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A Look at the Characteristics of Stevia Rebaudiana Bertoni: New Developments in Food Applications, Phytochemistry, and Health Benefits

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KEYWORDS

Dietary Supplements, Nutritious Foods, Natural Sweeteners, Clinical Research, And Health Advantages.

ABSTRACT: Native to Argentina, Brazil, and Paraguay, Stevia rebaudiana is a plant used as a sweetener and member of the Asteraceae family. In addition to having the potential to be a sweetener, stevia is a source of several nutrients that have a positive impact on human nutrition. The leaves of stevia include the chemical, rebaudioside, steviolbioside, and isosteviol and sweeter than sucrose with 0 calories. These steviol glycosides are valued commercially worldwide for their ability to replace sugar in food, drink, and nutraceuticals. They are also thought to have a sweet flavour. An overview of various extraction techniques, phytochemistry, and commercial stevia applications is given in this article. a variety of goods, including drinks, bread goods, dairy products, and confections. Numerous researches demonstrate the potential health advantages of stevia against a range of illnesses, including the antimicrobial, anti-obesity, cancer prevention, anti-oxidant, anti-hypertensive, and anti-diabetic qualities investigated in this work. According to clinical research, steviol glycosides—an important stevia phytochemical—are safe for ingestion by humans and do not cause either acute or serious toxic effects. This work potentially give an alternative perspective of stevia for the management of human ailments and contribute in creative stevia-based goods.

Introduction: The perennial shrub A particular type of stevia belongs to the family Stevia rebaudiana Bertoni. Compositae. Currently grown throughout North America, Europe, and Asia, it originated in South Americas (Vega-Galvez, Ah-Hen, Zura-Bravo, & Lemus-Mondaca, the year 2012). [1]. Currently, over 200 different There are recognised stevia subspecies to exist worldwide, nevertheless, mainly Stevia (Shivanna, Naika, Khanum, & Kabul, 2013)[2] Rebaudiana is a delicious plant. Stevia, also known, sometimes referred to In the form of a syrupy candy, or honeycomb leaves, gets It's delightful.

Objectives: Different Extraction Process and Identification of Stevioside with Pharmacological, Pharmacognostic Action.

Results & Conclusions: The need for novel low- or no-calorie sweeteners has surged recently due to the rise in the incidence of various metabolic diseases globally. There are several artificial sweeteners available on the market, but their usage is restricted because of potential negative side effects. Consequently, the quest for naturally occurring sugar alternatives has yielded some compounds with highly sweet tastes or taste-altering qualities. S. rebaudiana is a crop that is grown and harvested for its high intensity natural sweetening properties. It is an important source of phytochemical elements as a raw material that supports health and creates functional meals. components. Diterpene glycosides are a natural sweetener that is used extensively in foods and beverages. They are now available on the market. Compared to other artificial sweeteners now on the market, it is 200–300 times sweeter. Its low calorie index and non-toxic nature, as demonstrated by clinical and preclinical evidence, support its application in the food and beverage business. Harvesting practices, extraction methods, yield value, purification, and other business-related factors

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need to be given more attention. With better blending methods, the more recent stevia-based product version may have better flavour profiles and fewer or no adverse effects.

1. Introduction

The perennial shrub A particular type of stevia belongs to the family Stevia rebaudiana Bertoni. Compositae. Currently grown throughout North America, Europe, and Asia, it originated in South Americas (Vega-Galvez, Ah-Hen, Zura-Bravo, & Lemus-Mondaca, the year 2012). [1]. Currently, over 200 different There are recognised stevia subspecies to exist worldwide, nevertheless, mainly Stevia (Shivanna, Naika, Khanum, & Kabul, 2013)[2] Rebaudiana is a delicious plant. Stevia, also known, sometimes referred to In the form of a syrupy candy, or honeycomb leaves, gets It's delightful flavour from steviolglycosides, which contain According to Lemus Mondaca, Vega-Zura-Bravo, Gálvez was, and Ah-Hen (2012), for instance, 100–300 periods the amount of sweetness of dextrose[3].

