International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 2 Mar-Apr 2023, pp: 1706-1711 www.ijprajournal.com ISSN: 2249-7781

An Excellent Alternative Source of Sugar.

Dipasha Sugnani and Tushar Undegaonkar

Submitted: 10-04-2023 Accepted: 22-04-2023

ABSTRACT
This is a mini-review with scientific research findings in different studies on stevia as a natural sweetener and an excellent replacement for sugar. The intent of the article introduces the nutritional value and summarizes its pharmacokinetics and metabolism in the human body.Stevia is usually consumed in form of leaves and crude extracts. The review also examines the medicinal as well as food utility of stevia. Due to its diverse health benefitsstevia is usually recommended foracceptable intake, dietary exposure, impact on blood glucose and insulin concentrations, energy intake and weight management, blood pressure, dental caries, naturality and processing, taste and sensory properties, regulatory status, consumer insights, and market trends.Stevia is also important for commercial purposes in various countries, especially India,because of the unreasonable population suffering from diabetes.

I. INTRODUCTION, HISTORY, AND BOTANICAL INTERPRETATION

Stevia rebaudiana is a plant species in the genus Stevia of the family Asteraceae. It is commonly known as a candy, sweet, or sugar leaf.The plant is native to Paraguay and has a long history of use by the Guaraní people. It has been used as a sweetener by indigenous peoples ofnative South America for chiliads.[3]

It is known to the Guarani Indians as "Kaa he-he" (meaning sweet herb), Stevia was also utilized as a conventional medicine. It was used as a tonic for heart problems, high blood pressure, and digestive issues, to regulate blood sugar and nourish the liver.[3]

Stevia leaves have been used for more than 1,500 years. [1,2]Stevia, as a plant extract, was first commercially adopted as a sweetener by Japan in the 1970s on large scale, where it is still a popular ingredient today.Reb-A was the first commercial steviol glycoside launched in the marketplace. [4,5] The flowers are white with light purple accents and no fragrance. Plants produce fruit that is ribbed and spindle-shaped. Stevia prefers sandy-like soil. The plant prefers warm, moist, and sunny conditions. Germination from seed is difficult, and most plants are grown from cuttings. [1,2]

With continued increasing rates of obesity, diabetes, and other related comorbidities, in conjunction with global public policies calling for reductions in sugar intake as a means to help curb these issues, low- and no-calorie sweeteners (LNCSs, also known as high-potency sweeteners) especially stevia are gaining interest among consumers and food manufacturers.[5,6] This appeal is related to stevia being plant-based, zero calories and with a sweet taste that is 50–350 times sweeter than sugar, making it an excellent choice for use in sugarand calorie-reduced food and beverage products.[6]

CHEMICAL COMPOSITION AND NUTRITIONAL VALUE

Major elements that are required include magnesium, potassium, chlorine, sodium, phosphorous, and Sulphur, calcium is classified as a macronutrient. However, micronutrients include iron, cobalt, zinc, copper, selenium, iodine, molybdenum, chromium, manganese, etc. Stevia leaves have a good mineral profile with nutritionally essential elements in a reasonable amount, i.e., calcium, potassium, magnesium, iron, copper, manganese, zinc, and sodium in fresh and dried leaves.

Stevia contains **eight glycosides**. These are the sweet components isolated and purified from the leaves of stevia. These glycosides Sources:

- Stevioside
- Rebaudiosides A, C, D, E, and F
- Steviolbioside
- Glucoside A

The leaves of stevia contain protein, fat, fiber, carbohydrate, antioxidants, phenolic compounds, and glycosides which helps pragmatically in biochemical metabolism.[6]

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 2 Mar-Apr 2023, pp: 1706-1711 www.ijprajournal.com ISSN: 2249-7781

METABOLISM AND PHARMACOKINETICS OF STEVIA

Stevia is known to the scientific world for its sweetness and steviol glycosides (SGs). SGs are the secondary metabolites responsible for the sweetness of Stevia. They are synthesized by the SG biosynthesis pathway operating in the leaves. Most of the genes encoding the enzymes of this pathway have been cloned and characterized by Stevia. Out of various SGs, stevioside and rebaudioside A are the major metabolites. SGs including stevioside have also been synthesized by enzymes and microbial agents. These are non-mutagenic, non-toxic, and antimicrobial, and do not show any remarkable side effects upon consumption.[7]

