REVIEW ARTICLE

Health Benefits of the most Popular Alternative Sweetener, *Stevia rebaudiana*

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Abstract

Known for its natural sweetening properties, *Stevia rebaudiana* is among the most popular species belonging to the *Asteraceae* family. The genus Stevia comprises 154 species, including the Paraguayan sweet plant. Various glycosides found in the shrub's leaves impart it a sweet taste but have no caloric value. However, only *S. rebaudiana* has the ultimate level of sweetness among these species. Stevia extracts are high in steviol glycosides, which are sweetening agents that have antifungal, antibacterial, and antioxidant properties. This review's primary goal is to provide a current summary of stevia's antibacterial, antioxidant, and antidiabetic properties as well as its immune-boosting properties. In addition to its health benefits, stevia has been used in industry, specifically as food and food ingredients; as a substitute for sucrose; as animal feed and fertilizer; and as a solubilizing or foaming agent.

Key words: Anticancer, antidiabetic, antimicrobial, antioxidant, immunity booster, *Stevia rebaudiana*

INTRODUCTION

Stevia rebaudiana is a perennial shrub. It belongs to *Asteraceae* (the sunflower family). It is calorie-free due to the presence of steviol glycosides called stevioside and rebaudiosides.[1] Due to its sweet flavor, stevia is also referred to as a "honey leaf" or "candy leaf."[2] *S. rebaudiana* is primarily known as *ka'a he'ê* ("sweet herb") in Brazil and Paraguay.[3] More than 300 species are reported in the Stevia genus, out of which only 18 species have a sweetening nature.[4] *Stevia pheebophylla*, *Stevia bertholdii*, *Stevia salicifolia*, *Stevia micrantha*, *Stevia viscida*, *Stevia eupatoria*, *Stevia lemmonii*, *Stevia dianthoidea*, *Stevia crenata*, *Stevia engimatica*, *Stevia anisostemma*, *Stevia plummermma*, *S. rebaudiana*, and *S. viscida* are the most widespread species in this genus and family that can sweeten a meal. However, only *S. rebaudiana* has the ultimate level of sweetness among these species. The Stevia species is indigenous to South America, especially Brazil and Paraguay.[5] Santiago Bertoni, the then Director of the College of Agriculture at Asuncion, South America, was the first to discover *S. rebaudiana* in 1899.[6] The early uses of stevia leaves by indigenous people have been to make medicines and to sweeten beverages like herbal tea, mate tea, and green tea. In the 16thcentury, stevia was very popular in Spain; further, in the late 19th century, stevia gained enormous recognition across Europe. This recognition is due to its unique properties and the enormous efforts put forth by botanist Moises Santiago Bertoni.[7] Initially, it was known as Eupatorium rebaudianum; later botanist Bertoni renamed it *S. rebaudiana*. Bertoni stated in 1901 that a cup of tea may be sweetened with just a few leaves of stevia.[8] A few years down the line, in 1905, Dr Rebaudi, a chemist, named the plant *S. rebaudiana*.[9] He was the first person to extract and isolate the glycosides in the *Stevia*.

STEVIA DISTRIBUTION AND CULTIVATION

Stevia is grown commercially in several other nations, including Brazil, Canada, USA, China, Korea, Taiwan, Japan, and United Kingdom. Globally, China has the largest cultivated area for *S. rebaudiana*.[10] In India, stevia is grown in Maharashtra, Punjab, Rajasthan, Odisha and Kerala.[11,12] In the 1970s, Japan was the first country to use stevia to assess its impact on human health. Since then, the Japanese

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have been using stevia in their seafood, soft drinks, and candies.[13] The best climatic condition required by stevia for its growth is 80% relative humidity and a temperature of 20–28°Cat day time and 13–20°C during nighttime. The best season for stevia cultivation is March to September. However, during the rainy season (July to September), the stevia crop competes with the weed plants. Common weed species that compete with stevia are *Asteraceae*, *Poaceae*, *Fabaceae*, *Solanaceae*, *Malvaceae*, *Convolvulaceae*, *Caryophyllaceae*, *Brassicaceae*, *Rubiaceae*, *Primulaceae*, and *Plantaginaceae*. This competition, in turn, reduces stevia's branching and yield.[14]

