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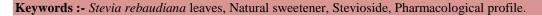
STEVIA (STEVIA REBAUDIANA): A REVIEW

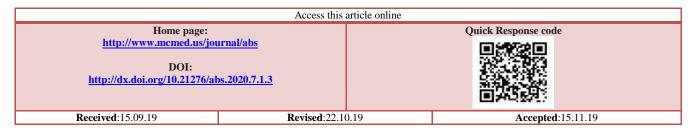
Vasuki K*, Murugananthan G, Suganya R, Renugaa Devi R

Swamy Vivekanandha College of Pharmacy, Elayampalayam, Tiruchengode, Tamilnadu, india.

ABSTRACT

Studies revealed that Stevia has been used throughout the world since ancient times for various purposes; for example, as a sweetener and a medicine. We conducted a systematic literature review to summarize and quantify the past and current evidence for Stevia. We searched relevant papers up to 2007 in various databases. As we know that the leaves of *Stevia rebaudiana* (Bert.) (Asteraceae) plants have functional and sensory properties superior to those of many other high-potency sweeteners, Stevia is likely to become a major source of high-potency sweetener for the growing natural food market in the future. Although Stevia can be helpful to anyone, there are certain groups who are more likely to benefit from its remarkable sweetening potential. These include diabetic patients, those interested in decreasing caloric intake, and children. Stevia is a small perennial shrub that has been used for centuries as a bio-sweetener and for other medicinal uses such as to lower blood sugar. Its white crystalline compound (Stevioside) is the natural herbal sweetener with no calories and is over 100-300 times sweeter than table sugar.





INTRODUCTION

Stevia rebaudiana is a small perennial growing up to 65-80 cm tall. Different species of Stevia contain several potential sweetening compounds [1,2], with S. Rebaudiana. Stevia is a semi-humid subtropical plant that can be grown easily. The soil should be in the pH range 6.5-7.5; well-drained red soil and sandy loam soil. Saline soils should be avoided to cultivate this plant. It is cultivated in Indian states: Rajasthan, Maharashtra, Kerela and Orissa. The increasing demands for natural sweeteners have driven the farmers in India toward largescale Stevia cultivation. The leaves of wild Stevia plants contain 0.3% dulcoside, 0.6% rebaudioside C, 3.8% rebaudioside A and 9.1% stevioside [3]. Stevia is a woody shrub that can reach 80 cm in height when it is fully matured. Leaves of this plant produce zero-calorie ent-kaurene diterpene glycosides (stevioside and rebaudiosides), a non-nutritive, high-potency sweetener,

and substitute to sucrose, being 300 times sweeter than sucrose[4]. It is recommended for diabetes and has been extensively tested on animals and has been used by humans with no side effects. It has also been reported that S. rebaudiana, as a non-calorie first natural sweetener used in medicinal green teas for treating heart burn. Therapeutic benefits that include antihypertensive, antidiabetic, antiinflammatory, anti tumor, antioxidant, antidiarrhoeal, diuretic and immunomodulatory actions [5]. 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

Corresponding Author Vasuki. K Email: - nalinikataria@rediffmail.com

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 [6].

Common Name of Stevia [7]:

Stevia, Candy leaf, Sweet leaf of Paraguay, Sweet-herb, Honey yerba, Honey leaf, Yaawaan.

Vernacular Names [8]:

Hindi: Meethi patti English: Sweet leaf, Honey leaf, Candy leaf, Sweet herb French: Stévia or Stévie Marathi: Madhu Parani Sanskrit: Madhu Patra Tamil: Seeni Tulsi Telugu: Madhu Patri



BOTANICAL DESCRIPTION:

Stevia rebaudiana, popularly known as 'candy leaf' is a sweet native herb of Paraguay. It became economically important for its significant contribution to the sugar and beverage industry throughout the world. This plant has been known to contain a calorie-free natural sugar in its leaves, which is an alternative to other artificially produced sugar substitutes. Stevia is conventionally propagated through seed and cutting, owing to its self-incompatibility, insufficient pollinator activity, and poor seed set, which results in the origination of heterozygous plants with varying concentration of glucosides in leaves, with low multiplication rate [9].

TAXONOMICAL CLASSIFICATION:

Kingdom: Angiospermae

Class: Dicotyledons Group: Monochlamydae Order: Asterales Family: Asteraceae Subfamily: Asteroideae Tribe: Eupatorieae Genus: Stevia Species: rebaudiana[10]

Cultivation:

Land preparation:

The land should be ploughed initially with a disc plough or harrowed to break down, the clods. Fine tilth of soil is required for Stevia cultivation. 1 to 2 ploughing has to be done after harrowing [11].

