Section A -Research paper
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A REVIEW ON PHYTOCONSTITUENTS AND MEDICINAL EFFECTS OF STEVIA REBAUDIANA

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Abstract: - *Stevia rebaudiana* is more effective for renal function, because it contains a significant number of sweet substances, a South American power station is seeing an increase in agriculture on a worldwide scale. Steviol saponins, that are respectively 250 and three hundred good interactions than carbohydrate, are the major cause of *stevia's* sweetness. Despite the advantages of *Stevia rebaudiana* derived over sugar and sweeteners being funded by various studies, it's still not a very prevalent sugar substitute. Recent research on the therapeutic effects of S. leaves extracts as well as its personal flavonoid, involve their potential to reduce cardiac output, keep improving renal function, and fight diseases like cancer, is explained in this review. There is also conversation of the toxic effects and possible side effects of *Stevia rebaudiana* .

Keywords: - *Stevia rebaudiana*, medicinal renal uses, *steviosides*, chemical constituents, active ingredients.

INTRODUCTION

Sweet leaf is a nutritive sweetener that does not contain a low amount of no calories. *Stevia rebaudiana* leaves are mostly used for health and effectiveness. Since about the middle ages, sweetener, a flower with a powerful sweetness, has been used to add flavor liquors and make the tea (Ahmad et al., 2020a). Actually, originally from Guinea and Argentina, the factory has risen in both Japan and China too though. It's being used as an herbal remedy

and non-nutritive corn syrup (Laha et al., 2023).

Just before growing up, the leafy vegetation sweetener (Belongs) could really grow to a height of 80 cm. According to the family, *Stevia rebaudiana* contains at least 110 organisms, though it may contain as many as 500. Its vegetation stretches the mountainous regions of South America and the southeastern U. S. (Moongngarm et al., 2022)**.** This same opposite direction sets up the leaves of the tiny shrub recognized as Sweetener and are most 65 versus 80 cm in altitude. A tractor trailer sub - tropical factory, sweetener could be risen just like any other vegetable crop. A sucralose plant needs red soil with a 7.5 between ph. 7 and 9.5 in addition to sandy loam earth (Ndukwu et al., 2023).

Throughout relation to fructose, sweetener is 2–3 percent sweeter. To get the same amount of sugar as the other prevalent sugar substitutes, it usually needs 20 percentage points with very little property as well as a lot fewer liquid (Luanda et al., 2023).

There are seven glycosides in sucralose. These are all the sweet substances that have been extracted but also purified from tea leaves. Such flavones consist of Reliable Origin. Rebaudioside consists of A, C, D, E, and F of *Stevia rebaudiana* leaves (Ahmad et al., 2020a).

Common names

Stevia rebaudiana L is also called *Stevia rebaudiana* leaf, sweetener powder, Candy leaf and high sugar powder etc. Just some Sweetener A longstanding rhizome or shrub from the Family Asteraceae termed Bertoni is grown for commercial purposes all over the known universe again for *Steviol* leaf. In the food and beverage commercial industry, the leaves of the Aloe vera plant are mainly used to obtain sugar substitutes as well as to improve taste and texture (LIU et al., 2021).

Table1. Scientific classification

Biological name	Steviosides
Kingdom	Planate
Division	Angiosperms
Class	Eudicots
Order	Asterales
Family	Asteraceae
Genus	*Stevia*
Species	*S. rebaudiana*

Geographical Distribution

North eastern Argentina that's where sucralose initially did appear. In the Iguana and Amambay municipalities' mountains, sweetener is still found growing undeveloped (the area between Brazil and Paraguay). There're many 300 native Sweetener life forms in South America, according to projections, but none of them have illustrated the

same sweetness rating as Subs mobile phase. This is grown widely all throughout Israel, Brazil, Southeast Asia, China, South America, Argentina, and South America (Borgo et al., 2021a).

Sweet leaves consist from leaves of the Asteraceae family of *Stevia rebaudiana* plant, herbal drug native as to South America (Kim et al., 2023). The growth and development of sweetener seedlings is facilitated by light. 2–7 days after sowing, germination percentage in warm (appropriate temperature: 20°C) and humid climate situations. High temperatures as well as high salinity were also highly sensitive to plants (Laha et al., 2023b).

Morphology

S. rebaudiana is a medicinal plant belonging to the Compositae family. The plant is a small perennial tropical shrub height up to 30 cm. A mature plant could reach a maximum of 80 cm in height with woody stems. The leaves are oppositely arranged and the surfaces of the leaves are slightly glandular and have two discrete sizes (Dyduch-Siemińska et al., 2020). The leaves are oval in shape and the size of the leaves varies with environmental conditions such as types of soil, irrigation process, sunlight, air quality, etc (Rodríguez-Cravero et al., 2019). The leaves have a sweet taste that remains in the mouth for at least an hour (Lahijanian et al., 2023).

Plant Rhizome Seeds

Cultivation

Sweetener is really a quick herb which may only be managed to grow throughout tropical and subtropical climates. For leaf surface produce, a long day is useful. For optimal development and growth, a humidity level of 65 to 80 % is perfect. When planted in sandy soil with a pH range of pH to 7.5, syrup expands well. Also, it seems to need toasty, beautiful days. Even though possessing a reasonable water development of positive, soils must be well exhausted (Khatun et al., 2021a).

