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Stevia Rebaudiana Bertoni: Composition and Functions : A Review

Hafiza Nazia Koser[1], Rabeea Mubarak[2], Sana Noreen[1], Bahisht Rizwan[1], Mudassir Khan[3], Zeenat Islam[1], Asra Abbas[2], Hifza Noor[2] and Nimra Naeem[2]

[1]University institute of diet and nutritional science, Faculty of Allied health sciences, The university of Lahore, Lahore **Pakistan**

[2]University institute of diet and nutritional science, Department of Allied health sciences, The university of Lahore, Lahore **Pakistan**

[3]Department of Healthcare Biotechnology, Atta-Ur-Rahman School of Applied Biosciences (ASAB), National University of Science and Technology (NUST), Islamabad**, Pakistan**

***Correspondence:** sananoreen.rizwan@gmail.com **Received 21-11-2020, Revised: 28-12-2020, Accepted: 29-12-2020 e-Published: 30-12-2020**

Stevia, which goes by the scientific name of Stevia Rebaudiana Bertoni, has been used since the late '80s. It has been used in making herbal tea and various diet especially for diabetic patients, and its numerous uses are gaining popularity in all fields in the health sector. It is also known as a zero caloric sweetener that serves as a bonus to those interested in weight loss. The presence of glycoside and stevioside in stevia acts as an anti-oxidative, anti-inflammatory, cardioprotective, and anti-cancerous. Therefore, this review article looks into the primary roles, composition, and doses, along with sensory evaluation tests, giving all kinds of readers a clear view of the significance in the daily live

Keywords: stevia, anti-diabetic, anti-hyperlipidemic, anti-inflammatory

INTRODUCTION

Stevia, of the Asteraceae family, is a plant herb and a natural sweetener known to be 100-300 times sweeter than sugar. It is mostly found in Paraguay, and primarily produced in Argentina, Brazil, Columbia, Paraguay, China, Japan, Malaysia, South Korea, Vietnam, Israel, Australia, Kenya, and the US (Singh et al., 2013). The plant that has been used by Guarani Indians in the past has an optimum temperature of 15-35 degrees and prefers a slightly acidic pH of 5.5-6.0 for it to grow (Ijaz, Pirzada, Saqib, & Latif, 2015; D. Soejarto, Compadre, Medon, Kamath, & Kinghorn, 1983). It is a small plant of 1m, and leaves are extending 3-4 cm (Ahmed & Mukta, 2017). This family covers around 230 varieties of species, and only two of them contain an increased content of steviol glycosides, namely S. rebaudiana and S. phlebophylla, which are accountable for the sweet taste. The presence of flavonoids, essential oils, and the phenolic content present makes it effective against diabetes, inflammation, cancerous activities, toxicities, hypertension, neurological and liver diseases, diarrhea and caries and is also used for wound healing and as a contraceptive (Gupta et al., 2013; Ijaz et al., 2015; Jitendra et al., 2012; Singh, et al., 2013). The development of Stevia rebaudiana can be classified into 4 stages, (a) germination, (b) development of seedling, (c) vegetative development (d) floral buds → pollination → fertilization (Ijaz et al., 2015). This article combines some of the recent works done on stevia so that the reader can get a clear view in loopholes for further research. This herb is an emerging and trending research in the field of

