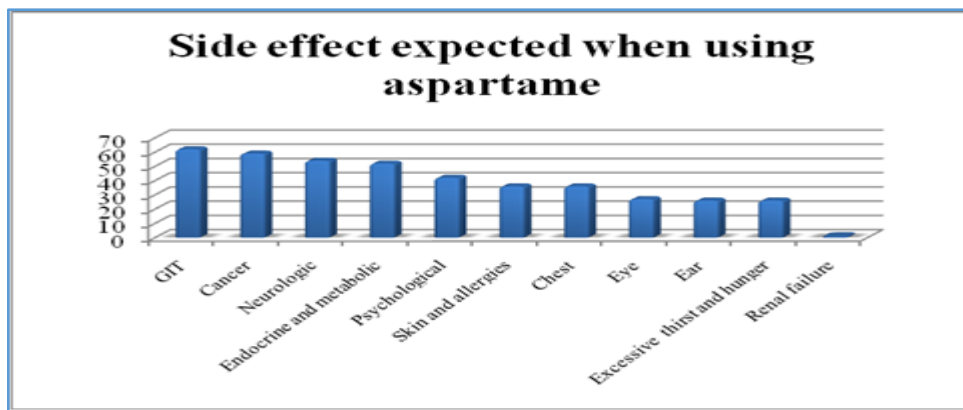


Figure (10): Frequency of Side effect expected when using aspartame among study population

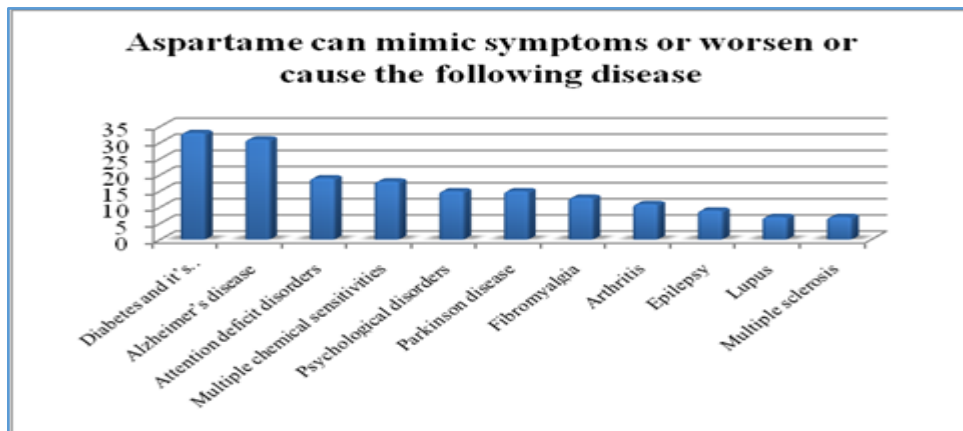


Figure (11): Frequency of aspartame can mimic symptoms, worsen, or cause the following disease among study population.

Discussion

Aspartame has been and for a very long time an overlooked entity an additive in the daily lives of patients, especially more that are seeking a change in life style towards certain health goals such as weight control, diabetes control, to ebb on excessive sugar and carbohydrate intake. In order to back drop this study against a background that reflects its emphasis on the dangerous outcomes, side effects, and end result of aspartame, we there should be a sufficient amount of literature that scientifically tackles this issue. However, highly discussed controversy looms over this subject due to political and medical reasons since its initial approval by the U.S. food and drug administration in 1974.