All Type:

Red soil and sandy loam types are best suitable for the cultivation of Stevia with pH between 6 to 7. Clayey loam soil does not show good results.

Raised Bed Preparation:

Forming raised beds is the best and economical way to grow Stevia. Raised bed of height half feet and width half feet is required. The distance between the 2 rows in bed is one feet. The distance between each plant in a row is half feet. With such spacing the plant population is around 50,000 plants per 'acre.

Irrigation:

Microsprinkler is the best method of irrigating Stevia plants. Flood or canal irrigation would not supply the required amount of water at the right time. Micro sprinklers, can be used to sprinkle the water once in a day in winter and 4 times in a day in summer or more depending upon the heat and relative humidity in the air; Watering frequency should be scheduled so that the plants do not wilt for want of water.

Organic Application and Plant Protection:

There is no such pest and disease incidence in this crop. In case any disease symptoms are noticed, spraying of neem oil diluted in water is the best organic method. For root grubs use castor oil mixed with cow manure and spray very little near the plant.

Weeding:

Removal of weeds can be done manually. Since the crop is grown in raised beds, Intercultural operations are easier by manual labour.

Maintenance:

Flowering of the plant should be avoided. Since Stevia has a significant apical dominance, the plant tends to grow tall and tanky. Pinching of the apical bud would enhance bushy growth of the plant with side branches. With good management the perennial plant can be maintained economically for 375 years.

Harvesting:

Harvesting of the leaves is done by plucking the leaves. If required in a small quantity. The entire plant with the side branches is cut leaving 10-15 cm from the basa.

Chemical Constituents:

Stevia it contains 100 phytochemicals. It is rich in terpenes and flavonoids. The two glycosides of Stevia are stevioside (5% - 10%) and rebaudioside-A (2% - 4%). Due to the non-caloric and sweetening properties, stevioside has increased their use [12]. Other sweet constituents include steviolbioside, rebausiosides A-E, dulcoside A, and. Stevia has some bitter taste due to presence of tannins, flavonoids, eseential oils. The chemicals presents with in Stevia are: Apigenin, Austroinulin, Avicularin, Caffeic Acid, Beta-Sitosterol, Caryophyllene Campesterol, Chlorogenic Acid, Centaureidin, Daucosterol, Chlorophyll, Cosmosiin, Cynaroside, Diterpene Glycosides, Dulcosides A-B, Foeniculin Formic Acid, , Gibberellin, Gibberellic Acid, Indole-3-Isoquercitrin, Acetonitrile, Isosteviol, Jhanol, Kaempfer, Kaurene, Lupeol, Polystachoside, Luteolin, Quercetin, Rebaudioside A-F, Sterebin, Quercitrin, Scopoletin A-H. Steviol. Steviolbioside. Steviolmonoside, Stevioside, Stigmasterol, Umbelliferone, Stevioside A-3, and Xanthophylls.

Pharmacological profile:

Anti-inflammatory: Methanolic extract of Stevia leaves showed marked inhibition of inflammatory activity induced by TPA in mice. Two active compounds, humulone and lupeol 3-palmitate were separated from hop and Stevia respectively[13].

Renal Effects on Chronic Administration: Administration of crude extract of Stevia dried leaves for 40 to 60 days induced systemic and renal vasodilation causing hypotension, diuresis and natriuresis [14].

Anti-Hypertension: Using stevioside capsules 250 mg 3 times daily, the study found stevioside to be a safe and effective compound or supplementary therapy for hypertension. Study showed stevioside caused vasorelaxation through an inhibition of Ca influx into the blood vessels[15].

Antioxidant: Study of ethanolic and ethyl acetate extracts of leaves indicate *Stevia rebaudiana* may be a useful as a potential source of natural antioxidants. Study showed that Stevia, besides its sweetness, can act as a source of antioxidants, even at the intracellular level [16].

Stevioside / Anti-Diabetic: Study on STZinduced diabetes in rats showed stevioside lowered blood glucose. It dose-dependently decreased the protein levels of phosphoenol pyruvate carboxykinase, reduced insulin resistance in diabetic animals. Study concludes stevioside regulates blood glucose by enhancing insulin secretion and insulin utilization in insulin-deficient rats [17].