2. Stevia, also known is a great source of vitamins, minerals, fatty acids, necessary amino acids that are required as well as additional health-promoting biologically active substances like hydrocarbons, flavonoids, phenolic compounds, phytosterols, non-glycosidic labdanediterpenes, chlorogenic acids, and crude fibre in addition to its sweet glycosides (Wolwer-Rieck, 2012). [4]. In many different countries, stevia is used extensively as a sugar replacement in foods, beverages, and pharmaceuticals. Products for commercial usage have been made using stevia derivatives (Abbas Momtazi-Borojeni, Esmaeili, Sahebkar & Abdollahi, 2017)[5].

3. Remarkably, stevia leaves outperform a variety of other high-potency sweeteners in terms of functionality and sensory appeal. As a result, stevia is projected could contribute significantly to the high-potency sweeteners availability for the growing organic meal market in the future (Goyal, Samsher, &Goyal, 2010).[7]. In addition to its industrial uses, numerous studies have demonstrated the health benefits of stevia, such as its ability to fight diabetes, obesity, cancer, hypertension, bacteria, and antioxidants According to Moguel-Ordonez, Ruiz-Ruiz, & Segura-Campos in 2015. and Borojeni et al., as well as Mahmoud Momtazi (2017).[8–9]. Moreover, no evidence of teratogenicity, carcinogenicity, mutagenicity, or acute or sub-acute toxicity has been found for the plant's steviol glycosides according to Abbas Momtazi-Borojeni et al., 2017) are an example.[10]. Numerous review studies have been carried out in response to the growing excitement about stevia's possible applications, documenting its biochemical makeup, nutritional qualities, and health benefits (Gantait, Das, & the Mandal, 2014; Goyal et al., 2010; Kobus-Moryson&Gramza-Michałowska, 2015; Lemus-Mondaca et al., Carrera-Lanestosa, Moguel-Ordonez, & Segura-Campos, 2017 as a whole Yadav & Guleria, 2012; Marcinek & Krejpcio, the year The following sources: ŠicŽlabur, Voća, Dobričević, Ježek, Bosiljkov, &Brnčić, 2013; Panpatil & Polasa, the year 2008; Rojas and collaborators, 2018; Ruiz-Ruiz, Moguel-Ordonez, & Segura-Campo, the year 2015) [10-19]. Nevertheless, the majority of these research are narrowly focused and were carried out more than five years ago. Because of this, an updated collection of the evidence on the health benefits is still lacking.

4. phytochemistry, commercial uses, and stevia's safety. Thus, the goal of this study is to provide a thorough and current summary of the health advantages, phytochemical makeup, and potential safety concerns associated with stevia. A review has also been done on the possible industrial uses of sweetener as a meal and meal component, as well as a sucrose substitute, fertiliser, &animal feed. Furthermore, this study aims to present a current overview of the characteristics and uses of steviol glycosides.

5. For instance, current research on the self-assembly patterns and amphiphilic structure of steviolglycosides, such as stevioside and It has been explored how to employ rebaudioside as an effective solubilizing agent or as a natural emulsifier to stabilise oil-in-water emulsions. Additionally, new approaches to enhance steviol glycosides' flavour profile have been examined.

2. Botany ethnobotany

Since the 18th century, nformation on Stevia, also known varieties from ethnobotany have been documented. The most recent version, which addressed the ethnopharmacological and ethnobotanical features of the genus Stevia, was made available in 2002 [6].