pharmaceuticals, as a functional food product and in the making of various foods and beverages to decrease the caloric intake and make it acceptable for consumer satisfaction. According to a study, the average protein (crude) was found to be 86.33 g/kg dry matter. Arginine, Lysine, Histidine, Phenylalanine, Leucine, Valine, Threonine and Isoleucine were found in the amounts of 0.81 g/100g, 0.15 g/100g, 0.34 g/100g, 0.88 g/100g, 1.30 g/100g, 0.94 g/100g, 0.75 g/100g and 0.72 g/100g respectively (Li et al., 2011)_Crude fat, crude fiber and ash was found to be 11.79g/kg, 284.68 g/kg, 96.56 g/kg DM respectively. Energy emitted by stevia is 9.77 MJ/kg on average (Gerdzhikova et al., 2018). These amounts vary in stems and leaves. In another study, the amount of moisture was found to be 10.73g, Energy 270kCal, Protein 13.68g, Fat 6.13g, Carbohydrates 63.1g, Ash 12.06g and crude fiber 5.03g (Gasmalla, Yang, Amadou, & Hua, 2014) (Table 1.1). The Moisture, Ash, Crude fat, Crude Protein and Crude fiber were found in amounts of 7.72%, 7.89%, 3.81%, 14.57%, 10.00%, 63.73% respectively in another study (Moguel-Ordoñez et al., 2015).

The plant leaves are also rich in certain minerals. Sodium (0.7mg/100g), Iron (366mg/100g) , Manganese (2.4mg/100g), zinc (20mg/100g) , Potassium (17.3mg/100g), Calcium (8.2mg/100g), Phosphorus (2.6mg/100g) (**Atteh *et al*., 2011; Gupta *et al*., 2013)**. Some of the studies also show that they also contain some levels of magnesium (1.86 g/kg DM), copper (10.2mg/kg) and nitrogen (13.81g/kg DM)(Gerdzhikova et al., 2018; Hu et al., 2010). References from other studies have been summarized in Table 1.2.

Stevia leaves are also rich in iminosugar steviamine, lipids, essential oils, sterebins, thiamine, niacin, beta carotene, Vitamin C, Vitamin B2, austroinulin, rebaudioxides, quercetin, isoquercitrin, xanthophyllus and trace elements (K. Singh, Chauhan, Yadav, & Kumar). Vitamin C, B2, Folic Acid are found to be 14.98mg/100g, 0.43mg/100g, 52.18mg/100g respectively (Kim, Yang, Lee, & Kang, 2011). Total no. of amino acids including lysine, histidine, phenylalanine, leucine, methionine, valine, threonine and isoleucine was found to be 7.67g/100g (Marcinek & Krejpcio, 2015).

The principal elements which give stevia their taste, are responsible for the various benefits of stevia and which make up stevia are the glycosides, compounds made by a simple sugar and some other compound by replacing a hydroxyl molecule in the sugar group making a glycosidic bond. Steviosides, steviols, Steviolbioside, Rebaudioside A, B, C, D, and dulcoside A are found in 2.0%, 0.70%, 1.2%, 5.0%, 0.50%, 2.0%, 3.3% and 1.0% DW respectively (Jaworska, Krynitsky, & Rader, 2012). Another study could not find out the levels of steviol, steviolbioside, rebaudioside B,D and dulcoside A. The amount of sstevioside, rebaudioside A and C were found to be 5.8%, 1.8% and 1.3% (Gardana, Scaglianti, & Simonetti, 2010). whose results are closer to a similar study (Atteh et al., 2011). Another study was only able to determine the levels of stevioside in stevi leaves. (6.26-10.10%). The levels of Rebaudioside A, C and Dulcoside A could not be determined (A Khiraoui et al., 2017). The percentage of steviosides in methanol and water extract was found to be 64.67 ± 0.47% (Abou-Arab, Abou-Arab, & Abu-Salem, 2010). References from other studies have been summarized in Table 1.3.

