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## Stevia the Ideal Sweetener: A Review.

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#### ABSTRACT

Stevia, a natural sweetener plant having medicinal and commercial importance is being used all over the world. *Stevia rebaudiana* Bertoni is the botanical name of stevia. It is a perennial shrub which belongs to the (Asteraceae) Compositae family. The leaves of the stevia shrub contain specific glycosides which produce a sweet taste but have no caloric value. It is estimated to be 300 times sweeter than cane sugar. Both xylitol and saccharine have been linked to tumor development and aspartame continues to prompt controversy in its reported wide range of negative side effects, hence Stevia seems to be the best alternative. 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.

Keywords: Stevia, sweetener, asteraceae

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#### INTRODUCTION

The overconsumption of refined sugars, especially sucrose, promotes inappropriate positive caloric balance, excessive weight gain and obesity [1- 3]. Non-caloric sweeteners may offer some hope to those who desire to avoid the debilitating diseases associated with excessive sugar consumption [4]. While aspartame and saccharine continue to dominate the non-caloric sweetener scene, a remarkable herb called stevia remains relatively obscure. Stevia is a small perennial shrub with green leaves that belongs to the aster (Asteraceae). They grow primarily in the Amambay mountain range of Paraguay but over 200 various species of stevia have been identified around the globe. *Stevia rebaudiana* is the only species at present which possesses an inordinate ability to sweeten. Stevia is a herb with incredible sweetening power. Its ability to sweeten is rated between 70 to 400 times that of white sugar. The mature plant grows up to 65-centimetres (26 inches) to as tall as 180 cm (72 inches). The suitable natural climate is semi-humid subtropical with temperature extremes from 21 to 43°C. What makes stevia so intriguing is that unlike other natural sweetening agents, it is completely calorie-free. Also the extracts of the leaf of stevia have shown beneficial antihypertensive, antihyperglycemic, antioxidant, non-cariogenic, chemoprotective, anti-inflammatory, immunomodulatory, and antiviral effects on human health [5]

#### Phytochemistry

The leaves of the stevia shrub contain specific glycosides which produce a sweet taste but have no caloric value. Stevioside is the primary glycoside involved in this effect. Dulcoside and rebaudioside are also major glycosides contained in the herb. Glycosides are organic compounds which contain a sugar component (glycone) and a non-sugar component (aglycone). Stevia leaves also contain protein, fibers, carbohydrates, phosphorus, iron, calcium, potassium, sodium, magnesium, rutin (flavonoid), iron, zinc, vitamin C and vitamin A.

#### **Forms of Stevia**

Powder, liquid formulas. Alcohol based extracts, fresh leaves, dried leaves, Tablets.

#### History

Stevia is a plant indigenous to mountainous regions of Brazil and Paraguay. For centuries, this herbal sweetener has been used by native cultures to counteract the bitter taste of various plant-based medicines and beverages. In addition, these native peoples have historically used stevia as a digestive aid and a topical dressing for wounds and other skin disorders. During the decade of the 1970s, the Japanese developed a new method which could better refine the glycosides contained in the stevia leaf. The result was a compound called stevioside which is from 200 to 300 times sweeter than white sugar. Stevia enjoyed substantial popularity during the 1980s as a natural sweetener and was found in a variety of consumer products. In 1986, however, the FDA abruptly seized stevia inventories and in 1991 claimed it was not suitable as a food additive.

#### **Other Sweeteners**

While white sugar, turbinado, fructose, honey and corn syrup all qualify as natural sweeteners, none of these are calorie-free. They can encourage weight gain, tooth decay, raise blood sugar quickly, and can also predispose certain individuals to yeast infections. These sugars can also contribute to indigestion, bowel disorders and, hyperactivity or ADD in children. Saccharin has been labeled with a warning that it has caused the development of cancer in laboratory animals. Cyclamates was banned few years ago for suspected carcinogenicity. Aspartame aggravates PMS (premenstrual syndrome), produces dizziness, disorientation, tunnel vision, ear buzzing, loss of equilibrium, numbing of hands and feet, inflammation of the pancreas, high blood pressure, eye hemorrhages and seizures.