Male Fertility Effects: Study on prepubertal rats showed chronic administration of *Stevia rebaudiana* extract tended to decrease plasma testosterone levels probably a putative affinity of glycosides of the extract for a certain androgen receptor. Results suggest extracts may decrease fertility of male rats [18].

Potential Use in Animal Feeds: The nutritional profile of stevia plant shows high levels of protein and gross energy that may be suitable for ruminant animals. It has a potential for use as energy diluent in monogastric diets due to slow ME and non-caloric nature [19].

Wound Healing: Study evaluated the healing effects of *S. rebaudiana* ethanol extracts on cutaneous wounds in rats using a full-thickness excisional wound model. Results showed significant reduction in wound area as evidenced by changes in arrangement of the healing tissue, re-epithelization and epithelial formation, together with decreased total number of cells, fibrocytes/fibroblasts ratio, neutrophils and lymphocytes and enhanced number of blood vessels and fibroblasts [20].

Energy metabolism: Stevioside has been found to interfere with oxidative phosphorylation in isolated mitochondrial cells by disrupting adenine dinucleotide translocation. Stevioside was found to stop the coupled respiration and it also causes inhibition of mitochondrial ATPase induced by the uncoupling agent, 2, 4dinitrophenol in rat liver mitochondria[21].

Effects on blood pressure: Different research reports based on effects of stevioside have claimed varying effects on kidney function and blood pressure regulation. It lowers mean arterial blood pressure alongwith decreasing renal vascular resistance, produces diuresis and increases fractional excretion of Na⁺ and K⁺ [22].

Chromosomal and mutagenic effects: Chromosomal abnormalities have been reported with stevioside at very high concentrations. In a Chinese hamster fibroblast cell line, stevioside did not induce chromosomal aberrations. No chromosomal effects of stevioside were noted in cultured human lymphocytes [23].

Food and culinary applications: Stevia extracts and steviosides are primarily used as a non-caloric sweetener and/or flavor enhancer in a wide range of food products and beverages, like tea, coffee, soft drinks, cordials, weight watcher diets, diabetic diets and fruit juices. It has also been used as a source of antioxidants and as an alcoholic beverage enhancer [24].

Glucoregulation activity: The traditional use of Stevia extract includes treating diabetes as it is found to increase insulin secretion and sensitivity, according to a clinical study. Isolated mouse pancreatic islet cells have also shown enhancement in insulin production by the action of Rebaudioside A. Stevioside is also known to promote glucose-activated insulin secretion, without affecting fasting insulinemia[24].

Hypotensive activity: Stevioside reduces blood pressure by affecting vascular resistance via inhibition of extracellular Ca 2+ influx and the release of a vasodilator prostaglandin. Stevioside also produces diuresis and natriuresis resulting in reduction of extracellular fluid volume [25].

Antimicrobial activity: *Stevia* has been shown to inhibit the growth and reproduction of bacteria that cause gum disease and tooth decay, making it an excellent addition to toothpaste and mouthwash for dental hygiene. Studies indicate that the major cariogenic organism, *Streptococcus mutans*, experiences growth suppression [26].

Anti-carcinogenic agent: Stevia leaf extracts and the presence of polyphenolic constituents have shown inhibitory effect on tumor initiation and promotion. Stevioside, isosteviol, steviol, leaf aglycones and other metabolites are known to inhibit the tumor formation in several ways: by blocking Epstein-Barr virus early antigen [27].

MARKETED PREPARATIONS: Sweet Leaf Stevia Sweetener

Sweet Leaf Stevia Sweetener is America's first zero-calorie, zero-carbohydrate, certified-paleo, nonglycemic-response sweetener. Use award-winning Sweet Leaf in place of sugars in foods and beverages for a delicious treat [28].

Sweet Leaf Sweet Drops Liquid Stevia : Sweet Leaf Sweet Drops Liquid Stevia is a tasty, convenient, and calorie-free way to flavor water, yogurt, oatmeal, smoothies, coffee, and so much more. Available in a wide variety of delicious, award-winning flavours [29].

Sweet Leaf Sweet Drops Liquid Stevia 50ml

Sweet Leaf Sweet Drops Liquid Stevia 50ml are available in a convenient, user-friendly BPA-free bottle. The sugar-free sweetness, with no artificial sweeteners and zero calories, is the ultimate companion for all your sweetening and flavoring needs [30].