Sensory Evaluation of different foods and drinks by the addition of Stevia: -

Addition of increased purity short chain Glucosyl stevia (having 4 or < alpha-1-4-glucosyl remainders) in the amounts of 0.03% in diet cookies, yogurt, and less caloric orange juice drink were renowned to have a full flavor and mouthfeel. Rebaudioside A and Glucosyl stevia in the composition of 0.003 and 0.05% respectively, when added to less caloric carbonated beverages showed no aftertaste, astringent or bitter taste and showed the highest quality of sweet taste. (Markosyan, 2012). The hardness of the short crust pastery decreased significantly by 55-56%. ENrgy, Carbohydrates and sugar levels also decreased pointedly (392 Cal, 36g, and 0g respectively) as compared to the controls, (452 Cal, 51g, and 15g respectiviely)(Król, Ponder, & Gantner, 2019). The highest score on a hedonic scale was of the sample that had 100% Rebaudioside A when simple sugar was replaced replaced by Rebaudioside A while making an orange juice in another study (Ardali, Alipour, Shariati, Taheri, & Amiri, 2014). While readying cake batters and replacing sugars with stevia leaves, a rise in gravity was seen as compared to the controls. Powdered stevia leaves in composition of 10% gained the maximum scores on the 9 point hedonic scale in terms of appearance, texture and overall acceptibility (Elsebaie & Mostafa, 2018). Stevia cookies showed the highest score with 17 supercritical

extract giving a pale yellow color going towards a light green color and the cookies start becoming darker when the concentration of stevia increases.

Table 1.1: Major nutrient composition of Stevia

	Li et al., 2011	Gasmalla,Yang,Amadou & Hua, 2014	Gerdzhikova et al., 2018
Crude Fat		6.13g	11.79g/kg
Crude Fiber		5.03g	284.68g/kg
Ash		12.06g	96.56g/kg
Energy		270kCal	9.77MJ/kg
Protein	86.33g/kg	13.68g	
Carbohydrates		63.1g	
Moisture		10.73g	

Table 1.2: Mineral content of Stevia

	Tadhani et al. 2006	Hu et al. 2010	Atteh et al.2011	Marcinek & Krejpcio ., 2015
Potassium	2.51g		17.3mg/100g	
Calcium	1.55g		8.2mg/100g	
Magnesium	0.50g	1.86g/kg		
Phosphorus	0.35g		2.6mg/100g	
Sodium	0.16g		0.7mg/100g	
Sulphur	0.12g			
Iron	363ppm		366mg/100g	
Manganese	98.30ppm		2.4mg/100g	
Zinc	63.90ppm		20mg/100g	
Copper	10.40ppm	10.2mg/kg		
Molybdenum	1.14ppm			
Selenium	0.57ppm			
Cobalt	0.27ppm			
Nitrogen		13.81g/kg		
Vitamin C				14.98mg/100g
Vitamn B2				0.43mg/100g
Folic Acid				52.18mg/100g

Table 1.3 : Major Bioactive Components (Stevia Rebaudiana)

	Gardana, Scaglianti, & Simonetti, 2010	Jawaroska, Krynitsky , & Rader., 2012	Prakash et al., 2014	Kobus-Moryson et al., 2015
		Dry Weight	Sweetening Power	Sweetening Power
Stevioside	5.80%	2.00%	210	200-450
Steviolbioside		1.20%	90	100-125
Rebaudioside A	1.80%	5.00%	200	150-450
Rebaudioside B		0.50%	150	30-350
Rebaudioside C	1.30%	2.00%	30	50-450
Rebaudioside D		3.30%	221	150-450
Rebaudioside E			174	150-300
Rebaudioside F			200	30-120
Rebaudioside M			250	
Dulcoside A		1.00%	30	50-125

The flavor, texture, taste and the overall acceptibility start diminishing as Stevia level increases (Chughtai & Farhan, 2017). This point is also supported by another study where substituting sucrose with stevia leaves powder and adding roasted flax seed flour changed the colour, texture and taste of biscuits and flavor and overall acceptability did not vary pointed in other different treatments. The 2 studies have been

opposed by another study where decreased caloric stevia yogurt cookies for patients with diabeties showed a good response from sensory panelists (Abdel-Salam, Ammar, & Galal, 2009). Food Additives Joint Expert Committee declared that extracts of stevia having 95% steviol glycosides or stevia in the dose of 4mg/kg bw/day is considered safe for human consumption (Mukhtar, Tiong, Bukhari, Abdullah, & Ming, 2016).