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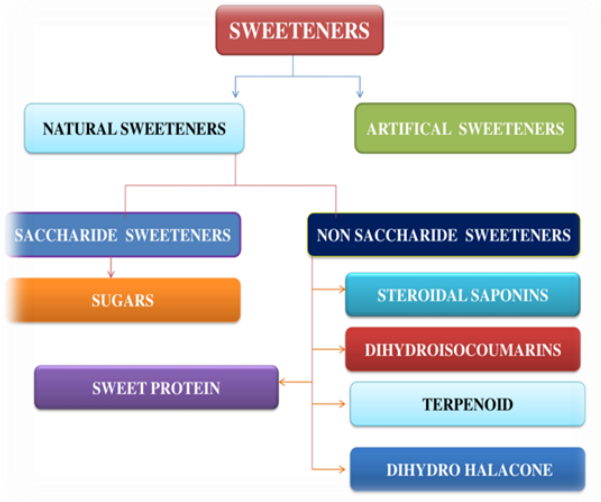
Here, a review of the texts from January 2002 to February 2021 was done to bring the knowledge on these subjects up to date. There are 29 species from Central and South America that have traditional usage. Several notable applications of Stevia species include treating skin issues, heart ailments, stomachaches, and diarrhoea. It is also used as a febrifuge, diuretic, antimalarial, and febrifuge.

Fig-01 Stevia Plant

Table-01 Distinguish stevia from additional synthetic sweeteners.

The Herb Stevia	substitute sweeteners
No energy	High in energy
0 on the glucose index	elevated glycemic index
Sustained heat up to 160 °C	Reduced stability in heat
Simple to process	not fully absorbed
not broken down and eliminated by the regular routes	In the blood, metabolised and absorbed
elevated safety	Insufficient safety
Excellent steadiness	Insufficient stability
Excellent solubility	Insufficient solubility
Not a cause of cancer	causing cancer
antioxidant qualities	not possess antioxidant qualities



(A) Fig.02 Stevia Leaf

(B) Fig.03 Stevia Plant

Table -02 Applications of Stevia species in ethnobotany

Animal species	Typical Name	Use of Ethnobotany	Place	Reference
S.	Comra	artistic.	Argent	[21,2
S.balansae	-	Antidiarrheal.	Paraguay	[23]
Ex Cortés, S. bogotensis Tr. ex	Clavito, Jarilla, and Eupatoria	febrifuge. Diaphoresis	Colombia	[24]
Perkins, S. cardiaca	-	cardiac conditions.	Bolivia	[24]
S. collina Gardn.	Ah, yeah	sugar substitute. As acidic	Brazil	[24]
Lag, S.	Pericó	therapy for	Guate	[23,2

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connata.	n de monte	stomachaches.	mala	4]
HBK S. elatior.	Pericón de monte	To relieve burns and Diuretic. Antimalarial. For	Mexico	[24,14]
Wild S. eupatoria (Spreng.)	Borrego herb, Borrego yerba, Borrego	stomach pain. Hypoglycemic agent.analgesic. Antiinflammatory.counteracts hypertension	Cuba	[23,24,25]
ar. vattuonei (Hicken) Castelra S. fiebrigii	-	artistic.	Argentina	[21]
	La pulga de	Inhibitory	the United States	[23,24]
Bip. Slinoides Sch.	-	Stringent in nature	-	[27]
Lucida Lag, S.	Arraña, yerba del aire, golondrina de la chirca, chilca, javillo, kebuj, mariposa, ma-li-	to heal injuries. to ease discomfort. Treatment for rheumatism. anti-inflammatory.	Mexico, Guatemala, Colombia, Venezuela	[23,24]
S. Macbridei Robins B. L. Robins var. anomala, B. L.	Huancayo-Jaunja	Bathed in it by ladies	Peru	[23,24]
S. Hieronis mercedensis var. mercedensis	Comrade	A decorative	Bolivia, Argentina	[22,28]
Nepetifolia S. HBK	Anis de ratón, peracón, and zazal	Treatment for dysmenorrhea	Mexico, Guatemala	[23,24]
S. palmeri Gray	Raniweri, raniwori	Odoriferous.	Mexico	[23]
S. petiolata (Cass) Sch. Bip	Guar me-guarmi	To give flavor to meat.	Peru	[23,24]
	Flor de María	anti-malarial. antipyretic. To make washes and	Mexico	[23,24]
S.	Ronin	ointments for	Mexic	[23]