Sugar Leaf

Sweet Leaf Sugar Leaf is a premium blend of Sweet Leaf Stevia and cane sugar. Sugar Leaf offers delicious taste, plus the browning and bulking qualities of sugar, but with 2/3 fewer calories than sugar ³¹.

Sweet Leaf Stevia Tabs

Sweet Leaf Stevia Tabs contain no calories or carbs. When added to your favorite hot beverage, Stevia Tabs begin dissolving instantly, deliciously sweetening your coffee, tea, or other hot beverage.

Uses of Stevia:

Stevia is safe for diabetics, as it does not affect blood sugar levels ³². Stevia does not have the neurological or renal side effects as other artificial sweeteners. Stevia possess anti-fungal and anti-bacterial properties in addition to its other versatile uses ⁶. It can be safely used in herbal medicines, tonics for diabetic patients and also in daily usage products such as mouthwashes and toothpastes ⁵. Mild Stevia leaf tea offers excellent relief for an upset stomach ³³.

CONCLUSION

Stevia rebaudiana is an herb that is used extensively in various areas of the world (without documentation of long-term use and effects) as a noncaloric sugar substitute which has many potential benefits to human beings especially in the field of diabetics, blood pressure, obesity etc. It is used as sugar substitutes in foods due its sweetness in many countries. Stevia provides an opportunity to develop foods rich in antioxidants which is a new functional foods. Various reports in animals and humans indicate that the safety of this herb is not yet completely determined. The current status of using this herb in the USA is as a 'dietary supplement'. Until further information is available, pharmacists should be advised to confirm to the FDA recommendation when counselling patients about this herb. Specifically, mild to moderate use as a supplement should be safe, but increased use for other pharmacological effects may not be warranted. Stevia a bio-sweetener.

REFERENCES

- 1. Smita N. Takarkhede. A Review on Stevia (*Stevia rebaudiana*): A Medicinal Plant. Asian Journal of Pharmaceutical Technology & Innovation, 2016, 04 (20); 558-62.
- 2. Rajesh. P, Rajesh Kannan. V and Thambi Durai. M. Effect of *Stevia rebaudiana* Bertoni ethanolic extract on anticancer activity of Erlisch's Ascites carcinoma induced mice. *Current biotica*, 2010, 3(4); 549-54.
- 3. Goyal S.K, Samsher and Goyal R.K. Stevia (*Stevia rebaudiana*) a bio-sweetener: a review. *International Journal of Food Sciences and Nutrition*, 2010, 61(1); 1-10.
- 4. Megeji N.W, Kumar J. K, Virendra Singh, Kaul V. K. and Ahuja P.S. Introducing *Stevia rebaudiana*, a natural zerocalorie sweetener, *Current Science*, 2005, 88(5); 801-04.