The entire steviol glycosides incompletely get absorbed when administered orally but it hydrolyses into steviol in the colon and most of it is then absorbed and the rest is excreted in faeces.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 2 Mar-Apr 2023, pp: 1706-1711 www.ijprajournal.com ISSN: 2249-7781

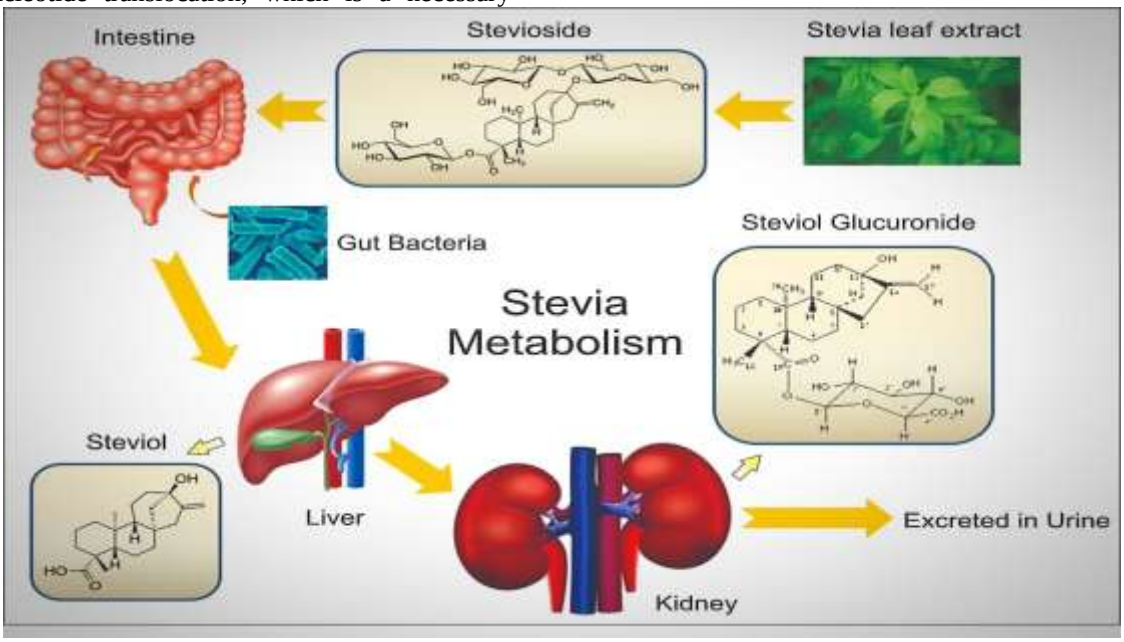
Stevia constituents seem to pragmaticallyinflect the insulin response: its effects seemingly depend on the glucose load and are terminated by the insulin receptor antagonist S961. In muscle and adipose tissue, binding of insulin to the insulin receptor (IR), triggers autophosphorylation and activation of its kinase activity. This induces the recruitment of the insulin receptor substrate 1 (IRS1), which conscripts phosphoinositide 3-kinase (PIRK), that in turn yields phosphatidylinositol (3, 4, 5)-triphosphate (PIP3) from PIP2. PIP3 recruits the phosphoinositide-dependent kinase 1, which activates the Akt pathway. In succession, Akt phosphorylates the Akt substrate of 160 kDa AS160, targeting multiple Rab GTPases on GLUT4-containing vesicles. This induces vesicle fusion resulting in GLUT4 integration into the cell membrane to expedite glucose uptake. Stevia extracts have also been found to upregulation GLUT4 transcription.[8]

On the cellular level, the energy metabolism of stevioside has been found to interfere with oxidative phosphorylation in isolated mitochondrial cellsby disrupting adenine dinucleotide translocation, which is a necessary process in the shuttling of high-energy phosphate groups generated in mitochondria to their sites of consumption.Stevioside (5 mM) was found to stop the coupled respiration and it also causes inhibition of mitochondrial ATPase induced by the uncoupling agent, 2, 4-dinitrophenol inliver mitochondria. The mitochondrial actions of stevioside have not been observed on intact cells but only reported on isolated organelles.[9]

Carbohydrate metabolism: Stevioside is found to reduce the transport rate of glucose into the liver to its half rate. Stevioside also inhibits the release of glucose in hepatic cells. In liver cells undergoing glycogenolysis, the intracellular andextracellular concentration gradient of glucose was found to get enhanced in presence of stevioside.[10]

Artificial sweeteners like Stevia work by activating the same signal pathways from the tongue to the brain. They switch on sweet taste receptors to fool the brain into thinking that sugar has landed on the tongue.