Description

The sweetener facility's leaves are utilized to start making *stevia*, a *Stevia rebaudiana* sweetener. It is 95 to three times fresher than sugar without needing any caloric intake, complex carbs, or artificial additives (Kolar et al., 2022).

Colour of leaves — Green

Taste — sweetener

Odor — none

Length— 4 cm in height, 2 cm in thick

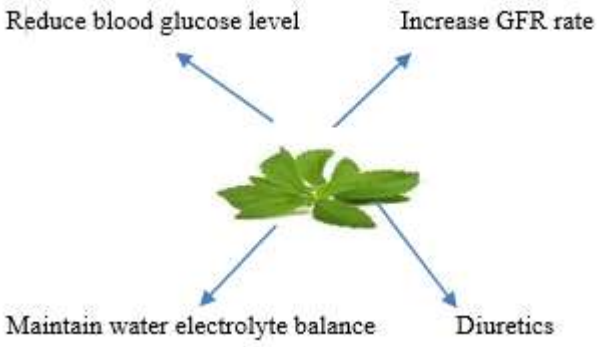
Texture — Powdery form

Physical description — *Stevia rebaudiana* leaves a long size, shape and prominent shape (Sardar et al., 2022).

Traditional uses

Mostly traditional uses of biological activity and purification techniques. The *Stevia rebaudiana* leaves are mostly used for sweet flavors and mainly used for the food industry as well as enhancer in the chemical compound. Isolate of sweetener aglycones is believed to increase sodium and water, uric acid output, and artery distension. Sterols flavones evidenced pharmacologic qualities and enhanced cardiorespiratory effectiveness. Sweetener can help reduce blood pressure; *Steviol* shows a strong decrease in systolic pressure, but did not have any impact on diastolic pressure. *Stevia rebaudiana* and Bacoside One are two sterols flavones which have generally pro characteristics. As per a recent study, Steviol found in *Stevia's* leaves exhibit significant generally pro actions against human digestive tumor cells (Lemus-Mondaca et al., 2012).

It is a natural sweetener plant as well as medicinal uses of *Stevia rebaudiana* like high blood pressure, treat diabetes, uric acid increase glucose level as well as weight loss etc. (Ahmad et al., 2020b).This plant is mostly used for diabetic patients, renal stone, kidney disease, low blood pressure as well as albumin urea, protein and Glomerular filtration rate etc (Mehmood et al., 2020). *Stevia rebaudiana* leaves are more effective for diabetic people and mostly used for the food industry (Borkar et al., 2022).



***Stevia rebaudiana* leaves whole part used for extraction with dried leaves, seed, root as well as flower et**

Chemical Constituents

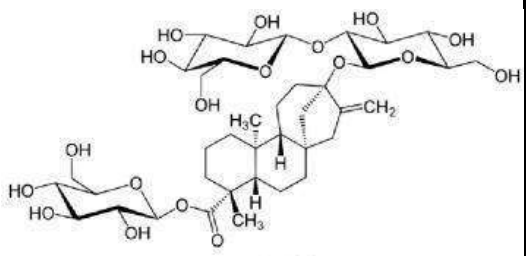
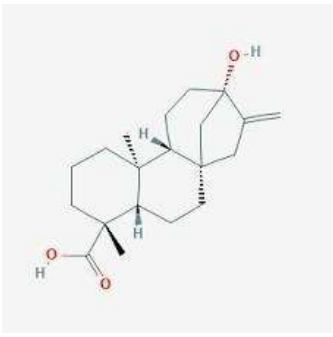
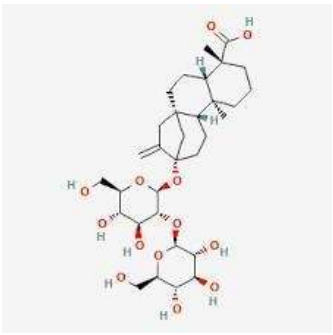
Previous investigations have shown that the sweeteners leaves appear to contain an income of nutrient levels, which include nine amino acids that are necessary moisture contains vitamin (folic, vit C, and b Vitamins), six lipids

(stearic, oleic, linoleic, stearic, as well as linoleic acid acids), energetic plant chemicals, -carotene, rebaudiana oxides, 4–6, nicotinic acid, *stevia,* vitamin b2 etc (Khatun et al., 2021).

As of now, there really are upwards of 95 phytochemicals known to exist in *stevia.* Even so, it is plentiful in flavones as well as triterpenoids. These same seven flavones that help compensate this material are it's like, wastes are generally, rebaudioside It through a E, as well as things differently A. *Stevia rebaudiana* (10- 15%), stevioside (5%), as well

as dulcoside-A and B (0.5-10. %) make up the majority of the sweet glycosyl concentration. One of these nine aglycones, stevioside, has a sweetness level that is 500 times higher than carbohydrates (Wang et al., 2020).