- Reshu Gupta, Vidushi Yadav and Manvi Rastogi. A review on importance of natural sweetener, a zero calorie plant -Stevia - having medicinal and commercial importance. *International journal of food and nutritional sciences*, 2014, 3(3); 90-94.
- 6. Hossain MF, Islam MT, Islam MA and S Akhtar. Cultivation and uses of Stevia (*Stevia rebaudiana* Bertoni): A Review. *Afr. J. Food Agric. Nutr. Dev.*, 2017, 17(4); 12745-57.
- Suresh V, Preethi Fetricia J, Saranya V, Sarithra S and Tamilselvan K. Uses of Stevia (Stevia rebaudiana). Journal of Medicinal Plants Studies, 2018, 6(2); 247-48.
- 8. Alagesapoopathi C. Endemic Medicinal Pants. MJP Publishers, New Delhi, 2013, P.no. 190.
- 9. Saikat Gantait, Arpita Das and Joydeep Banerjee. Geographical Distribution, Botanical Description and Self-Incompatibility Mechanism of Genus Stevia. Sugar Tech, 2018, 20(1); 1-10.
- 10. Ranjan R, Jaiswal J and Jitendra Jena. Stevia as a natural sweetener. *International Journal of research in pharmacy and chemistry*, 2011, 1(4); 1199-202.
- 11. https://agrihunt.com/articles/horti-industry/cultivation-of-stevia/
- 12. "Stevia Sweeteners Now Approved in Israel". Greenprophet.com. 2012.
- 13. Ken Yasukawa, Susumu Kitanaka and Shujiro Seo. Inhibitory Effect of Stevioside on Tumor Promotion by 12-O-Tetradecanoylphorbol-13-acetate in Two-Stage Carcinogenesis in Mouse Skin. *Biological & Pharmaceutical Bulletin*, 2002, 25(11); 1488-90.
- 14. Melis M.S. Chronic administration of aqueous extract of *Stevia rebaudiana* in rats: renal effects. *Journal of Ethnopharmacology*, 1995, 47(3), 129-34.
- 15. Lee CN, Wong KL, Liu JC, Chen YJ, Cheng JT and Chan P. Inhibitory effect of stevioside on calcium influx to produce antihypertension. *Planta Med.*, 2001, 67(9); 796-9.
- 16. Bender C, Graziano S and Zimmermann BF. Study of *Stevia rebaudiana* Bertoni antioxidant activities and cellular properties. *Int J Food Sci Nutr.*, 2015, 66(5); 553-8.
- 17. Chen TH, Chen SC, Chan P, Chu YL, Yang HY and Cheng JT. Mechanism of the hypoglycemic effect of stevioside, a glycoside of Stevia rebaudiana. *Planta Med.* 2005, 71(2); 108-13.
- 18. Melis MS. Effects of chronic administration of *Stevia rebaudiana* on fertility in rats. *J Ethnopharmacol.* 1999, 67(2); 157-61.
- 19. Atteh J, Onagbesan O, Tona K, Buyse J., Decuypere E. and Geuns J. Potential use of *Stevia rebaudiana* in animal feeds. *Arch. Zootec.*, 2011, 60 (229): 133-6.
- Goorani S, Zangeneh M.M., Zangeneh A, Poorshamohammad C, Abiari M, Moradi R, Najafi F, Tahvilian R. Study of Wound Healing Potential of *Stevia rebaudiana* Ethanol Extract in Male Rats. *Research Journal of Pharmacognosy*, 2018, 5(1); 23-30.
- Shaifali Mathur, Neha Bulchandani, Suman Parihar and Gyan Singh Shekhawat. Critical Review on Steviol Glycosides: Pharmacological, Toxicological and Therapeutic Aspects of High Potency Zero Caloric Sweetener. *International Journal of Pharmacology*, 2017, 13 (7); 916-28.
- 22. Elmfeldt D, Nordlander M and Edgar B. Renal effects of felodipine--a review. Kidney Int Suppl. 1992, 36; 54-60.
- 23. Maitree Suttajit, Usanee Vinitketkaumnuen, Umnat Meevatee, and Duang Buddhasukh. Mutagenicity and Human Chromosomal Effect of Stevioside, a Sweetener from *Stevia rebaudiana* Bertoni. *Environmental Health Perspectives Supplements*, 1993, 101(3): 53-56.
- Abudula R, Jeppesen PB, Rolfsen SE, Xiao J and Hermansen K. Rebaudioside a potently stimulates insulin secretion from isolated mouse islets: studies on the dose-, glucose-, and calcium-dependency. *Metabolism*, 2004, 53(10); 1378-81.
- 25. Carlos R. Tirapelli, Sergio R. Ambrosio B , Ana M. de Oliveira and Rita C. Tostes. Hypotensive action of naturally occurring diterpenes: A therapeutic promise for the treatment of hypertension. *Fitoterapia*, 2010, 81; 690 -702.
- Yadav C and Sanoop P.V. An Invitro Study to Compare and Evaluate The Antimicrobial Efficacy of Two Natural Sugar Substitutes, Xylitol and *Stevia Rebaudiana* on *Streptococcus Mutans*. Sri Lanka Dental Journal, 2017, 47 (3); 1-5.
- 27. Takao Konoshima and Midori Takasaki. Cancer-chemopreventive effects of natural sweeteners and related compounds. *Pure and Applied Chemistry*, 2002, 74(7); 1309-16.
- 28. https://www.justtouch.com/product-category/stevia-sweetner-substitute/
- 29. https://sweetleaf.com/sweet-products/
- 30. https://sweetleaf.com/stevia_products/sweetleaf-50ml-liquid-stevia-sweet-drops/
- 31. https://sweetleaf.com/stevia_products/sugarleaf/
- 32. Parinya Samakkarnthai, Manaporn Payanundana, Nattapol Sathavarodom, Chonpiti Siriwan and Apussanee Boonyavarakul. Effect of Stevia on glycemic and insulin responses in obese patients-a randomized, double-blind, placebo-controlled crossover study. *Diabetes*, 2018, 67(1); 90-93.

33. Walia U.S. and Walia S.S. Crop management. Sceintific Publishers, New Delhi, India, 2015. P. 512.

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