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plummerae Gray	o	exposed wounds	o	
Hook S. puberula	Lima-lima	Utilised for a replacement for the beverage and Sweetener. Food additive	Peru	[23,24]
S. Bertoi rebaudiana	Sweet fern from Paraguay stevia	contraband. used as an antidiabetic to regulate arterial	Paraguay and Brazil	[6,10]
	Herba envidia, zazale de olor, yerba de la mula, hierba del aire y mucho más. Santa Rita de Hierba	Treatment for rheumatism. cathartic. for parasitic disturbance of the intestines. Negative in nature. For colds and fevers	Mexico, USA	[23,24]
Hieron sanguinea S.S. saturei ifolia (Lam.)	Malvisco	artistic.	Argentina	[21]
var. The bip. ex Klotzsch Schas a. saturei ifolia	Romerillo	artistic.	The nations of Argentina, Brazil, and Uruguay	[21]
S. serrata Cav.	Hiperi cón, Q'ang'aj, Ronino, Uriki, Chapo, Otoni nawa, yerba picante, anis silvestre had, and hiperi con arrie	to prepare poultices and soaps for open wounds. Used for snake bites and wounds on the foot. as a cough cure. Regarding digestive issues	Guatemala, Mexico	[23,24,29]
S. subpubescens Lag.	Zazal, Herba de la Quintana	like a postpartum bathing. therapy for stomachaches. to ease arthritic joints.	Mexico	[23,24]
S. trifida Lag.	Manzanillais de drinking water	Management for dysentery	the United States	[23,24]
S. Yalae Hernández	-	artistic.	the country of Argen	[21]

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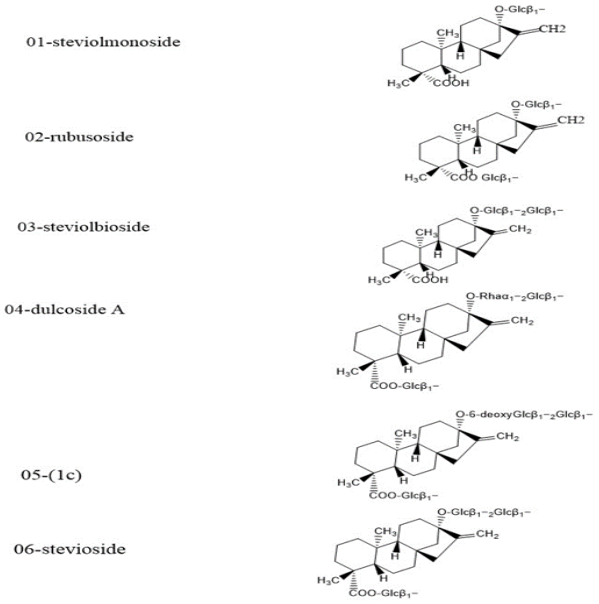
			tina	

Steviol Glycosides

[30,31,32,33,34,35,36]