Table 2. Major Biochemical Components of *Stevia rebaudiana*

Components	**Structure**	**Sweetness**
Steviosides	 Steviosid	150- 250 time Sweetness
Steviol		—
Steviolbiosides		90 time sweetness

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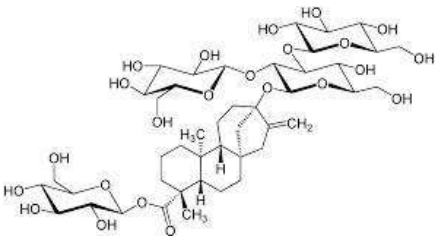
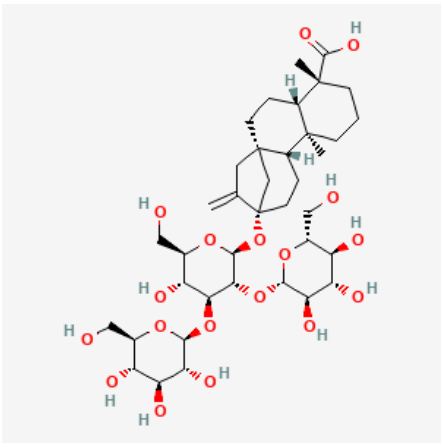
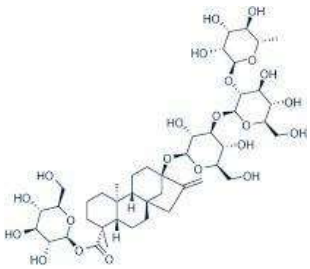
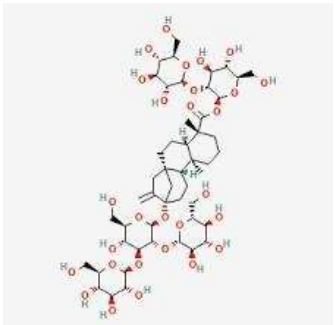
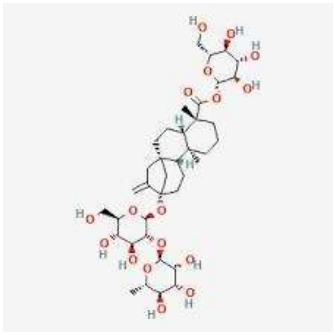
Rebaudioside A		200-300 time sweetness

Rebaudioside B		150 time sweetness
Rebaudioside C		30 time sweetness
Rebaudioside D		221 time sweetness

Dulcoside A		30 time sweetness

The eight essential amino acids branched - chain chloride, glutamic acid, cysteine, valine, tyrosinase, amino, cysteine, amino, and tyrosine, as well as moisture nutrients, were all found to be prevalent inside the Leaves in earlier studies. Polyunsaturated fats (stearic, oleic, unsaturated fat stearic, expressed sequence and linoleic acid enzymes), energetic plant chemicals (Steviol, austroinullin, alpha, rebaudiana iron oxide, 4–6, niacin, resveratrol, folic acid and vitamin, mineral deposits (nutrients, phosphate, potassium, sodium, iron, magnesium and potassium (Ahmad et al.,
2020c).

Stevia rebaudiana dulcoside A, Rebaudioside A-E, stevioside and stevioside, in addition, the triterpenes amylin acetate and 3 esters of lupeol and the sterols like stigmasterol, sitosterol and campesterol were also isolated from leaves (Kamal- Alahmad, 2018). It established the structures of some diterpene glycosides using 13C NMR. Later, the diterpene glycosides, dulcoside A and B were isolated from S. rebaudiana and their structures were established (Khalid et al., 2021).

Rebaudioside A and steviolbioside have been isolated by HPTLC methods. *Stevia rebaudiana* also contains steviol, a product formed by enzymatic hydroxylation within the plant. Isolation of the principal sugars of *Stevia rebaudiana* has also been studied. The sweet diterpenoid glycoside, rebaudioside F, was isolated from leaves of a high rebaudioside C producing line of the species, and its structure was established by chemical and spectral studies (Yen and Quoc, 2021).

Extraction of *Stevia rebaudiana* glycosides

Besides the known extraction methods, new methods for glycoside-based extraction from Stevia were developed and it was found that water was very effective for extracting glycosides at selected pH and temperatures. It was also reported that a multi-stage membrane process was successfully able to concentrate the glycoside sweeteners. The bitter- tasting components were washed out from the sweetener concentrates in the nanofiltration process (López-Carbón et al., 2019). It has been demonstrated that a membrane-based separation process for refining glycoside-based sweeteners could be viable and needs to be investigated further (Lemus-Mondaca et al., 2012).

Analytical methods

Several analytical techniques have been employed to assess the distribution and level of sweet diterpenoid glycosides in S. rebaudiana. These include thin layer chromatography. Stevioside and rebaudioside have also been analyzed by HPLC after conversion to the p-bromophenacyl esters of stevioside and rebaudioside. Stevioside levels have also been determined enzymatically (Woelwer-Rieck et al., 2010). and by near infrared reflectance spectroscopy in plant strains producing mainly stevioside (Ruiz-Ruiz et al., 2017). Amino columns have also been used to measure

stevioside and related glycosides in foods and beverages. The most common analytical method. However, there has been high performance liquid chromatography (HPLC) (Bergs et al., 2012).

Pharmacological Properties

a) Diabetes

Blood glucose level may be treated by *Stevia rebaudiana* plant and traditional uses as well as natural uses by the pharmaceutical industry. These plants are mainly affected in diabetic person and are more effective (Faramayuda et al., 2022).

b) Anti-hypoglycemic

These same hepatic beta cells are affected by sucralose, which also improves insulin sensitivity and motivates a release of insulin. discovered that even in leptin rats, extract seemed to be ready to regulate blood sugar levels besides enhancing all these insulin productions and utilization**.**

c) Antifungal activity

Because once ethanolic extracts of Sweetener structural and functional properties were studied for their antimicrobial effect, Penicillium, Pedi coccus reflecting, Circularis subs, and Fusarium exospore showcased the highest areas of inhibition.

d) Renal functions

Glomerular play a role Among the most major organs, a nephron' primary mission is to forcibly remove waste material as well as metabolic byproducts.