A specific area of the brain called the caudal nucleus of the solitary tract, or cNST gets induced. [9,10]



HEALTH BENEFITS OF STEVIA

This natural sweetener can suppress glucose levels, crucially increase glucose tolerance and stabilize blood sugar levels. Artificial sweeteners such as saccharin can raise blood sugar and change the bacterial composition in the gut which can then cause glucose intolerance. [10,11]

Stevia is often touted as a safe and healthy sugar substitute that can sweeten up foods without the negative health effects linked to refined sugar. It's also associated with several impressive health benefits, such as:

- Reduced calorie intake
- Blood sugar levels

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 2 Mar-Apr 2023, pp: 1706-1711 www.ijprajournal.com ISSN: 2249-7781

- Maintain oral health
- Possible anticancer potential
- May regulate blood pressure
- Prevent osteoporosis[11]

Along with all the health benefits mentioned above stevia is also known to possess anti-diarrheal, anti-hyperglycaemic, antihypertensive, diuretic, anti-inflammatory, anti-diarrheal, and immune-modulatory actions[8,11] Certain glycosides in stevia extract have been found to dilate blood vessels. They can also **increase sodium excretion and urine output**.[12]

THERAPEUTIC PROPERTIES OF STEVIA:

Stevia has immense pharmacological and therapeutic applications as suggested by many preclinical and clinical studies; these are innocuous and possess antioxidant, antimicrobial, antifungal, and anti-carcinogenic activity. [13,14]

The leaves naturally retain diterpene glycosides stevioside, rebaudiosides A-F, steviolbioside, and dulcoside, which are responsible for its sweet taste and have a commercial value all over the world as a sugar substitute in foods, beverages, or medicines.[14,15] The therapeutic effects of stevia include[16]

Anti-hyperglycemic-

Stevia has the potential to increase the activity of pancreatic cells, and insulin sensitivity, and promote insulin production and utilization. It is helpful in the treatment of Type-2 diabetics.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 2 Mar-Apr 2023, pp: 1706-1711 www.ijprajournal.com ISSN: 2249-7781

Anti-hypertensive-

Stevioside reduces blood pressure by preventing calcium ions from entering the endothelial cells of the blood vessels and thus lowering vasoconstriction in hypertensive patients.

Antioxidant-

Stevia composes great aggregatesof natural antioxidants including opigenin, kaempferol, and quereitrin. This helpaverts DNA strand damage, angiotensin-induced cell propagation, and endothelin secretion.[17]

Anti-carcinogenic-

Steviol glycoside consists of four constituents: stevioside, rebaudiosides A, rebaudioside C, and ducloside A, which vehemently inhibits the inflammation caused by 12-0-tetradecanoylphorbol-13-acetate (TPA), indicating its anti-carcinogenic activity.

Antimicrobial-

Stevia can evade the growth and reproduction of harmful bacteria and prevent other infections.

Anti-inflammatory and immunomodulatory -

Stevia is also beneficial in decreasing inflammation and immune modulation. It reduces the synthesis of inflammatory agents in lipopolysaccharide (LPS)-induced THP-1 cells by intervening in the I-Kappa-B kinases (IKK-beta) and Kappa B signalingpathways.[17]

RISKS AND SIDE EFFECTS:

The FDA suggests stevia glycosides like Reb-A are "Generally recognized as safe." But the approval of whole-leaf stevia or crude extract of stevia for usage in various marketed products of stevia is because of a lack of authentic safety information.[18]

Some stevia products also contain sugar alcohol hence people with sensitivity to sugar alcohol such as erythritol may experience bloating, abdominal cramps, nausea, and diarrhoea.[19]

