IJFANS
International Journal of Food And Nutritional Sciences

Volume 3 Issue 3 Apr-Jun-2014, www.ijfans.com e-ISSN: 2320-7876

INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES

Official Journal of IIFANS

INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES

e-ISSN 2320 –7876 *www.ijfans.com*

Vol.3, Iss.3, Apr-Jun 2014

© 2012 IJFANS. All Rights Reserved

Review Paper *Open Access*

A REVIEW ONIMPORTANCE OF NATURAL SWEETENER, A ZERO CALORIE PLANT – STEVIA - HAVING MEDICINAL AND COMMERCIAL IMPORTANCE

Reshu Gupta, Vidushi Yadav and Manvi Rastogi*

Teerthanker Mahaveer University Moradabad.

*Corresponding Author: manvimanu1@gmail.com

ABSTRACT

Sugar is an inseparable part of the food we consume. Artificial sweetener (A sugar substitute) is a food additive that duplicates the effect of sugar in taste, but usually has less food energy. Besides its benefits, animal studies have convincingly proven that artificial sweeteners cause weight gain, brain tumors, bladder cancer and many other health hazards.Stevia is a natural sweetener plant and estimated to 300 times sweeter than sugar cane. Stevioside is regenerated as a valuable natural sweetening agent because of its relatively good taste and chemical stability. Products can be added to tea and coffee, cooked or baked goods, processed foods and beverages, fruit juices, tobacco products, pastries, chewing gum and sherbets. The direct effect of stevioside on transport activity of glucose in skeletal muscle study divulged that insulin action on muscle glucose transport might be improved due to the low concentration of stevioside, signifying that stevioside has the imminent action in the glucose transport system in skeletal muscle. Also, it has a potential commercial value and that is why private and public biotechnology companies are producing stevia in huge quantity and marketing its products. Stevia is such a versatile herb with sweetness that possesses anti-fungal and anti-bacterial property also. It can be safely used in herbal medicines, tonics, for diabetics and also in the daily usage products like mouth washes, and tooth pastes. Leaves of this plant produce zero-calorie, a non-nutritive, high potency sweetener and substitute to sucrose.

Key words: stevia, stevioside.

INTRODUCTION

Obesity and its related health problems like diabetes, dislipidemia, heart disease, hypertension stroke etc. are the results of a great advancement in life style, poor dietary habits, lack of exercise and stress, apart from genetic contribution. Of all, the most alarming related health problem is diabetes. Consumption of sugar sweetened beverages is a major cause of obesity and diabetes. There is an alarming increase in the incidence of diabetes in India and with world's largest population being noted, India is labeled as" Diabetic capital of world". Therefore, substituting sugar with low calorie sweeteners may be efficacious in reducing the weight and its related healthproblems. So, sugar substitutes like saccharin, sucralose and aspartame gained importance in reducing calorie intake. However they are artificial substitutes. Recently, it has been evident that prolonged use of artificially sweetened beverages / or prolonged use of aspartame lead to an increase in frequency of brain tumors in humans which is a major concern (Fowler *et.al.,* 2088).

Stevia is a perennial herb that belongs to the Asteraceae family. It is a natural sweetener plant having medicinal and commercial importance is being used all over the world and estimated to be 300 times sweeter than cane sugar (B. Ahmed *et.al*., 2011). Stevia, commonly known in Sanskrit as "madhu patra," meaning sweet leaf is natural and healthy alternative to sugar and artificial sweeteners. It is also known as "honey yerba" and "honeyleaf" and by some other variations of these names. It is a famous perennial shrub, belongs to the family asteraceae, genus stevia and species rebaudiana. It is extensively grown in the subtropical regions, and has been available since decades for its wide use as a sweetener in beverages and to mask the bitter taste of certain herbal medicinal plants in several countries like Brazil, Japan, and Paraguay etc (Parsons, 2001).

It has also been reported that S. rebaudiana, as a non-calorie first natural sweetener used in medicinal green teas for treating heart burn and other ailments (Vanek et.al., 2001) even though there are more than 200 species of the genus Stevia, only S. rebaudiana gives the sweetest essence (Savita *et.al.,* 2004). Japanese have been using stevia and its products in cooked or baked goods, processed foods and beverages, fruit juices, tobacco products, pastries, chewing gum and sherbets (Brandle, 1992).

In 1970's while cyclamate and saccharin were suspected as carcinogens, Japan began cultivating stevia as an alternative which soon gained popularity and got commercialized. As it possesses flavor enhancing property

it is used in food products and soft drinks like Coco-cola, Pepsi etc. (Carakostas *et.al.,* 2008). Today it is widely cultivated in countries like China, Korea, Thailand, Brazil, Peru, Paraguay and Isreale etc.