MORPHOLOGICAL FEATURES

S. rebaudiana is somewhat bushy shrub. It typically grows to a height of 60–100 cm. The shrub has a brittle stem, small elliptic leaves and widespread roots. *S. rebaudiana* has green-colored sweet leaves with no aroma.[15] Net-like venation is seen in the leaves.[16] Stevia flowers are white in color with a pale purple color on their necks.[17] It thrives well in warm, semi-humid settings. This shrub requires well-aerated soils with abundant sunlight for its development and glycoside buildup.[18] Stevia requires soil pH around 6–7 and richness in organic matter for its growth.[6] It is propagated by cutting stems and cell cultures.[19] *S. rebaudiana* can withstand a broad range of temperatures. The change in environmental situation affects the stevioside concentration and leaf production.[20] Storing stevia seeds at 0°C or even very low temperatures protects them from germination. Further lowering of the temperature reduces the chances of seed germination by 50% for more than 3 years.[21] Before flowering, stevia leaves have a high concentration of sweetness, so they are immediately harvested. After harvesting, the leaves are cut and processed to extract their sweet content.[9] Table 1 displays the *S. rebaudiana* botanical classification.

CHEMICAL CONSTITUENTS PRESENT IN *S. REBAUDIANA*

The main component that imparts stevia sweetness is stevioside ($C_{38}H_{60}O_{18}$), and rebaudiosides A ($C_{44}H_{70}O_{23}$) are also referred to as steviol diterpene glycosides.[22] The major constituents present in *S. rebaudiana* have been mentioned in Table 2. In addition to the presence of sweet glycosides, stevia contains a variety of health-promoting bioactive substances, such as non-glycosidic labdane diterpenes, phytosterols, flavonoids, chlorogenic acids, phenolic compounds, crude fibers, triterpenes, and hydrocarbons.[23]

Table 1: Botanical classification of *Stevia rebaudiana*

Domain	Eukaryota
Kingdom	Plantae
Class	Angiosperms (flowering plants)
Order	Asterales
Family	*Asteraceae* (sunflower family)
Genus	Stevia
Species	*Stevia rebaudiana*

There are more than 30 different steviol glycosides present in stevia.[24] This component was discovered by French researchers Briedel and Lavieille in 1931. Stevioside and rebaudioside A imparts high-intensity sweetness roughly 300 times sweeter than sucrose.[25] Initially, stevioside was isolated in 1931, and later in 1952 its chemical structure was documented.[24] Sweet glycosides are mostly found in the leaves of *S. rebaudiana*. It was reported that extract obtained from stevia leaf shows improvement in the health of patients suffering from amnesia, rheumatism, lumbago, anemia and neuralgia.[26] It is reported that the presence of a hydroxyl group at C-13 and a carboxyl group at C-19 is responsible for imparting sweetness in Stevia.[6]

Further, *S. rebaudiana* contains carbohydrates, fats, protein, and dietary fibers.[27,28] reported that carbohydrates like fructooligosaccharides and polysaccharides are also present in stevia's roots and leaves. Both of these carbohydrates, if consumed, help in controlling sugar levels in the blood and in lipid metabolism. Researchers[29] and[30] reported that nine essential amino acids (glutamate, aspartate, methionine, tyrosine, proline, alanine, isoleucine, lysine, and serine) and eight non-essential amino acids (aspartate, serine, glutamic acid, proline, glycine, alanine, cysteine, and tyrosine) are also present in *S. rebaudiana* leaves. A further six fatty acids (linoleic acid, linolenic, oleic, stearic, palmitoleic, and palmitic acid) are also present in stevia leaves.