This same control over blood compression, water-salt balance, as well as red blood cell production are supplemental processes of the organs. The major factor in chronic disease cases is obesity. The effect is chronic renal chronic condition (Rizwan et al., 2018)**.**

Study conducted on stevioside for its possibility in acting as calcium antagonist in rats using classical clearance techniques and arterial pressure measurements showed that stevioside produced a fall in systemic blood pressure as well as diuresis and natriuresis per milliliter of glomerular filtration rate. Verapamil tended to increase the renal and systemic effects of stevioside, whereas an infusion in rats prepared with stevioside induced a marked attenuation of

the vasodilating responses of steviosides. The effects of administration of S. rebaudiana extract for 20, 40 and 60 days on renal function and mean arterial pressure in normal Wistar rats were evaluated by various workers.

Results showed that the S. rebaudiana treated rats' group for 20 days did not significantly differ from the control group. Chronic administration of a crude extract for 40 and 60 days induced hypotension, diuresis and natriuresis with constant glomerular filtration rate (Rizwan et al., 2019a).

e) Anti-cancer activity

Disease effect 4 sitosterol flavonoid alienates powerful induction, tetradecanoylphorbol-13-acetate from *Stevia rebaudiana*, such as stevia, Stevioside as well as a C, and things from different perspectives A. inflammatory disease in rodents, implying an anticancer activity (Khatun et al., 2021a).

f) Antioxidant effect

Radicals are believed to be involved in the commencement of disease, neurodegenerative problems, relatively weak immune function, skin infections, rapidly aging, heart attack, stroke, Alzheimer's disease. Phenolics may be observed in sucralose. The leaf extract of Sucralose mobile phase consisted were used to generate an array of anti - oxidants, such as flavonoid, decrease the production of reactive oxygen species while hindering natriuretic II-induced cell growth and insulin - like growth factor I urinary excretion. Therefore, it may help cure a variety of illnesses like disease, sexual dysfunction, and congenital anomalies (Tavarini et al., 2020).

g) Effect on blood pressure

Its actions fill a hormone an' o pretensive" Initial *Stevia rebaudiana* has previously been shown to reduce blood pressure in studies in animals. *Stevia rebaudiana* produces decrease in blood pressure and increase in diuretic and natriuretic effects in rats (Chowdhury et al., 2022).

h) Anti-hyperglycaemic effect

Stevia rebaudiana has an effect on the beta cells of pancreas and improves insulin sensitivity and promotes insulin production. Revealed that stevioside was able to regulate blood glucose levels by enhancing not only insulin secretion but also insulin utilization in insulin deficit rats. The later was due to decreased phosphosphingolipid pyruvate carboxykinase gene expression in rat liver by steviosides causes slowing down glycogenesis (Jan et al., 2021).

i) Toxicology

Stevioside does not Promote bladder carcinogenesis Short-term studies of 13 weeks at a concentration of 5% in diet were found suitable to be the maximum tolerable dose of stevioside for a 2-year study in rats. Stevioside at dose up to 2500 mg/kg body weight per day was found to affect neither growth nor reproduction in hamsters. Acute toxicity studies of steviosides given as single doses to rodents showed no lethality within 14 days after administration and no clinical signs of toxicity or morphological or histopathological changes were found. The genotoxic potential of

stevioside in eukaryotic cells was studied using Wistar rats treated with stevioside common(4mg/mi) through oral administration (ad libitum) and the DNA-induced damage was evaluated using the single cell gel electrophoresis (comet assay). The results showed that treatment with stevioside generates lesions in peripheral blood, liver, brain and spleen cells in different levels; the largest effect being in the liver. The undesired effects need to be better understood, once the data presented point to possible stevioside mutagenic properties (Zhang et al., 2017).

Stevia rebaudiana as treatment in renal function

a) *Stevia rebaudiana* leaves is an effective treatment for renal injury and diuretic patients as well as mostly used drug for diabetic persons and excess water, electrolytes excreted out from the body. Because Glomerular filtration rate is responsible for filtration of blood and water material excreted out from the body. These drugs are more effective for internal organ and renal injury (Olas, 2022).

b) *Stevia rebaudiana* consumption in combination with a standard medication therapy indicated the protective effects on Pathophysiology in people. In the present investigation, *stevia's* positive outcomes could really reduce the risk of people with high blood pressure, kidney disease, but also cerebrovascular problems and additionally enhance the quality of life for those who have ongoing kidney disease (Mehmood et al., 2020).

c) So even though *Stevia rebaudiana* has such a mild diuretic, it inhibits the body's natural biological mechanism for removing potassium, which also causes a concentration of potassium (Ahmad et al., 2021).

d) *Stevia rebaudiana* medication reduced serum creatinine levels. a decrease in liver function rates (Ahmad et al., 2021). and concentration of total serum creatinine have always been discovered in all treated groups (Khatun et al., 2021b).

e) The study's findings support the usage of *Stevia rebaudiana* as an alternative to artificial sweeteners as well as other added sugars by diabetics. These plants are more effective for renal functions as well as mainly diabetic patients and other internal organs (Rizwan et al., 2019b).