Apart from its sweetness stevioside along with related compounds which include rebaudioside A and steviol offer many therapeutic benefits that include antihypertensive, antidiabetic, anti-inflammatory, anti tumor, antioxidant, antidiarrhoeal, diuretic and immunomodulatory actions. Steviol interacts with the drug transporters and for this property of its, Steviol is proposed as drug modulator (Goyal et.al., 2010, Boonkaewwan et.al., 2008 and Chatsudthipong, 2009).

MECHANISM OF ACTION

The taste buds on the tongue react to the glucose in the glycoside. Those glycosides with more glucose (rebaudoside) taste sweeter than (stevioside) that tastes less sweet. Some of the taste buds react to the bitter taste of aglycone (Genus, 2003 and Goyal *et.al.,* 2010).

PHARMACOKINETICS

Gardana et.al in their study showed that, in the gut, rebaudioside and stevioside are hydrolyzed to steviol and glucose. The glucose released in the process is used by bacteria in colon and not absorbed into blood stream. Steviol was absorbed and conjugated to glucuronide. The half life (t½) for both glycosides is approximately 14hrs.It is excreted as steviolglucuronide through urine and feces (Koyama *et.al.,* 2003, Gardana *et.al.,* 2003 and Wheeler *et.al.,* 2008).

USES OF STEVIA AND ITS PRODUCTS

Stevia has its legendary due to its various mode of actions such as, sweetener, hypoglycemic, hypotensive (lowers blood pressure), cardiotonic (tones, balances and strengthens the heart), antimicrobial activities (Taylor, 2005). Different studies and documents proved that stevia has its own and natural constituents which are very much helpful for human health. Among various uses, sweetener is the main use of stevia. Some ethnological uses has been recorded (Taylor, 2005) which are enlisted in the table 1.

Table 1- Ethnomedical uses of stevia (Taylor, 2005)

Country	Ethnomedical uses
Brazil	Usually used for cavities, depression, diabetes, fatigue, heart support, hypertension, hyperglycemia, infections, obesity, sweet cravings, tonic, urinary insufficiency, wounds
Paraguay	Diabetes
South America	diabetes, hypertension, infections, obesity
United States	candida, diabetes, hypertension, hyperglycemia, infections, and as a vasodilator

COMMERCIALIZATION OF STEVIA

According to the document in the Dietary Supplement Health and Education Act (DSHEA) in 1994, in USA stevia did not have GRAS (Generally Recognized As Safe) status for eating, therefore, banned for human food. Then Doug Kinghorn of the Herb Research Foundation formed a review for American Herbal Products Association (AHPA) and on the basis of scientific evidence and historical use, stated that stevia was safe. So many researches and studies finally proved that stevia has no terrible effects in human and can be taken for having diverse medicinal uses of stevioside. Though stevia is the natural sweetest plant in the world since leaves contain diterpene glycoside which enriches sweet taste, it is not metabolized and calories free. GD Searle and Company which was later on bought by Monsanto in 1985 stated that more than 200 objective studies have found stevia as NutraSweet to be safe. The papers were re-evaluated by relevant regulatory authorities like the FDA and as named Neotame is the new sweetener to be marketed by the company. Some available stevia products in USA market are enlisted in the table 2.

Table 2.Commercially obtainable stevia products in USA market

Product	Type	Manufacturer
Stevia	Crystals	At Stevia LLC (Valley Forge, PA, USA)
Stevia extracts	Powder	Life Extension Foundation (Fort Lauderdale, FL, USA)
JAJ Stevioside	Powder	JAJ Group, Inc. (Jacksonville, FL, USA)
Stevia liquid extract	Liquid	Baar Products, Inc. (Downingtown, PA, USA)
Stevia Dark Liquid Concentrate	Liquid concentrate	Stevia Now (Shrub Oak, bNy, USA)
Stevia Pure Powder Extracts	Powder extract	Stevia Now
Stevia Tablets	Tablets (100-400 mg)	Stevia Now

THERAPEUTIC BENEFITS

ANTI-HYPERGLYCEMIC EFFECT

Animal studies have shown that stevia has a revitalizing effect on the beta cells of pancreas, also improves insulin sensitivity and promotes additional insulin production. Chen TH and co-workers found that stevioside was able to regulate blood glucose levels by enhancing not only insulin secretion but also insulin utilization in insulin deficit rats. The later was due to

decreased phosphophenol pyruvate carboxykinase gene expression in rat liver by stevioside's action of slowing down glucogenesis. Stevioside reduces the postprandial blood glucose levels. Several human trials conducted in normal healthy volunteers have shown that extracts of stevia rebaudiana leaves could increase glucose tolerance in humans. Therefore stevia may be advantageous in the treatment of type 2 diabetes (Jeppesen et.al., 2006, Chen et.al., 2005, Anton *et.al.*, 2010, Gregersen *et.al.*, 2004 and Barriocanal *et.al*., 2008).