The amount of sugar in kulfi and kheer reduced to 75% and 67% by the addition of stevia which resulted in reduced energy levels (Kaur, Kochhar, Boora, & Javed, 2019). Similarly, normal table sugar can be efficiently replaced by administration of 0.15% steviol glycosides of 15 degrees Bx (amout of sugar in an aquoues solution) in yogurt (Sherpa, 2018). The alteration in taste, according to a research study is possibly because of the presence of sesquiterpene lactones, essential and aromatic oils, tannins, and flavonoids (D. D. Soejarto, Kinghorn, & Farnsworth, 1982). Formation of herbal hot drinks which were sweetened with 50% stevia instead of simple sugar was the one which was the most acceptable followed by 75% substitution in comparison to control (Wafaa, Azza, & El-Ola, 2016). In a study of substituting sugars with stevia in the production of ice cream, the results suggested that all of the formulations tested could have a commercial potential (Aranda-Gonzalez, Perera-Pacheco, Barbosa-Martín, & Betancur-Ancona, 2016).

Anti- diabetic effects of stevia

Studies show that the incentive of the production of insulin is directly dependant on the quantity of steviosides and Calcium ions. Steviosides affect insulin sensitivity by enhancing the acceptance of glucose and improving protein expression thereby resulting in depolarization of Beta cells of pancreas by closing Potassium channels and the opening of calcium channels (Mohd-Radzman, Ismail, Jaapar, Adam, & Adam, 2013). as explained in Fig 1. The rebaudiosides A in stevia significantly reduces the concentration of glucose in blood and being protective of the because of their similar structures (Holvoet et al., 2015). However, a conflicting study stated that rebaudioside A did not have any effect on glucose levels of blood (Mohd-Radzman, Ismail, Adam, Jaapar, & Adam, 2013). In the livers of mice having resistance to insulin, Glycosides as a whole is shown to enhance the metabolism of glucose and bile, catabolisation of fats, the transportation and the storing of lipids (Marcinek & Krejpcio, 2016). The action of stevia to enhance the result of insulin on the membranes, enhnce the making of insulin, and to maintain blood glucose levels has also been stated in another study (Chughtai & Farhan, 2017; He et al., 2019). The stopping of advanced glycated end products (AGE's), which are harmful substances formed when protein or fats combine with sugar in blood causing micro and macro vascular damages in diabetic patients, were seen with stevia in vivo and in vitro (Aswar, Gogawale, Miniyar, & Patil, 2019). S. rebaudiana also acts by inhibiting the activity of alloxan, a toxic substance of glucose that destroys B cells selectively (Nadaf & Naikwadi, 2015). Glycosides of Stevia are shown to enance the insulin secretion in humans by action on the pancreatic Beta cells directly without effecting the channels of the Potassium ions and cAMP (Cyclic 3'5' AMP), a significant enhancer of glucose-induced insulin secretion by the beta-cells of the pancreas (Furman, Ong, & Pyne, 2010) indicating and proving the fact that steviosides and steviols can be considered as important hypoglycemic agents. A small single amount of 1000g was able to significantly decrease the levels of glucose by 18% in diabetic patients.