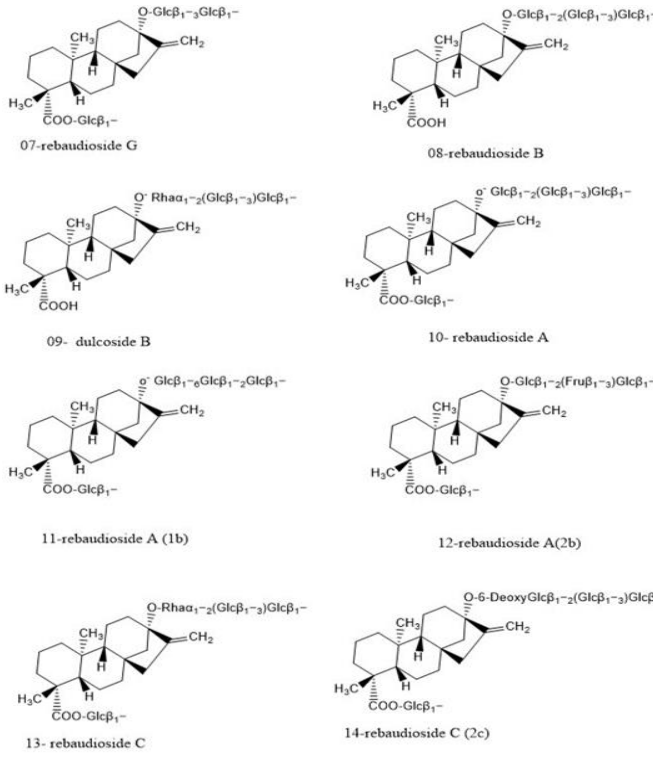


Fig.04 Chemical Structure

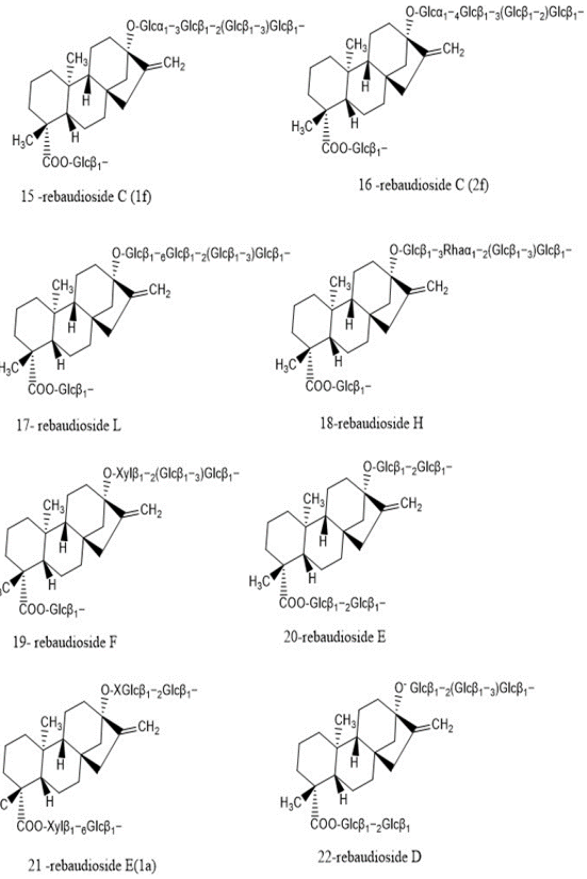


Fig.05 Chemical Structure

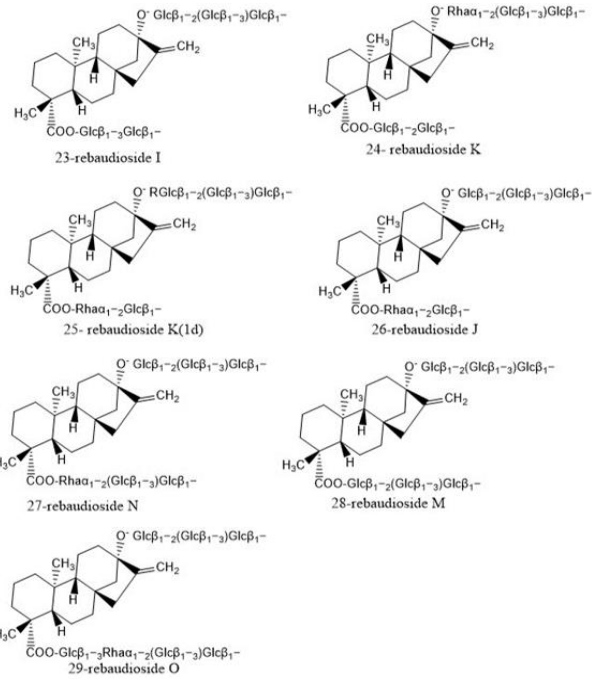


Fig.06 Chemical Structure

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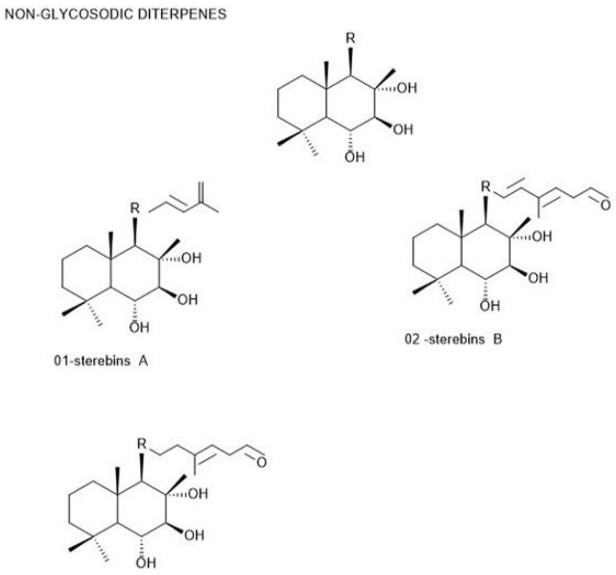

Fig.07 Chemical Structure

New Steviol Glycosides with Changes in the ent-Kaurene Backbone [37,38]

Non-Glycosodic Diterpenes

Fig.08 Chemical Structure

Fig.09-(A)Stevia plant(B) Stevia Flower(C)Stevia Plant(D) Dried leaf(E)Crushed Stevia leaf

Tests were conducted on S. rebaudiana crude leaf extract (in vivo) in several systems against various infections. Stevia has shown to be a highly potent antibacterial. The results indicated that Table 9 (a and b) of the methanolic extract had the strongest favourable reaction against all microorganisms. The extracts' enhanced solubility in these organic solvents may account for their stronger antibacterial activity in both formaldehyde and methanol, which Extracts from stevia have shown to be efficient in opposition to the greatest number of bacterial strains. Six distinct bacteria, including Bacillus subtilis, Salmonella mutans, Staphylococcus aureus and the growth of E. Coli were subjected to the antimicrobial properties of Stevia rebaudiana extracts in a variety of solvents. fungus strains were. But according to Debnath (2008), A small number of mushrooms reported reported to be suppressed by leaf extractions. The main and secondary metabolites that the plants produced were thought to have the therapeutic qualities (Faizi et al., 2003). In our investigations, we discovered that while just one fungus shown inhibition to the leaf extract, all The rebaudiana lichen extract reduced the growth of microorganisms in the different solvents. Similar tests were conducted by Adebolu and Oladimeji (2005), who discovered the antibacterial activity of Ocimum sp. leaves. The effectiveness of several