In addition to this, stevia contains phytochemicals, vitamins and minerals.[31-33] Characteristic phytochemicals present in *S. rebaudiana* are *β*-carotene, thiamine, steviol, stevioside, riboflavin, rebaudiosides, niacin, dulcoside, and austroinullin.[6] Stevia stems contain volatile oils, flavonoids (traces), and structural fibers.[34] Whereas alkaloids, phenolic chemicals, and saponins (bioactive glycosides) are found in the root. Flowers contain anthocyanin colors, flavonoids, moderate glycosides, and essential oils.[35]

The stevia plant is a rich source of vitamins and minerals. It contains water-soluble vitamins such as Vitamin B_{12}, Vitamin C, and folic acid. The plant also contains several essential macro- and micronutrients, including selenium, potassium (K), calcium (Ca), magnesium (Mg), sodium (Na), iron (Fe), zinc (Zn), and manganese (Mn), which have been associated with antiviral and immune-enhancing effects. Vitamins A, C, and B-complex, including thiamine and riboflavin, are among the many vitamins found in stevia. Folic acid is present in significant amounts in leaves, followed by vitamin C.[36]

According to toxicology tests, stevia's secondary metabolites do not have any teratogenic, mutagenic, or carcinogenic

effects, and using it as a sweetener has not been linked to any adverse reactions.[37,38]

S. REBAUDIANA IN THE FOOD INDUSTRY

In the United States of America, using stevia as a food additive in food products was banned, which had created a major restriction on the stevia industry's commercialization; later, in 1995, the Food and Drug Administration approved it as a nutritional supplement.[39] Internationally, steviol glycosides were declared as a safe product in the year 2004.[40] Remarkably, stevia leaves outperform other high-potency sweeteners in terms of their functional and sensory qualities. As a result, stevia is anticipated to play a significant role in the future supply of high-potency sweeteners for the expanding natural food market.[41] In recent times, food industries are replacing sucrose with stevia powder and gaining consumers' acceptance. After knowing the health benefits of stevia, customers are using stevia in *seafoods, cereals, yoghurt, beverages, ready-to-eat foods, etc.*[42] Due to stevia's sweetness-imparting properties, it is used as a sugar substitute in bakeries, jams, biscuits and chocolates.[43] Now beverages companies (Coca-Cola and PepsiCo) started producing drinks with stevia instead of sugar in 2013. Stevia-based drinks reported 30% fewer calories as compared to the ones manufactured with sugars. These drinks are currently offered for sale in several nations across the world.[44] It is reported that stevia sweetener is not fermentable, is acid stable and is heat stable up to 200°C.[45,46] Hence, stevia leaves are used in the preparation of herbal teas, coffee, salads and sauces. Recently, tabletop sweeteners have also begun using stevia.[47] *S. rebaudiana* is thoroughly assessed in this introduction by looking at its botanical traits, chemical makeup, healthy covering, and economic potential in light of the global movement toward better and more sustainable production systems.[48]

STEVIA'S HEALTH BENEFITS

It is a healthy sugar substitute or sugar alternative with many health advantages. Current research worldwide focuses on stevia's anti-inflammatory, antioxidant, anticancer, antidiabetic, and antimicrobial qualities.[49] Many pharmaceutical businesses are using *S. rebaudiana* leaves to make ayurvedic and pharmaceutical products.[50] Stevia has long been used as a natural sweetener and herbal remedy for diabetes and gastrointestinal issues.[51] In addition, studies have demonstrated that stevia helps in resolving digestive issues, skin conditions, and the typical adverse effects of metabolic syndrome.[4] Figure 1 summarizes the multifunctional health benefits of *S. rebaudiana*, emphasizing its antimicrobial, antioxidant, antidiabetic, immune-boosting, and anticancer properties.