Frequent consumption of sucrose-rich "sweets," is associated with increased risks for breast cancer [6-9], pancreatic cancer [10], increases the frequency of mutations in the colonic mucosa [11] and is associated with increased risk of colon cancer [12]

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The adhesion of *C. albicans* and *C. tropicalis* is facilitated in the presence of a high concentration (500 *mM*) of fructose, glucose, maltose, and sucrose [13,14].

#### Diabetes

Stevia leaf extract has been used traditionally in the treatment of diabetes [15,16]. Evidence from preclinical studies suggests that stevioside enhances both insulin secretion and insulin sensitivity. The increase in insulin sensitivity induced by the components of stevia leaves may be related to inhibition of hepatic expression of phosphoenolpyruvate carboxykinase (PEPCK) and gluconeogenesis coupled with stimulation of hepatic glycogen synthesis [17,18]. Another component of stevia leaf extract, rebaudioside A, has been shown to stimulate insulin secretion by isolated mouse pancreatic islets [19]. Stevioside also enhances glucose-stimulated insulin secretion but does not affect fasting insulinemia [20,21]. In a 6-week study, stevioside-fed diabetic rats displayed significantly enhanced first-phase insulin responses with concomitant suppression of glucagon secretion and attenuation of blood glucose concentration excursions [22]. Similar beneficial effects appear to occur in humans. In an acute, paired cross-over study, twelve men and women with type 2 diabetes consumed a standard test meal supplemented with either 1 g of stevioside or 1 g of maize starch (control) [23]. Compared to the effects of maize starch, stevioside consumption was associated with significantly greater attenuation of peak postprandial blood glucose concentrations and increase in the insulinogenic index.

#### Obesity

Stevia is an ideal dietary supplement for anyone who wants to lose or maintain their weight. Because it contains no calories, it can satisfy cravings for sweets without adding extra pounds.

#### Dental

Stevia can be used as an oral tonic to prevent tooth decay and gingivitis. Stevia extracts are sometimes added to toothpaste or mouthwashes to initiate this effect. Stevia is used insome Brazilian dental products with the assumption that the herb can actually help to prevent tooth decay and retard plaque deposits (Bonvie, 53).

#### Cancer

Stevioside, the stevia leaf aglycones, steviol and isosteviol, and their metabolites have been reported to inhibit tumor promotion by blocking Epstein-Barr virus early antigen (EBV-EA) induction [24]. The hydrolysis product of stevioside, isosteviol, potently inhibits DNA replication and human cancer cell growth *in vitro* (with LD50 values of 84 to 167  $\mu$ Mol) [25]. Carcinogenic organism, *Streptococcus mutans*, experiences growth suppression and secretes less acid and when grown on media containing stevioside than when grown on sucrose, glucose or fructose) [26-29]

#### **Blood Pressure**

Studies in rats and dogs have demonstrated that stevioside induces vasorelaxation [29-31]. This effect was tested in a year-long randomized, double-blind, placebo-controlled study of 106 hypertensive subjects who consumed capsules containing either stevioside (750 mg daily) or placebo [32]. the subjects consuming stevioside exhibited significantly greater decreases in systolic and diastolic blood pressures.

#### **Antioxidant Action**

Stevia leaf extract exhibits a high degree of antioxidant activity and has been reported to inhibit hydroperoxide formation in sardine oil with a potency greater than that of either DL- $\alpha$ -tocopherol or green tea extract [33,34]. The antioxidant activity of stevia leaf extract has been attributed to the scavenging of free radical electrons and superoxides. An ethyl acetate extract of a methanolic extract of *Stevia rebaudiana* leaves contains a relatively high concentration of total polyphenols and flavonoids and prevents lipid peroxidation, free radical propagation and DNA strand excision at 0.1 mg/mL [35].

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#### Microorganism

Stevia leaf extracts exhibit significant antiviral and antimicrobial activity.Fermented aqueous extracts of stevia leaves have exhibited strong antimicrobial, antibacterial and antifungal activity towards a wide range of pathogenic bacteria, including enterohemorrhagic *Escherichia coli*, without affecting normal intestinal flora [36,37]. Hot water extracts of stevia leaf inhibit the replication of human rotavirus *in vitro* by blocking viral attachment to cells [36]. The fact that stevia has the ability to inhibit the growth of certain bacteria helps to explain its traditional use in treating wounds, sores and gum disease.