ANTIHYPERTENSIVE EFFECT

Physiological and Pharmacological experiments have suggested that stevioside from the leaves of stevia act as a typical systemic vasodilator. Melis MS et al in their studies have demonstrated that stevioside from stevia rebaudiana leaves provoked hypotension, diuresis and natriuresis in both normal and hypertensive rats. An increase in the renal plasma flow and glomerular filtration in rats had been observed in normal rats and the effect was attributed to the vasodilatation of afferent and efferent arterioles (Melis, 1996 and Melis, 1995). Human studies have also suggested its beneficial role in hypertension for its vasodilator property. It was suggested that 750 – 1500 mg/ day of stevioside, reduces systolic blood pressure by 10 – 11 mmHg and diastolic blood pressure by 6 -14 mmHg within one week of starting the treatment (Ferri et..al., 2006 and Maki et.al., 2008). It is found that stevioside causes vasorelaxation by inhibition of Ca++ influx into the blood vessels (Ulbricht et.al., 2010). Therefore stevia could prove to be beneficial in hypertensive patients.

ANTI- OXIDANT EFFECT

Being natural stevia is potential source of natural antioxidants. Varieties of antioxidants were obtained from the extracts of stevia rebaudiana, they include, opigenin, kaempferol and quereitrin that inhibited DNA strand damage. Isosteviol, a derivative of stevioside inhibits angiotensin II induced cell proliferation and endothelin I secretion while attenuation of reactive oxygen species generation (Ghanta *et.al.*, 2004 and Stoyanova *et.al.*, 2011). Hence it could be beneficial in a variety of diseases like cancer, reproductive problems and developmental defects.

ANTI -CANCER EFFECT

Although limited evidence are available, animal studies by Yasukawa et al indicate that the four isolates of steviol glycoside - stevioside,rebaudiosides A & C and ducloside A from stevia rebaudiana have a strong inhibitory effect on 12- 0- tetradecanoylphorbol-13-acetate (TPA) induced inflammation in mice which is suggestive of its anticancer effect (Raskovic et.al., 2004 and Yasukawa, 2002).

ANTIMICROBIAL EFFECT

Evidential research reports indicate that derivatives prepared by stevia isolates which included octa - acetylombuoside, ombuine and retusine were found to have antimicrobial action against few types of gram positive bacteria (Tomita *et.al.*, 1997).

ANTI-INFLAMMATORY AND IMMUNO-MODULATORY EFFECT

Stevia has been found to attenuate synthesis of the inflammatory mediators in LPS stimulated THP-1 cells by interfering with the I Kappa B kinases (IKKbeta) and Kappa B signaling pathway thus beneficial as anti-inflammatory and immunomodulatory substance (Bookaewan *et.al.*, 2006).

MISCELLANEOUS

Stevia is also rich in beta carotene, ascorbic acid, protein, calcium, iron, magnesium, phosphorus and numerous other phytochemicals. Hence the herbal derivative apart from its sweetening property also is beneficial with its nutritive value. Other proposed uses include alcohol abuse, anti-inflammatory, anti-mutagenic, antitumor, diuretic, digestive aid, food additive, immunomodulation and obesity (Chatsudthipong, 2009).

ADVANTAGES OF STEVIA

In comparison to the artificial sweeteners Stevia possess several advantageous properties that include;

1. Appetite regulation / suppression.
2. .Being zero calorie sweeteners, assists in weight management / weight loss (as it reduces craving for sweets).
3. No major safety concerns.
4. .Ideal for cooking and baking as it is non-fermentable and heat stable up to 200°C.
5. Calorie value is 2.7kcal/gm.
6. Intense in its sweetening property.
7. Cheaper as compared to other sweeteners.
8. Safe and beneficial in management of diabetes and obesity.

DRUG INTERACTIONS

1. It has diuretic effect so it decreases the excretion of lithium with resultant increase in plasma lithium concentration and leads to lithium toxicity (Melis, 1996).
2. Given along with antidiabetic agents like glimepride, pioglitazone etc. may cause decrease in blood sugar levels hence needs close monitoring of blood sugar levels.
3. Stevia may also interact with monoketocholate (a substance that may affect glucose and lipid levels), diuretics, anti-inflammatory, anticancer agents or hypocalcaemia agents (Raskovic *et.al.*, 2004).
4. Verapamil tends to increase the renal and systemic effects of stevia (Melis, 1991).