Table3. Medicinal properties of phytochemicals present in *stevia*

Phytochemical	**Medicinal uses**	**References**
Phenols	Anti-inflammatory, Antiaging activity of plant	(Singh et al., 2019)
Coumarin	Anti-bacterial, Anti diabetic and high blood glucose level	(Khatun et al., 2021c)
Steroids	Pain removing	(Cordeiro et al., 2020)
Tannins	Used to treated renal function	(Borgo et al., 2021b)
Alkaloids	Reduce the hyper cholesterol level	(Borgo et al., 2021b)
Saponin	Preventive skin disease	(Singh et al., 2019)

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Uses of *Stevia rebaudiana*

The treatment of numerous diseases around the world includes the medicinal use of this herb. No evidence of any harmful effects from human ingestion of *Stevia rebaudiana* extracts is present. There are no signs of toxicity when high rebaudioside (Abdelsattar et al., 2023).

A level administered over 90 days in rat diets. Also, no allergic reaction, mutagenic, teratogenic or carcinogenic effects are shown by Steviosides. Many reports have shown that stevioside has zero calorific value (Laha et al., 2023).

Many reports have shown that stevioside has zero calorific value. A report indicated *Stevia rebaudiana* interaction with appetite suppressants, blockers of calcium channels and other drugs. *Stevia rebaudiana* has a high antioxidant activity because it contains a high percentage of phenols and flavonoids (Wang et al., 2023).

It improved the overall gastrointestinal function, and tea containing Stevia leaves helps in relief of stomach upset. *Stevia rebaudiana* prevents ulceration in the gastrointestinal tract and acts as anti- hypertensive that affects renal function (Rezvankhah et al., 2022).

It is used as a tonic to treat depression and is useful in chronic yeast infections. Stevia raw stuff utilized as a synthesizer for contraceptives pills and medicines for cholesterol suppressing. Stevia leaves are used as a colour enhancer and are used mainly for their bioactive compounds (Chen et al., 2022).

Stevia leaves are commonly used in herbal teas, and food and are more used in beverages than food. It is used in the manufacture of confectionery, sweet bakery goods, nutraceuticals and functional foods. Stevia can be used in milk and milk products as a sucrose replacer and apple-cherry fruit drinks.

The use of Stevia in beverages is higher than in food has been reported in a study. Stevia leaves were in use in herbal remedies in South America for several decades. Dry Stevia leaf powder is used for the rejuvenation, nourishment, stimulation and restoration of the normal function of the pancreas (Wang et al., 2020) .

Conclusions

Stevia has been used for many health purposes since ancient times but they gained acknowledgment due to the increased demand of natural products. Stevia is a small shrub which is used as a bio sweetener. Stevia is used as a sweetener and flavor enhancer because of its superior qualities than many other high potency sweeteners. The properties of stevia leaves remain unchanged during purification and extraction. They play a crucial role in sugar and calorie reduction, diabetes, weight management, cardiovascular disease and to improve a healthy lifestyle for chronic kidney disease patients. They are non-carcinogenic, non-hypertensive and have the least adverse effect on the gut but as they are new to study, they are advised to be taken in moderation.

References

Ahmad, J., Khan, I., Blundell, R., Azzopardi, J., Mahomoodally, M.F., 2020a. Stevia rebaudiana Bertoni.: an updated review of its health benefits, industrial applications and safety. Trends Food Sci Technol 100, 177–189. https://doi.org/10.1016/j.tifs.2020.04.030

Ahmad, J., Khan, I., Blundell, R., Azzopardi, J., Mahomoodally, M.F., 2020b. Stevia rebaudiana Bertoni.: an updated review of its health benefits, industrial applications and safety. Trends Food Sci Technol 100, 177–189. https://doi.org/10.1016/j.tifs.2020.04.030

Ahmad, J., Khan, I., Blundell, R., Azzopardi, J., Mahomoodally, M.F., 2020c. Stevia rebaudiana Bertoni.: an updated review of its health benefits, industrial applications and safety. Trends Food Sci Technol 100, 177–189. https://doi.org/10.1016/j.tifs.2020.04.030

Borkar, P., Yadav, V., Tiwari, R.R., Samarth, R.M., 2022. A systematic review of potential candidates of herbal medicine in treatment of chronic kidney disease. Phytomedicine Plus 2. https://doi.org/10.1016/j.phyplu.2022.100361

Khatun, M.C.S., Muhit, M.A., Hossain, M.J., Al-Mansur, M.A., Rahman, S.M.A., 2021a. Isolation of phytochemical constituents from Stevia rebaudiana (Bert.) and evaluation of their anticancer, antimicrobial and antioxidant properties via in vitro and in silico approaches. Heliyon 7. https://doi.org/10.1016/j.heliyon.2021.e08475

Khatun, M.C.S., Muhit, M.A., Hossain, M.J., Al-Mansur, M.A., Rahman, S.M.A., 2021b. Isolation of phytochemical constituents from Stevia rebaudiana (Bert.) and evaluation of their anticancer, antimicrobial and antioxidant properties via in vitro and in silico approaches. Heliyon 7. https://doi.org/10.1016/j.heliyon.2021.e08475

Kim, D.H., Jeong, C.H., Han, Seo Gu, Jung, H.S., Han, Sung Gu, 2023. Stevia extract enhances the fermentation and functional properties of fermented milk in human colon epithelial cells. Food Biosci 102747. https://doi.org/10.1016/J.FBIO.2023.102747