Aspartame has been used as a sweetener in many products due to its low caloric value , and this discussing and assessing its abundance within the population in from of a used beverages or delicacy sweetener will be through assessing the knowledge and awareness of pharmacists about its abundance within a range of products, and though assessing this wide spread abundance , and awareness or lack of it within the community pharmacists society we can determine the need to further investigate the speculations Stated regarding it harmful effect since the lager the base of population using this product the larger the incandescens that may appear in future tense within several year. A study tackling its safety was done at northeastern Ohio University College of medicine, this study managed only to recommend discouragement of this sweetener in-patient with history of mood disorders, regarding the awareness survey done amongst Community pharmacists mentioned that 49% of aspartame users might develop neurological problems. But to assess the awareness of community pharmacists regarding this matter we must first look at the population providing such data the demographic data illustrating

the population of community pharmacists displayed the majority of those falling under the scope of this study to be bachelor Degree holder, juniors, due to the jobs available in Sudan for those graduating newly and recently finishing their internship or housmanship, Are only community pharmacy jobs (77%), the knowledge they show may be shadowed by speculation, where their lack of experience could be subject to personal opinion more than scientific data or actual cases. Master degree holders held a weak percentage of(22%) also weakened by the travel of most master degree holders and a more(1%)representing only 1 PHD holder encountered in this study their knowledge was furthermore stressed to the edges of speculation when questioned if they knew the number of products containing aspartame , this also displayed that a large number(51%) were not aware of the aspartame products available in the market which may lead to them to go undetected when dispensing . and since very low are screen for the rare genetic conditions of phenylketonuria there is no possible way to know whether or not this aspartame user is harming himself or not. Regarding the number of products containing aspartame in Sudan and respectively the awareness of the community pharmacists whether these products actually contain aspartame or not, we will have to discuss the abunduacny of aspartame products worldwide, aspartame as stated by articles and studies of dr. lendensmith, is and can be found in over (6000) products often referred to as (sugar free or diet products).Exemplified in breath mints, cereals, sugar free gums, cacao mixes, coffee beverages, soft drinks and much more. community pharmacists in Sudan could only name the obvious through mentioning alternative sweeteners , sussina TM being the most mentioned with a percentage of (71.4%) and Ahermestas the least mentioned with a percentage of(2.9%), these products are all products used instead of sugar to sweeten beverages and taking delicacies realizing non mentioned only gums , candy sweets, drinks , or food rendering these overlooked and uncategorized the knowledge of community pharmacists as aspartame containing products.

Aspartame, being a very abundant sweetener and low calorie product is sometimes considered an aid to help weight loss , given such knowledge it is highly suggested and mentioned though word of mouth from patients to patient to aid in decreasing sugar intake and to help with weight loss, this has rendered aspartame as a highly dispensed product community pharmacists have reported that up to 10 patients are dispensed aspartame(74.5%) of the time , and 3.6% of the time more than 30 patients per day. controversy still remains evident as the American diabetes association actually recommends aspartame to diabetic patients even though a diabetes specialist through a study has showed that aspartame actually precipitates clinical diabetes, causes poor diabetic control in patients using insulin's or oral hypoglycemic and leads to the aggravation of diabetic complications such as retinopathy, cataracts, neuropathy and gastropathesis. Due to the lack of clinical studies on the harmful effects of aspartame and the even shadowing controversy Of medical and political controversy that hindered the progression of such studies, community pharmacists and medical researchers have had to rely on their medical and scientific knowledge and the knowledge of pharmacological metabolites to determine the possible harmful effect caused by excitatory amino acids, phenylalanine, methanol and DKP. Side effects mentioned by community pharmacists in this study were mainly GIT having the largest percentage of(56.4%) ,(53.6%) cancer, and 0.9% renal failure as the lower possible side effects , which were on par when received by the medical articles regarding aspartame side effects, which were mostly the same , alongside other endocrine, eye and ear, skin allergies , chest and neurological side effects, giving confirmation that aspartame is and probably a much more hazardous chemical than reported .