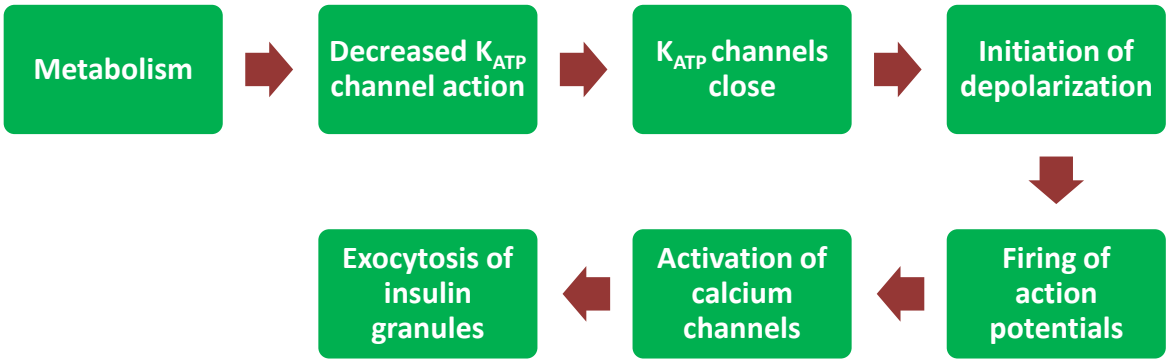

Figure 1: (Rorsman, Braun, & Zhang, 2012)

Anti-hyperlipidemic effects of Stevia

Stevia is also cast off as a heart refresher that maintains blood pressure heart rate and other cardiovascular activities. In humans, the extraction from the leaf of stevia by hot water decrease the blood pressure, by lowering the levels of blood cholestrol. When the cholesterol levels are lowered, the arteries tend to relax, the coagulation of blood is also reduced, improving regeneration of cells and toughening vessels (Suresh, Fetricia, Saranya, Sarithra, & Tamilselvan, 2018). The role of stevia in heart health is also supported by other studies. It is shown to relax the heart muscles and lower the amount of cholesterol in blood. Rebaudiana A, a bioactive coponent of stevia is also shown to balance blood pressure and is a protective agent against cvd's. The process by which stevia acts on the heart is similar to the way the Ca channel blockers work; by dilating the heart muscles thereby reducing blood pressure (Katz, 1986; Maki et al., 2008). In a study, stevia was used long term in women having high levels of cholesterol in blood, and it was seen that LDL and triglycerides levels decreased and HDL levels improved significantly. The results have been supported by other studies where 20 women having high cholesterol levels given a dose of 20 ml of stevia extract in 200 ml water decreased tryglycerides, LDL and cholesterol while enhancing HDL levels which shows a direct relation to heart health (Gupta et al., 2013). The rise in lipids can also be because of increase in the activity of hormone sensitive lipase (HSL), responsiple for hydrolyzing lipids and water soluble substances (Kraemer & Shen, 2002) inhibited by insulin and stimulated by hormones such as catecholamine and adrenocorticotrophic hormones (Aswar et al., 2019). Extracts of S. Rebaudiana using methanol as the extracting osolvent also showed significant decrease in cholesterol, triglycerides, LDL and VLDL levels from 231.2 ± 18 to 91.6 ± 9.4; 284.6 ± 12.5 to 120.7 ± 10.1; 179.4 ± 18 to 30.2 ± 9.9 and 62.6 ± 7.09 to 24.1 ± 2 respectively and improved HDL levels 19.6 ± 1.5 to 37.3 ± 1.5 (S. Singh et al., 2013). Also supported by another study (U. Ahmad et al., 2018).