Stevia is usually considered safe for diabetic patients but the marketed products that consist of dextrose or maltodextrin should be treatedwith vigilance. There's solicitude regarding the raw stevia herb that it may harm certain vital organs and systems of the human body.[19,20]

A few side effects that may be caused by stevia are as follows:

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 2 Mar-Apr 2023, pp: 1706-1711 www.ijprajournal.com ISSN: 2249-7781

- Kidney damage. Stevia is considered a diuretic, meaning that it increases the speed at which the body expels water and electrolytes from the body in urine.
- Gastrointestinal symptoms.
- May Lead to sore muscles.
- Allergic reaction.
- Hypoglycaemia or low blood sugar.
- Low blood pressure.
- Stevia May Cause Numbness.
- Nausea
- Bloating
- Dizziness
- Numbness
- Muscle pain
- Abdominal fullness
- Endocrine disruption.[21]

II. CONCLUSION:

This mini-review with scientific facts was desired to acknowledge various communities about the cumulative particulars of Stevia.

The review article mainly sums up the aggregates about Stevia such as its botanical description, nutritional values, therapeutic applications, and commercial importance.

REFERENCES:

[1]. https://en.wikipedia.org/wiki/Stevia
[2]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4890837/
[3]. https://www.britannica.com/plant/stevia-plant
[4]. https://academic.oup.com/jn/article/148/7/1186S/5049670
[5]. https://actascientific.com/ASMI/pdf/ASMI-04-0765.pdf
[6]. https://chemistnotes.com/physical/adsorption-isotherm-and-its-types/
[7]. https://www.medicalnewstoday.com/articles/319837
[8]. https://pubmed.ncbi.nlm.nih.gov/22823347/
[9]. https://www.organicfacts.net/health-benefits/other/stevia.html
[10]. https://www.endocrinologynetwork.com/view/using-lipid-biomarkers-to-predict-diabetic-neuropathy-with-gregory-weiss-md
[11]. https://www.indigo-herbs.co.uk/natural-health-guide/benefits/stevia
[12]. https://www.stylecraze.com/articles/side-effects-of-stevia/
[13]. https://www.sciencedirect.com/science/article/pii/B9780128159729000330#:~:text=In%20addition%20to%20providing%20sweetness,%2C%20anthocyanins%2C%20and%20phenolic%20acids.
[14]. https://www.researchgate.net/figure/Antihypertensive-action-of-stevioside-Inhibition-of-Ca-2-influx-in-vascular-smooth_fig2_329895045#:~:text=Inhibition%20of%20Ca%202%2B%20influx%20in%20vascular%20smooth%20muscle%20resulting,reduction%20in%20systemic%20vascular%20resistance.&text=Stevia%20rebaudiana%20(Bertoni)%2C%20a,belonging%20to%20the%20Asteraceae%20family.
[15]. https://www.news-medical.net/health/Is-Stevia-Safe.aspx#:~:text=Antimicrobial%E2%80%94stevia%20has%20the%20ability,decreasing%20inflammation%20and%20immuno%2Dmodulation.
[16]. https://www.semanticscholar.org/paper/Nutritional-and-therapeutic-values-of-Stevia-A-Gupta-Purwar/6af92436e87e6a2f4102806baceacac84dbf7f9e
[17]. https://www.sciencedirect.com/science/article/pii/B9780128159729000330#:~:text=In%20addition%20to%20providing%20sweetness,%2C%20anthocyanins%2C%20and%20phenolic%20acids.
[18]. https://www.lybrate.com/topic/stevia-benefits-and-side-effects
[19]. https://www.news-medical.net/health/Is-Stevia-Safe.aspx#:~:text=Antimicrobial%E2%80%94stevia%20has%20the%20ability,decreasing%20inflammation%20and%20immuno%2Dmodulation.
[20]. https://www.researchgate.net/figure/Antihypertensive-action-of-stevioside-Inhibition-of-Ca-2-influx-in-vascular-smooth_fig2_329895045#:~:text=Inhibition%20of%20Ca%202%2B%20influx%20in%20vascular%20smooth%20muscle%20resulting,reduction%20in%20systemic%20vascular%20resistance.&text=Stevia%20rebaudiana%20(Bertoni)%2C%20a,belonging%20to%20the%20Asteraceae%20family.
[21]. https://www.healthline.com/health/food-nutrition/stevia-side-effects#benefits