Aspartame, has also been linked to serious diseases and disease syndromes, but it is also sometimes misdiagnosed because aspartame symptoms are not as apparent or obvious as said and usually next other disease which could be misleading. Community pharmacists have mentioned some of these diseases whilst most of them actually knew or ever heard of aspartame to begin with, literature has mentioned disease such as psychological conditions, Alzheimer's, Parkinson's, ADHD, and others as serious syndrome and disease to be dealt with apart from the number of community pharmacists that had no idea what is aspartame or its harmful cases were, a satisfying number of the study sample mentioned the worsening of diabetes (30%), Alzheimer's (28%), ADHD (17.3%) and psychological disorders (15.8%) alongside other conditions as a result of aspartame poisoning or intoxication.

Conclusion:

Almost 68% from community pharmacists didn't know the number of products that contain aspartame in their places they work. The majority of community pharmacists expect side effects can be developed due to aspartame regular use by patients but majority didn't know what are the exact side effects and the exact diseases that can be worsened when using aspartame.

In conclusion more studies should be conducted to fortify the general concept of the poisonous hazard of aspartame and fill the gaps of knowledge found within community, clinical and hospital pharmacists alongside other health professionals.

Recommendations:

Experimental researches must be done on aspartame side effects in man and animals to study safety profile.

There must be a notification about aspartame side effects and diseases worsened by using aspartame to the all doctors, pharmacists and patients.

Reference

1. www.independent.co.uk/news/worlds-top-sweetener-is-made-with-gm-bacteria-1101176.html, June 29, 2010.
2. Method for production of L-phenylalanine by recombinant E. coli (<http://patft.uspto.gov/netacgi/nph-parser>). June 27, 2010.
3. "Has aspartame an aftertaste". Institute of Food Technologists. Sept/Oct 1985. http://grande.nal.usda.gov/ibids/index.php?mode2=detail&origin=ibids_references&therow=419684. June 27, 2010.
4. Magnuson BA, Burdock GA, Doull J (2007). "Aspartame: a safety evaluation based on current use levels, regulations, and toxicological and epidemiological studies". *Crit. Rev. Toxicol.* 37 (8): 629–727. doi:10.1080/10408440701516184. PMID 17828671. Citing: Mazur, R.H. (1984). Discovery of aspartame. In *Aspartame: Physiology and Biochemistry* (L. D. Stegink and L. J. Filer Jr., Eds.). Marcel Dekker, New York, pp. 3–9. June 27, 2010.
5. <http://www.ncbi.nlm.nih.gov/pubmed/8373935>. June 25, 2010.
6. Betty Kovacs and William C. Shiel Jr. http://www.medicinenet.com/artificial_sweeteners/page8.htm - 52k, May 8, 2010.
7. Wurtman and Walker, "Dietary Phenylalanine and Brain Function," *Proceedings of the First International Meeting on Dietary Phenylalanine and Brain Function.*, Washington, D.C., May 8, 1987 <http://www.mac-archive.com/ns/side.html> - 11k. May 8, 2010.
8. www.diethealthclub.com/articles/24/diet-and-wellness/the-truth-about-aspartame.html - 30k, December 31, 2010.
9. Sucralose breakthrough could smash Tate & Lyle monopoly.