#### Toxicity

The safety of stevia leaf extracts has been demonstrated repeatedly [39]. Stevioside has been without effects in acute and chronic toxicity studies in rats [40,41]. The bioactive compounds in stevia leaf extract do not pose a risk of genetic damage in humans [43]. Stevia leaf extracts and stevioside have produced no adverse effects on laboratory animal fertility, mating performance, pregnancy, number of fetuses, or growth and fertility of offspring [44-47]

#### **Current Usage**

Currently, stevia is commercially grown in Paraguay, Brazil, Uruguay, Central America, Israel, China, Thailand, and the United States. It is considered an important natural sweetener in both Japan and Korea, and has been safely used in these countries for decades. Japanese use stevia in sweet sauces, pickles, beverages, etc., making Japan one of the largest single consumers of stevia in the world.

In September 2009, the French Government (*via* interministerial decree) became the first government in the European Union (EU) to approve Stevia extracts consisting of at least 97% Rebaudioside A (Reb A) as food and beverage sweeteners. Following the recent U.S. FDA recognition of high purity Reb A from key producers as "Generally Recognized as Safe (GRAS)" [48], the global market is now looking forward to approval from the European Food Safety Association (EFSA).

#### CONCLUSION

Because sugar cravings are so hard to control, a product like stevia can be of enormous value in preventing roller coaster blood sugar levels. Stevia can help to satisfy the urge to eat something sweet without changing blood sugar levels in a perfectly natural way and without any of the risks associated with other non-nutritive sweeteners. Little additional study is required to advance to the next step: stevia as an approved sweetener for global use in human food products. The safety of stevia leaf extracts and their phytonutrient components sets the stage for high quality randomized, double-blind, placebo-controlled human clinical trials that can confirm the effectiveness of stevia leaf extracts and their phytonutrient components in both general and specific disease-preventive and therapeutic settings.

#### REFERENCES

- [1] Malik VS, Schulze MB, Hu FB. Am J Clin Nutr 2006; 84: 274-88.
- [2] Linardakis M, Sarri K, Pateraki MS, Sbokos M, Kafatos A. BMC Public Health 2008; 8: 279.
- [3] Harrington S. J Sch Nurs 2008; 24: 3-12.
- [4] Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. JAMA 2006; 295: 1549-55.
- [5] Chatsudthipong V, Muanprasat C. Pharmacol Ther 2009; 121: 41-54.
- [6] Agurs-Collins T, Rosenberg L, Makambi K, Palmer JR, Adams- Campbell L. Am J Clin Nutr 2009; 90: 621-8.
- [7] Bradshaw PT, Sagiv SK, Kabat GC, et al. Cancer Causes Control 2009; 20: 1509- 1515.
- [8] Tavani A, Giordano L, Gallus S, et al. Ann Oncol 2006; 17: 341-5.
- [9] Potischman N, Coates RJ, Swanson CA, et al. Cancer Causes Control 2002; 13: 937-46.
- [10] Larsson SC, Bergkvist L, Wolk A. Am J Clin Nutr 2006; 84: 1171-6.
- [11] Dragsted LO, Daneshvar B, Vogel U, et al. Cancer Res 2002; 62: 4339-45.
- [12] Slattery ML, Benson J, Berry TD, et al. Cancer Epidemiol Biomarkers Prev 1997; 6: 677-85.
- [13] Pizzo G, Giuliana G, Milici ME, Giangreco R. New Microbiol 2000; 23: 63-71.