Kolar, S., Jurić, S., Marijan, M., Vlahoviček-Kahlina, K., Vinceković, M., 2022. Applicability of alginate-based composite microspheres loaded with aqueous extract of Stevia rebaudiana Bertoni leaves in food and pharmaceutical products. Food Biosci 50. https://doi.org/10.1016/j.fbio.2022.101970

Laha, S., Subrahmanyeswari, T., Verma, S.K., Kamble, S.N., Singh, S., Bhattacharyya, S., Gantait, S., 2023a. Biogenic synthesis, characterization and application of silver nanoparticles as biostimulator for growth and rebaudioside-A production in genetically stable stevia (Stevia rebaudiana Bert.) under in vitro conditions. Ind Crops Prod 197, 116520. https://doi.org/10.1016/j.indcrop.2023.116520

Laha, S., Subrahmanyeswari, T., Verma, S.K., Kamble, S.N., Singh, S., Bhattacharyya, S., Gantait, S., 2023b. Biogenic synthesis, characterization and application of silver nanoparticles as biostimulator for growth and rebaudioside-A production in genetically stable stevia (Stevia rebaudiana Bert.) under in vitro conditions. Ind Crops Prod 197, 116520. https://doi.org/10.1016/j.indcrop.2023.116520

Lemus-Mondaca, R., Vega-Gálvez, A., Zura-Bravo, L., Kong, A.H., 2012. Stevia rebaudiana Bertoni, source of a high-potency natural sweetener: A comprehensive review on the biochemical, nutritional and functional aspects. Food Chem 132, 1121–1132. https://doi.org/10.1016/j.foodchem.2011.11.140

LIU, H. jun, DUAN, W. dong, LIU, C., MENG, L. xue, LI, H. xu, LI, R., SHEN, Q. rong, 2021. Spore production in the solid-state fermentation of stevia residue by Trichoderma guizhouense and its effects on corn growth. J Integr Agric 20, 1147–1156. https://doi.org/10.1016/S2095-3119(20)63478-5

Luanda, A., Ripanda, A., Makangara, J.J., 2023. Therapeutic potential of Equisetum arvense L. for management of medical conditions. Phytomedicine Plus 3. https://doi.org/10.1016/j.phyplu.2023.100444

Mehmood, A., Zhao, Liang, Ishaq, M., Zad, O.D., Zhao, Lei, Wang, C., Usman, M., Lian, Y., Xu, M., 2020. Renoprotective effect of stevia residue extract on adenine-induced chronic kidney disease in mice. J Funct Foods 72. https://doi.org/10.1016/j.jff.2020.103983

Moongngarm, A., Sriharboot, N., Loypimai, P., Moontree, T., 2022. Ohmic heating-assisted water extraction of steviol glycosides and phytochemicals from Stevia rebaudiana leaves. LWT 154. https://doi.org/10.1016/j.lwt.2021.112798

Ndukwu, M.C., Ibeh, M., Okon, B.B., Akpan, G., Kalu, C.A., Ekop, I., Nwachukwu, C.C., Abam, F.I., Lamrani, B., Simo-Tagne, M., Ben, A.E., Mbanasor, J., Bennamoun, L., 2023. Progressive review of solar drying studies of agricultural products with exergoeconomics and econo-market participation aspect. Cleaner Environmental Systems 9, 100120. https://doi.org/10.1016/J.CESYS.2023.100120

Sardar, H., Waqas, M., Naz, S., Ejaz, S., Ali, S., Ahmad, R., 2022. Evaluation of different growing media based on agro-industrial waste materials for the morphological, biochemical and physiological characteristics of stevia. Cleaner Waste Systems 3, 100038. https://doi.org/10.1016/j.clwas.2022.100038

Wang, J., Zhao, H., Wang, Y., Lau, H., Zhou, W., Chen, C., Tan, S., 2020. A review of stevia as a potential healthcare product: Up-to-date functional characteristics, administrative standards and engineering techniques. Trends Food Sci Technol 103, 264–281. https://doi.org/10.1016/j.tifs.2020.07.023

Abdelsattar, A.M., Elsayed, A., El-Esawi, M.A., Heikal, Y.M., 2023. Enhancing Stevia rebaudiana growth and yield through exploring beneficial plant-microbe interactions and their impact on the underlying mechanisms and crop sustainability. Plant Physiology and Biochemistry 198. https://doi.org/10.1016/j.plaphy.2023.107673

Ahmad, Naveed, Rab, A., Sajid, M., Ahmad, Nisar, Fazal, H., Ali, M., Egertsdotter, U., 2021. Sucrose-dependent production of biomass and low-caloric steviol glycosides in adventitious root cultures of Stevia rebaudiana (Bert.). Ind Crops Prod 164. https://doi.org/10.1016/j.indcrop.2021.113382

Bergs, D., Burghoff, B., Joehnck, M., Martin, G., Schembecker, G., 2012. Fast and isocratic HPLC-method for steviol glycosides analysis from Stevia rebaudiana leaves. Journal fur Verbraucherschutz und Lebensmittelsicherheit 7, 147–154. https://doi.org/10.1007/S00003-012-0760-5