10. Dailey JW, Lasley SM, Mishra PK, Bettendorf AF, Burger RL, Jobe PC (May 1989). "Aspartame fails to facilitate pentylenetetrazol- induced convulsions in CD-1 mice" *Toxicology and applied pharmacology* 98 (3): 475-486.
11. M. Vallender, S. Young, 2009, *Monographs medicinal and Pharmaceutical Substances, British Pharmacopoeia Volume I & II*, London, Crown Copyright, pp 435-439.
12. M. Vallender, S. Young, 2009, *Monographs medicinal and Pharmaceutical Substances, British Pharmacopoeia Volume I & II*, London, Crown Copyright, pp 435-439.
13. S. C Sweetman, 2009, *Martindale: The Complete Drug Reference Thirty-sixth edition*, Pharmaceutical Press, UK, pp 1930.
14. R. H. Bravo, L. L. Braden, D. Craig B., S. S. de Mars, 2009, *United States Pharmacopoeia*, by Rodyan, USP website at <http://www.usp.org>.
15. D. A. Warrell, T. M. Cox, J. D. Firth, Edward J., J R., M.D. Benz, 2003, *Oxford Textbook of Medicine 4th edition*, Oxford Press.
16. M. A. Chisholm-Burns, B. G. Wells, T. L. Schwinghammer, P. M. Malone, J. M. Kolesar, J. C. Rotschafer, J. T. Dipiro, 2008, *Pharmacotherapy Principles and Practice, USA*, McGraw-Hill.
17. K. Baxter, 2008, *Stockley's Drug Interactions, Eighth edition*, UK, Pharmaceutical Press.
18. K. R. Olson, I. B. Anderson, N. L. Benowitz, P. D. Blanc, R. F. Clark, T. E. Kearney, J. D. Osterloh, 1999, *Poisoning and Drug Overdose, third edition*, USA, McGraw-Hill.
19. C. Ashley, A. Currie, 2009, *the Renal Drug Handbook, Third Edition*, Radcliffe Publishing.
20. J. Martin, 2011, *British National Formulary 61 Edition*, BMJ Group and Pharmaceutical Press.
21. J. Swarbrick, 2007, *Encyclopedia of Pharmaceutical Technology Volume 1, Third Edition*, USA, Informa Healthcare.
22. M. Sittig, *Pharmaceutical Manufacturing Encyclopedia Volume 1, Second Edition*, United States of America, Noyes.
23. D. Aulton, 2002, *Pharmaceutics the Science of Dosage Form Design, 2nd edition*, Edinburgh, Churchill Livingstone.
24. R. C. Rowe, P. J. Sheskey, M. E Quinn, 2009, *Handbook of Pharmaceutical Excipients, Sixth Edition*, UK, Pharmaceutical Press.
25. S. L. Blachford, K. Krapp, 2003, *Drugs and Controlled Substances Information for Students*, United States of America, Thomson Gale.
26. L. V. Allen, Jr., N. G. Popovich, H. C. Ansel, 2011, *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, Ninth Edition*, USA, Lippincott Williams & Wilkins.
27. D. Jones, 2008, *FAST-track Pharmaceutics –Dosage Form and Design, First Edition*, UK, Pharmaceutical Press.
28. S. Cox G., 2008, *Pharmaceutical Manufacturing Handbook: Production and Processes*, USA, John Wiley and Sons.
29. T. K. Ghosh, B. R. Jasti, 2005, *Theory and Practice of Contemporary Pharmaceutics*, USA, CRC Press.
30. Clayden, 2000, *Organic Chemistry*, UK, Oxford Press.
31. D. A. Skoog, D. M. West, F. James H., S. R. Crouch, 2004, *Fundamentals of Analytical Chemistry Ninth Edition*, USA, Brooks Cole.
32. Saad, F. Ahmad K., A. Hayee, M. Sajjad N., 2014, A Review on Potential Toxicity of Artificial Sweeteners vs Safety of Stevia: A Natural Bio-sweetener, *Journal of Biology, Agriculture and Healthcare*, Vol.4, No.15, pp 138-9.

33. J. Abraham, F. Mathew, 2014, Taste Masking Of Pediatric Formulation: A Review on Technologies, Recent Trends and Regulatory Aspects, International Journal of Pharmacy and Pharmaceutical Sciences, Vol. 6, Issue 1, pp 13.
34. V. Vummaneni, D. Nagpal, 2012, Taste Masking Technologies: An Overview and Recent Updates, International Journal of Research in Pharmaceutical and Biomedical Sciences, Vol. 3, pp 512, 516, 517.
35. M. Asif, 2013, Low Caloric Sweeteners for Diabetes and Obesity Care and Their Clinical Inferences for Tackle the Prevalence, Journal of Pharmaceutical Care, pp 105-109.
36. L. Stanley, 2013, External Scientific Report: Review of data on the food additive aspartame, European Food Safety Authority, Supporting Publications, pp 3-4.

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