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- [14] Abu-Elteen KH. Microb Ecol Health Dis 2005; 17: 156-62.
- [15] Megeji NW, Kumar JK, Singh V, Kaul VK, Ahuja, PS. Curr Sci 2005; 88: 801-4.
- [16] Soejarto DD, Kinghorn AD, Farnsworth NR. J Nat Prod 1982; 45: 590-9.
- [17] Chen T, Chen S, Chan P, Chu Y, Yang H, Cheng J. Pharmacol Planta Med 2005; 71: 108-13.
- [18] Yang PS, Lee JJ, Tsao CW, Wu HT, Cheng JT. Neurosci Lett 2009; 454: 72-5.
- [19] Abudula R, Jeppesen PB, Rolfsen SE, Xiao J, Hermansen K. Metabol 2004; 53: 1378-81.
- [20] Xiao J, Hermansen K. Diabetes 2005; 54: A131.
- [21] Chen J, Jeppesen PB, Nordentoft I, Hermansen K. Metabol 2006; 55: 1674-80.
- [22] Jeppesen PB, Gregersen S, Rolfsen SE, et al. Metabol 2003; 52: 372-8.
- [23] Gregersen S, Jeppesen PB, Holst JJ, Hermansen K. Metabol 2004; 53: 73-6.
- [24] Akihisa T, Hamasaki Y, Tokuda H, Ukiya M, Kimura Y, Nishino H. J Nat Prod 2004; 67: 407-10.
- [25] Mizushina Y, Akihisa T, Ukiya M, et al. Life Sci 2005; 77: 2127-40.
- [26] Grenby TH. Int Dent J 1991; 41: 217-24.
- [27] Grenby TH. Pure Appl Chem 1997; 69: 709-14.
- [28] Phillips KC. In: Developments in Sweeteners (T.H. Grenby, ed.) p 1-43. Elsevier Applied Science, London, 1987.
- [29] Lee CN, Wong KL, Liu JC, Chen YJ, Cheng JT, Chan P. Planta Med 2001; 67: 796-9.
- [30] Wong KL, Chan P, Yang HY, et al. Life Sci 2004; 74: 2379-87.
- [31] Liu JC, Kao PK, Chan P, et al. Pharmacol 2003; 67: 14-20.
- [32] Chan P, Tomlinson B, Chen Y, Liu J, Hsieh M, Cheng J. Br J Clin Pharmacol 2000; 50: 215-20.
- [33] Xi Y, Yamaguchi T, Sato M, Takeuchi M. Japan Soc Food Sci Technol 1998; 45: 317-22.
- [34] Xi Y, Yamaguchi T, Sato M, Takeuchi M. Japan Soc Food Sci Technol 1998; 45: 310-6.
- [35] Ghanta S, Banerjee A, Poddar A, Chattopadhyay S. J Agric Food Chem 2007; 55: 10962-7.
- [36] Tomita T, Sato N, Arai T, et al. Microbiol Immunol 1997; 41: 1005-9.
- [37] Ghosh, S, Subudhi E, Nayak S. Intern J Integrat Biol 2008; 2: 27-31.
- [38] Takahashi K, Matsuda M, Ohashi K, et al. Antiviral Res 2001; 49 :15-24.
- [39] Geuns JMC, Buyse J, Vankeirsbilck A, Temme L. J Food Agric Environ 2004; 2: 290-1.
- [40] Hagiwara A, Fukushima S, Kitaori M, Shibata M, Ito N. Gann 1984; 75: 763-8
- [41] Xili L, Chengjiany B, Eryi X, et al. Food Chem Toxicol 1992; 30: 957-65.
- [42] Toyoda K, Matsui H, Shoda T, Uneyama C, Takada K, Takahashi M. Food Chem Toxicol 1997; 35: 597-603.
- [43] Brusick, DJ. Food Chem Toxicol 2008; 46 Suppl 7: S83-91.
- [44] Shiotsu, S. Tech J Food Chem 1996; 4: 108-13.
- [45] Oliveira-Filho RM, Uehara OA, Minetti CA, Valle LB. Gen Pharmacol 1989; 20: 187-91.
- [46] Geuns JMC, Bruggeman V, Buyse JG. J Agric Food Chem 2003; 51: 5162-7.
- [47] Usami M, Sakemi K, Kawashima K, Tsuda M, Ohno Y. Eisei Shikenjo Hokoku 1995; 113: 31-5.
- [48] http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRec ognizedasSafeGRAS/GRASListings/ucm154988.htm.