ADVERSE EFFECTS AND CONTRAINDICATIONS

- Generally it is considered to be safe, with minimal side effects that include; nausea, abdominal fullness, myalgia, muscle weakness, dizziness, asthenia and allergy (Genus, 2003 and Goyal et.al., 2003).
- It is used with caution in diabetes as it is known to reduce the blood sugar levels.
- In hypertensive patients it is used with caution as it is likely to reduce the blood pressure.
- It may affect the renal activity and perfusion, sodium excretion and urinary flow hence, cautious use is indicated in patients with renal disease or with impaired renal function (Melis, 1996).
- With lack of evidence for its effect on pregnancy and lactation Stevia is not recommended during pregnancy and lactation.

CONCLUSION

Stevia is now being used worldwide for having its various magnitudes. It has been proved that historically it has medicinal values and some stimulating actions. Stressful and sedentary life styles of present days alarmingly increase the incidence of diabetes, hypertension and obesity affecting mainly the young adults. If adequate care and regularity in treatment is neglected these problems lead to complications, which further increase morbidity and mortality rate. Among different chemical constituents, stevioside has a potential mode of actions in controlling type 2 diabetes. Therefore, peoples are used to ingest it without any confusion. Due to the demand, biotechnology companies are commercially producing stevia through tissue culture and marketing stevia in different form such as leaf powder, liquid and fresh leaves. Stevia has a natural sweetening activity and pharmaceutical properties, therefore, it can be concluded that some extensive high throughput biotechnological techniques should be implemented for the better known of stevia properties in animal health.

A little health conscience knowledge and modification of life style will help us fight these conditions. Stevia being herbal natural product, with virtually calorie free status causing less harm, benefits several health conditions and has a bright future with other medicinal values apart from its use as a sweetener.

REFERENCES

- Anton SD, Martin CK, Han H, Coulon S, Cefalu WT, Geiselman P, Williamson DA. (2010): Effect of stevia, aspartame and sucrose on food intake, satiety and postprandial glucose and insulin levels. Appetite. 55(1): 37-43.
- B. Ahmed, M. Hossain, R. Islam, A. Kumar Saha, A. Mandal. (2011): A review on natural sweetener plant – stevia having medicinal and commercial importance. ISSN 0002- 1954: 75- 91.
- Barriocanal LA, Palcois M, Benitez G, et al. (2008): Apparent lack of pharmacological effect of steviol glycosides used as sweeteners in humans. A pilot study of repeated exposure in some normotensive and hypotensive individuals and in type 1 and type 2 diabetics.RegulToxicolPharmacol. 51: 37-41.
- Bookaewan C, Toskulkao C, Vongsakul M. (2006): Anti inflammatory and immunomodulatory activities of stevioside and its metabolite steviol on THP-1 cells. J Agric Food Chem. 54 (3): 785-789.
- Boonkaewwan C, Ao M, Toskulkao C, Rao MC. (2008): Specific immunomodulatory and secretory activities of stevioside and steviol in intestinal cells. J Agric Food Chem. 56: 3777-84.
- Brandle, J.E., Rosa N. (1992): Heritability of yield, leaf-steam ratio and stevioside content estimated from a ladrace cultivar of Stevia rebaudiana. Can. J. Plant Sci. 72: 1263-1266.
- Carakostas MC, Curry LL, Boileau AC, et al. (2008): Overview: the history, technical function and safety of reaudioside A, a naturally occurring steviol glycoside, for use in food and beverages. Food ChemToxicol. 46 Suppl 7: S1-S10.
- Chatsudthipong V, Muanprasat C. (2009): Stevioside and related compounds: therapeutic benefits beyond sweetness. PharmacolTher. 121 (1): 41-54.
- Chen TH, Chen SC, Chan P et al. (2005): Mechanism of the hypoglycemic effect of stevioside, a glycoside of stevia rebaudiana. PlantaMed.71 (2): 108-113.
- Ferri LA, Alves-Do-Prado W, Yamada SS, Gazola S, Batisla MR, Bazotte RB. (2006): Investigation of the antihypertensive effect of oral crude stevioside in patients with mild essential hypertension. Phytother Res. 20(9):732-6.
- Fowler SP, Williams K, Resendez RG, Hunt KJ, Hazuda HP, Stern MP. (2008): Fueling the obesity epidemic? Artificially sweetened beverage use and long term weight gain. Obesity (Silver Spring) 16(8): 1894-900.
- Gardana C, Simonetti P, Canzi E, Zanchi R, Pietta P. (2003): Metabolism of stevioside and rebaudioside A from stevia rebaudiana by human microflora. J Agr Food Chem. 51:6618-6622
- Genus JM.(2003): Stevioside.Phytochemistry. 64:913-21.
- Ghanta S, Banerjee A, Poddar A, Chattopadhyay S. (2007): Oxidative DNA damage preventive activity and antioxidant potential of stevia rebaudiana (Bertoni) Bertoni: A natural sweetener. J Agric Food Chem. 26:55 (26):10962-67.