Antioxidants, anti-inflammation and wound healing effect of Stevia

The leaves of stevia are shown to have an increased degree of antioxidant action ascribing to their scavenging activity of free radicals and super oxides thereby reducing inflammation which has been supported by many studies (Abdelkarim Khiraoui et al.; Shukla, Mehta, Bajpai, & Shukla, 2009; Tarka & Roberts, 2010). Extracts of stevia raised the actions of superoxide dismutase which plays a role as an effective antioxidant against oxidative stress in the body (Younus, 2018), catalase, an enzyme that converts hydrogen peroxide to water and oxygen (US. National Library of Medicine), glutathione peroxidase, which is also an anti-oxidative enzyme protecting cells from oxidative damage (Lubos, Loscalzo, & Handy, 2011) and reduces acetylcholinesterase, an enzyme that breaks down acetyl choline into acetate and choline (Zhao et al., 2019). The reduction in inflammatory cytokine expressions like TNF-α, IL- 6, IL- 10, IL- 1 beta, macrophage inflammatory protein 1-alpha (MIP-1α), CD11b and CD14 have also been seen with S. rebaudiana (Ranjbar & Masoumi, 2018). S. rebaudiana was also seen to effect wound healing. Thick exterior wounds of 2x2cm were made on 32 rats on their backs. Stevia showed potent decrease of wounds. Changes were also seen in tissue healing, epithelial cells reformation and reduction in neutrophils, lymphocytes, the ratio of fibrocytes to fibroblasts, and the increased no. of vessels and fibroblasts on Day 20th (Goorani et al., 2018). These results are also in line with another study where the researchers found out that applying mg/kg body weight of stevia on the wounds reduces the area of these wounds after 2 weeks (Das, 2013). Aqueous extract of stevia has been shown as an antioxidant, anti-inflammatory, and anti-fibrotic agent, because of its property of propagating NRF2 expression, protein that controls antioxidant expressions which protect from oxidative stress normally caused by inflammation or any kind of injury, NF-KB expressions and by blocking profibrogenic pathways thereby averting fibrosis (Ramos-Tovar et al., 2019).

Other functions of Stevia

Administration of 5mg/kg dose of stevia showed a noteworthy rise in ejaculation frequency and intromission frequencies in Streptozotocin induced diabetic male rodents. There was no effect on the amount of testosterone and other sexual performances (Ghaheri et al., 2018). Sativoside have also shown anti- cancer activity like Buckwheat and can be used for synthesis of

silver nanoparticles (Deshmukh & Kedari, 2014; Mudassir et al., 2018; Sane et al., 2020). Hexane extract of S.rebaudiana showed inhibitory action against Staphylococcus aureus (strain 921), Staphylococcus epidermidis (strains 965, 982, and 735), and Pseudomonas aeruginosa (strains RO3 and RO4) which shows that this herb can be considered as a potent antibiotic in the pharmaceutical industry and anti-inflammatory silver nanoparticles can be synthesized from stevia (Miranda-Ar et al., 2017; Mudassir et al., 2018). In vivo administration of 2.67g of dried leaves of stevia for 30 days in HTN rodents, important positive effects were seen such as improved Glomerular Filtration Rate (GFR), rise in renal plasma flow, and the elimination of Sodium (Cosola, Sabatino, di Bari, Fiaccadori, & Gesualdo, 2018). Initiation of renal vasodilation thereby reducing blood pressure and diuresis was also seen with aqueous extract of stevia leaves (N. Ahmad, Fazal, Abbasi, & Farooq, 2010). Extract of stevia leaves in amounts of 400 mg/kg showed a pointed decrease in AST, ALT, GGT, ALP and T. bilirubin levels while studying the liver protective functions of Stevia in contradiction to thioacetamide induced liver toxicity (Das & Kathiriya, 2012).

Conclusion

S. rebaudiania Bertoni is a well-known sweet herb due to its pharmacological and nutraceutical properties. Stevia and its metabolites have commercial value in number of countries as sugar substitutes in foods, beverages and medicines. It has many bio active components which provides additional health benefits beyond the basic needs. Studies have reported the health promoting of this natural herb Stevia which is well known as therapeutic agent and an efficient medication for curing chronic diseases. Stevia has a major thermogenic impact because of this it serves as a hypolipidemic and thermogenic agent in problems related to obesity. It still seems to be a "miracle" plant with endless advantages for mankind besides can thus be taken at a very reasonable price as a high-quality nature gift.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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AUTHOR CONTRIBUTIONS

HNK: Conceptualization and methodology. HNK, RM, SN and BR: Writing original draft. MK, ZI and AA: Visualization and investigation. HN and NN: Data validation. HNK, SN and MK: Writing-reviewing and editing. All authors read and approved the final version.

ORCID

Sana Noreen https://orcid.org/0000-0002-4040-5454

Mudassir Khan https://orcid.org/0000-0002-8184-3557

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