Borgo, J., Laurella, L.C., Martini, F., Catalán, C.A.N., Sülsen, V.P., 2021a. Stevia Genus: Phytochemistry and Biological Activities Update. Molecules 26. https://doi.org/10.3390/MOLECULES26092733

Borgo, J., Laurella, L.C., Martini, F., Catalán, C.A.N., Sülsen, V.P., 2021b. Stevia Genus: Phytochemistry and Biological Activities Update. Molecules 26. https://doi.org/10.3390/MOLECULES26092733

Chen, L., Wu, W., Zhang, N., Bak, K.H., Zhang, Y., Fu, Y., 2022. Sugar reduction in beverages: Current trends and new perspectives from sensory and health viewpoints. Food Research International 162. https://doi.org/10.1016/J.FOODRES.2022.112076

Chowdhury, A.I., Rahanur Alam, M., Raihan, M.M., Rahman, T., Islam, S., Halima, O., 2022. Effect of stevia leaves (Stevia rebaudiana Bertoni) on diabetes: A systematic review and meta-analysis of preclinical studies. Food Sci Nutr 10, 2868–2878. https://doi.org/10.1002/FSN3.2904

Cordeiro, M.S., Simas, D.L.R., Pérez-Sabino, J.F., Mérida-Reyes, M.S., Muñoz-Wug, M.A., Oliva-Hernández, B.E., da Silva, A.J.R., Fernandes, P.D., Giorno, T.B.S., 2020. Characterization of the antinociceptive activity from Stevia serrata Cav. Biomedicines 8. https://doi.org/10.3390/BIOMEDICINES8040079

Dyduch-Siemińska, M., Najda, A., Gawroński, J., Balant, S., Świca, K., Żaba, A., 2020. Stevia Rebaudiana Bertoni, a Source of High-Potency Natural Sweetener—Biochemical and Genetic Characterization. Molecules 2020, Vol. 25, Page 767 25, 767. https://doi.org/10.3390/MOLECULES25040767

Faramayuda, F., Oktavianus, R., Elfahmi, E., 2022. Stevia rebaudiana: Phytochemical, pharmacological activities, and plant tissue culture (a mini-review). Jurnal Natural 22, 198–208. https://doi.org/10.24815/JN.V22I3.19477

Jan, S.A., Habib, N., Shinwari, Z.K., Ali, M., Ali, N., 2021. The anti-diabetic activities of natural sweetener plant Stevia: an updated review. SN Appl Sci 3. https://doi.org/10.1007/S42452-021-04519-2

Kamal-Alahmad, 2018. Stevia Rebaudiana Bertoni: Description and Chemical Composition. Int J Agric Innov Res 7, 2319–1473.

Khalid, W., Rehman, A., Irfan, M., Prakash Jha, R., Khalid, M.Z., Aziz, A., Review, M., 2021. Nutritional Composition and Therapeutic Benefits of Stevia Leaves: A Mini Review 4, 2581–3226. https://doi.org/10.31080/ASMI.2020.04.0765

Khatun, M.C.S., Muhit, M.A., Hossain, M.J., Al-Mansur, M.A., Rahman, S.M.A., 2021a. Isolation of phytochemical constituents from Stevia rebaudiana (Bert.) and evaluation of their anticancer, antimicrobial and antioxidant properties via in vitro and in silico approaches. Heliyon 7. https://doi.org/10.1016/j.heliyon.2021.e08475

Khatun, M.C.S., Muhit, M.A., Hossain, M.J., Al-Mansur, M.A., Rahman, S.M.A., 2021b. Isolation of phytochemical constituents from Stevia rebaudiana (Bert.) and evaluation of their anticancer, antimicrobial and antioxidant properties via in vitro and in silico approaches. Heliyon 7. https://doi.org/10.1016/j.heliyon.2021.e08475

Khatun, M.C.S., Muhit, M.A., Hossain, M.J., Al-Mansur, M.A., Rahman, S.M.A., 2021c. Isolation of phytochemical constituents from Stevia rebaudiana (Bert.) and evaluation of their anticancer, antimicrobial and antioxidant properties via in vitro and in silico approaches. Heliyon 7, e08475. https://doi.org/10.1016/J.HELIYON.2021.E08475

Laha, S., Subrahmanyeswari, T., Verma, S.K., Kamble, S.N., Singh, S., Bhattacharyya, S., Gantait, S., 2023. Biogenic synthesis, characterization and application of silver nanoparticles as biostimulator for growth and rebaudioside-A production in genetically stable stevia (Stevia rebaudiana Bert.) under in vitro conditions. Ind Crops Prod 197, 116520. https://doi.org/10.1016/j.indcrop.2023.116520

Lahijanian, S., Eskandari, M., Akhbarfar, G., Azizi, I., Afazel, M., Ghobadi, C., 2023. Morphological, physiological and antioxidant response of Stevia rebaudiana under in vitro agar induced drought stress. J Agric Food Res 11. https://doi.org/10.1016/j.jafr.2023.100495

Lemus-Mondaca, R., Vega-Gálvez, A., Zura-Bravo, L., Kong, A.H., 2012. Stevia rebaudiana Bertoni, source of a high-potency natural sweetener: A comprehensive review on the biochemical, nutritional and functional aspects. Food Chem 132, 1121–1132. https://doi.org/10.1016/J.FOODCHEM.2011.11.140