Table 2: Major chemical constituents present in various parts of *Stevia rebaudiana*

Plant Part	Steviol glycosides	Flavonoids and polyphenols	Fiber/ cellulose	Essential oils	Other notes
Leaves	High	High	Moderate	Low	Major source of sweetness
Stems	Low	moderate	High	None	Strong fiber, structural use
Roots	None	moderate	Moderate	None	Therapeutic attention
Flowers	Trace	High	Moderate	moderate	High antioxidant movement

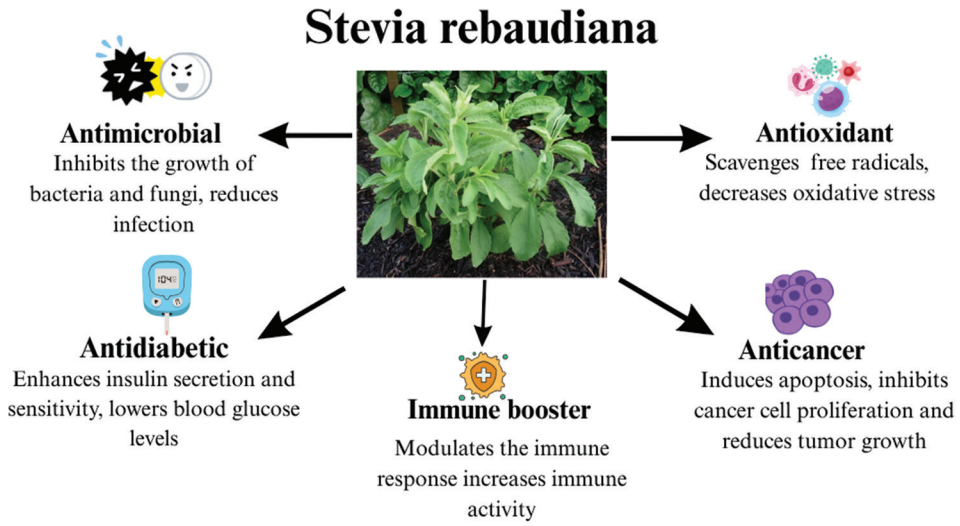

Figure 1: Health-promoting properties of *Stevia rebaudiana*

S. REBAUDIANA AS AN IMMUNITY BOOSTER

In *S. rebaudiana,* a wide range of bioactive constituents are discovered, which help in immunity boosting and provide other health benefits like antioxidant, anti-inflammatory, antibacterial, and anticancer effects.[24] *S. rebaudiana* leaves are rich in antioxidants, usually flavonoids and phenolic compounds such as quercetin, kaempferol, and chlorogenic acid.[52] These antioxidants enhanced the immune system's defenses against infections and chronic inflammation by diminishing oxidative damage to cells and tissues. The plant has strong antioxidant, anti-inflammatory, and antibacterial qualities due to the presence of phytochemicals such as stevioside, rebaudioside A, flavonoids, phenolic acids, and essential oils. These qualities are all crucial for boosting immune responses. *S. rebaudiana* can be used as a natural remedy to boost immunity because it triggers several biological reactions, including antimicrobial effects that fight pathogens, immunomodulatory actions that support balanced immune responses, anti-inflammatory effects that reduce chronic inflammation, and antioxidant activities that neutralize dangerous free radicals. These reactions work together to fortify the immune system by increasing immune cell activity, lowering oxidative stress, and improving resistance to infections.

STEVIA AS AN ANTIDIABETIC AGENT

Diabetes mellitus affects a large population globally.[53] *S. rebaudiana* attracted a lot of interest as a natural antidiabetic drug because of its potent sweetening qualities, especially due to stevioside and rebaudiana A. Artificial synthetic sweeteners are facing stiff competition from *S. rebaudiana*. These artificial sweeteners, such as saccharin, acesulfame potassium, sucralose, and aspartame, are safe and non-nutritive, but they contain chemical additives. Consequently, diabetic patients are not finding these artificial sweeteners acceptable.[51] *S. rebaudiana*, on the other hand, has garnered significant attention as a natural antidiabetic drug due to its potent sweetening properties and the added benefit of not causing blood glucose spikes. The leaf extract stabilizes blood sugar by enhancing β-cell activity in the pancreas, which further increases the insulin amount.[54]