- Goyal SK, Samsher RK, Goyal. (2010): Stevia (Stevia rebaudiana) a bio-sweetener- a review.Int J Food SciNutr. 61(1):1-10.
- GregersenS, Jeppesen PB, Holst JJ, Hermansen K. (2004): Antihyperglycemic effects of stevioside in type 2 diabetic subjects. Metabolism. 53:73-6.
- Jeppesen PB, Gregersen S, Poulsen CR, Hermansen K. (2000): Stevioside acts directly on pancreatic beta cells to secrete insulin: actions independent of cyclic adenosine monophosphate and adenosine triphosphate sensitive K+ channel activity. Metabolism. 49: 208-14 .
- Koyama E, Kitazawa K, Ohori Y, et al.(2003): In vitro metabolism of the glycoside sweeteners, stevia mixture and enzymatically modified stevia in human intestinal microflora. Food ChemToxicol. 41(3):359-374.
- Maki KC, Curry LL, Carakostas MC et al. (2008): The hemodynamic effects of rebaudioside A in healthy adults with normal and low normal blood pressure. Food ChemToxicol. 46: Suppl 7:S40-6.
- Melis MS. (1995): Chronic administration of aqueous extracts of stevia rebaudiana in rats renal effects. J Ethnopharmacol. 47: 129-34.
- Melis MS, (1996): A crude extract of stevia rebaudiana increases the renal plasma flow of normal and hypertensive rats.Braz J Med Biol.Res. 29:669-75.
- Melis MS, Sainati. (1991): AR. Effect of calcium and verapamil on renal function of rats during treatment with stevioside. J Ethnolpharmacol. 33:257-622.
- Parsons WT, Cuthbertson EG. (2001): "Noxious weeds of Australia." Edn 2, CSIRO Publishing, Collings wood, Australia, ISBN 978-0-643-06514-7.
- Raskovic A, Jakovijevic, Mikov M, et al. (2004): Joint effect of commercial preparations of stevia rebaudiana Bertoni and sodium monoketocholate on glycemia in mice.Eur J Drug Metab Pharmacokinetics. 29 (2): 3-86.
- Savita, S.M., Sheela, K., Sunanda, S., Shankar, A.G., Ramakrishna, P., Sakey S. (2004): Health implications of Stevia rebaudiana. J. Hum. Eco. 15: 191-194.
- Stoyanova S, Genus J, Heideg E, Den Ende WV. (2011): The food additives inulin and stevioside counteract oxidative stress.Int J Food SciNutr. 62:207-214.
- Taylor, L. (2005): The Healing Power of Natural Herbs. Garden City Park, NY: Square One Publishers, Inc.. pp. (excerpted at weblink). ISBN 0-7570- 0144-0. http://rain-tree.com/stevia.htmhttp://rain-tree.com/stevia.htm.
- Tomita T, Sato N, Aria T, et al. (1997): Bactericidal activity of a fermented hot water extract from stevia rebaudiana Bertoni towards enterohaemorrhagic Escherichia Coli 0157:H7 and other food borne pathogenic bacteria. MicrobiolImmunol. 41: 1005-9.
- Ulbricht C, Isaac R, Milkin T, Poole EA, Rusie E, Grimes Serrano JM, Weissner W, Wonder RC. (2010): An evidence based systematic review of stevia by the Natural Standard Research Collaboration. CardiovascHaematol Agents Med Chem. 8(2): 113-27.
- Vanek, T., Nepovim, A., Valicek, P. (2001): Determination of Stevioside in plant material and fruit teas. J. food comp. anal. 14: 383-388.
- Wheeler A, Bioleau AC, Winkler PC, Compton JC, Prakash I et al. (2008): Pharmacokinetics of rebaudioside A and stevioside after single dose in healthy men. Food Chem Toxicology, 04.041.
- Yasukawa K et al. (2002): Inhibitory effect of stevioside on tumor promotion by 12-0-tetradecanoylphorbol-13-acetate in two stage carcinogens in mouse skin. Pharm Bull. 25(11): 1488-90.