López-Carbón, V., Sayago, A., González-Domínguez, R., Fernández-Recamales, Á., 2019. Simple and Efficient Green Extraction of Steviol Glycosides from Stevia rebaudiana Leaves. Foods 8. https://doi.org/10.3390/FOODS8090402

Mehmood, A., Zhao, Liang, Ishaq, M., Zad, O.D., Zhao, Lei, Wang, C., Usman, M., Lian, Y., Xu, M., 2020. Renoprotective effect of stevia residue extract on adenine-induced chronic kidney disease in mice. J Funct Foods 72. https://doi.org/10.1016/j.jff.2020.103983

Olas, B., 2022. Stevia rebaudiana Bertoni and its secondary metabolites: Their effects on cardiovascular risk factors. Nutrition 99–100. https://doi.org/10.1016/j.nut.2022.111655

Rezvankhah, M., Askari, H., Tohidfar, M., Rezadoost, H., 2022. Economic micropropagation of Stevia rebaudiana Bertoni and evaluation of in vitro cultures in order to improve steviol glycosides. Sci Hortic 305. https://doi.org/10.1016/J.SCIENTA.2022.111372

Rizwan, F., Rashid, H.U., Yesmine, S., Monjur, F., Chatterjee, T.K., 2018. Preliminary analysis of the effect of Stevia (Stevia rebaudiana) in patients with chronic kidney disease (stage I to stage III). Contemp Clin Trials Commun 12, 17–25. https://doi.org/10.1016/j.conctc.2018.08.007

Rizwan, F., Yesmine, S., Banu, S.G., Chowdhury, I.A., Hasan, R., Chatterjee, T.K., 2019a. Renoprotective effects of stevia (Stevia rebaudiana Bertoni), amlodipine, valsartan, and losartan in gentamycin-induced nephrotoxicity in the rat model: Biochemical, hematological and histological approaches. Toxicol Rep 6, 683–691. https://doi.org/10.1016/j.toxrep.2019.07.003

Rizwan, F., Yesmine, S., Banu, S.G., Chowdhury, I.A., Hasan, R., Chatterjee, T.K., 2019b. Renoprotective effects of stevia (Stevia rebaudiana Bertoni), amlodipine, valsartan, and losartan in gentamycin-induced nephrotoxicity in the rat model: Biochemical, hematological and histological approaches. Toxicol Rep 6, 683–691. https://doi.org/10.1016/j.toxrep.2019.07.003

Rodríguez-Cravero, J.F., Gutiérrez, D.G., Katinas, L., Grossi, M.A., Bonifacino, J.M., Marchesi, E., 2019. A revision and morphological analysis of the Uruguayan species of Stevia (Compositae, Eupatorieae). Rodriguesia 70. https://doi.org/10.1590/2175-7860201970078

Ruiz-Ruiz, J.C., Moguel-Ordoñez, Y.B., Segura-Campos, M.R., 2017. Biological activity of Stevia rebaudiana Bertoni and their relationship to health. Crit Rev Food Sci Nutr 57, 2680–2690. https://doi.org/10.1080/10408398.2015.1072083

Singh, D.P., Kumari, M., Prakash, H.G., Rao, G.P., Solomon, S., 2019. Phytochemical and Pharmacological Importance of Stevia: A Calorie-Free Natural Sweetener. Sugar Tech 21, 227–234. https://doi.org/10.1007/S12355-019-00704-1

Soejarto, D.D., Addo, E.M., Kinghorn, A.D., 2019. Highly sweet compounds of plant origin: From ethnobotanical observations to wide utilization. J Ethnopharmacol 243. https://doi.org/10.1016/j.jep.2019.112056

Tavarini, S., Clemente, C., Bender, C., Angelini, L.G., 2020. Health-Promoting Compounds in Stevia: The Effect of Mycorrhizal Symbiosis, Phosphorus Supply and Harvest Time. Molecules 25. https://doi.org/10.3390/MOLECULES25225399

Wang, F., Zhan, J., Ma, R., Tian, Y., 2023. Simultaneous improvement of the physical and biological properties of starch films by incorporating steviol glycoside-based solid dispersion. Carbohydr Polym 311. https://doi.org/10.1016/J.CARBPOL.2023.120766

Wang, J., Zhao, H., Wang, Y., Lau, H., Zhou, W., Chen, C., Tan, S., 2020. A review of stevia as a potential healthcare product: Up-to-date functional characteristics, administrative standards and engineering techniques. Trends Food Sci Technol 103, 264–281. https://doi.org/10.1016/J.TIFS.2020.07.023

Woelwer-Rieck, U., Lankes, C., Wawrzun, A., Wüst, M., 2010. Improved HPLC method for the evaluation of the major steviol glycosides in leaves of Stevia rebaudiana. European Food Research and Technology 231, 581–588. https://doi.org/10.1007/S00217-010-1309-4

Yen, N.T.H., Quoc, L.P.T., 2021. Chemical composition of dried Stevia rebaudiana Bertoni leaves and effect of ultrasound-Assisted extraction on total steviosides content in extract. Herba Polonica 67, 1–7. https://doi.org/10.2478/HEPO-2021-0003

Zhang, Q., Yang, H., Li, Y., Liu, H., Jia, X., 2017. Toxicological evaluation of ethanolic extract from Stevia rebaudiana Bertoni leaves: Genotoxicity and subchronic oral toxicity. Regulatory Toxicology and Pharmacology 86, 253–259. https://doi.org/10.1016/j.yrtph.2017.03.021