STEVIA AS AN ANTIMICROBIAL AGENT

S. rebaudiana contains bioactive substances that may reduce the growth of several harmful bacteria. Its antibacterial activity is mostly related to the presence of secondary metabolites such as flavonoids, tannins, phenolic acids, terpenoids, and the steviol glycosides (particularly stevioside and rebaudioside A), which are primarily responsible for its sweetening effect.[55] These substances have a variety of antimicrobial activity mechanisms, such as oxidative damage, breakdown of microbial cell membranes, interference with cellular metabolism, and reduction of biofilm formation.[56] Studies using aqueous, ethanolic, and methanolic extracts of *S. rebaudiana* have demonstrated significant antibacterial action against a variety of Gram-positive and Gram-negative microorganisms, such as *Salmonella typhi*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus*.[57] In addition, antifungal qualities against *Aspergillus niger* and *Candida albicans* have also been observed in *S. rebaudiana*. In addition, extracts containing *S. rebaudiana* demonstrated encouraging outcomes when used with conventional antibiotics, suggesting that they might help boost antibiotic activity and combat germs that are resistant to drugs. Due to its natural origin, biocompatibility, and broad-spectrum antimicrobial conditioning, *S. rebaudiana* is a viable candidate for further study as a natural antibacterial agent.[58] It could be distributed as a sustainable alternative or supplement to synthetic antimicrobials in global efforts to combat antibiotic resistance and reduce reliance on chemical-based preservation agents.[59] *S. rebaudiana* is a helpful herb for non-calorific flavoring and can be used to create antiseptic therapy that is safe, efficient, and environmentally friendly. Because it is sweet and has antibacterial properties, it is the most versatile ingredient in the food industry. It improves flavor, lowers the risk of microbial contamination, and extends shelf life.[60] Nowadays, stevia-based mouthwashes, toothpastes, and chewing gum are being designed to battle oral microorganisms that cause gum disease and tooth decay, which include *Streptococcus mutans* and *Lactobacillus acidophilus*, among others.[61] In contrast to artificial sweeteners or sugar, which can lead to dental cavities, stevia not only avoids feeding dangerous bacteria but may also actively minimize their growth, facilitating better oral hygiene.

STEVIA AS AN ANTICANCER AGENT

Globally, the second leading cause of death after diabetes is cancer.[24] One of the most significant effects of stevia compounds is the induction of apoptosis, a natural defence against unchecked cell division and cancer.[62] Stevia derivative chemicals effectively induce cell death in malignant tissues.[63] *S. rebaudiana* affects cellular machinery and possesses strong antioxidant capabilities.[64] Stevia contains flavonoids and phenolic acids, such as quercetin, kaempferol, and chlorogenic acids, which significantly neutralize reactive oxygen species and prevent oxidative damage to cellular macromolecules, including proteins, lipids, and DNA. Stevia also has anti-inflammatory properties, which are important in general.[65] One of the most fascinating things about stevia is that stevioside and its derivatives may make cancer cells more sensitive to medications like doxorubicin, cisplatin, and 5-fluorouracil.[66] Furthermore, stevia-mediated green nanoparticle synthesis has been addressed for the delivery of anticancer medications in new fields.[67]

CONCLUSION

Stevia offers a natural, safe, and potentially therapeutic substitute for artificial sweeteners, which may have adverse metabolic effects. *S. rebaudiana* possesses strong antimicrobial properties. The bioactive components of stevia prevent many fungi, viruses, and bacteria from growing. Moreover, stevia is a natural sweetener that shows promise for the food and cosmetics industries. It may also be used as an extract agent to improve industry, health, and infection prevention. However, it is more than just a sugar alternative. Antioxidant, antidiabetic, antibacterial, and anti-inflammatory qualities imply several advantages that go far beyond sweetening. *S. rebaudiana* may be essential to the development of functional foods and natural health treatments in the future as studies of its therapeutic potential continue. This review is based wholly on previously published secondary data and does not contain any original experimentation. Other areas of future research involve the biotechnological enhancement of steviol glycosides through metabolic engineering, clinical validation of therapeutic properties of stevia in human populations, and the development of standardized protocols for extraction and formulation to enhance applicability within the nutraceutical and pharmaceutical industries. The entire potential of this wonderful plant will require careful development, clinical testing, and continued scientific investigation.

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