medicinal plants' aqueous and methanol extracts was studied by Parekh et al. in 2005. Potential antimicrobial properties of twelve therapeutic herbs. The antibacterial properties of a plant called S. rebaudiana fermentation with warm water extracted were documented by Tomita et al. (1997) against Enterohemorrhagic bacterial infection This157:47 and other microorganisms that cause illnesses linked to food. It was discovered that the ideal solvent for producing strong antibacterial activity was methanolic extract. The possibility that the antibacterial action was caused by the secondary metabolite "stevioside" has been raised (Nakamura and Tamura, 1985). What was the secondary metabolite likewise the The best soluble in functioned as an antibacterial agent while it happened in system of methanol as solvents. Improved susceptibility and a zone of inhibition were frequently seen upon dilution of the plant leaf extract (in order to ascertain the minimal inhibitory concentration). The reason behind this might be that the extract was too viscous to effectively permeate and disperse in the medium when it was pure; but, upon dilution, it was able to do so with ease (Parekh et al., 2005). This is The recreated within the cell plantlets' increased antibacterial properties might be attributable to the increased quantity of extracellular compounds; thus, result, these plantlets are exploited as a reservoir of superior plantlets. Consequently, this plant might be exposed to more separation of the medicinal antibiotics and other pharmacological analysis. The antibacterial activity of dried Stevia leaves extracted in methanol and chloroform (in vivo).Steviol components have been used as antibacterial agents, according to evidence (Meireles et al., 2006).[45] In addition to preventing the

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growth of Streptococcus mutans UA159 and inhibiting its formation of biofilms (Escobar et al., 2020) [46],

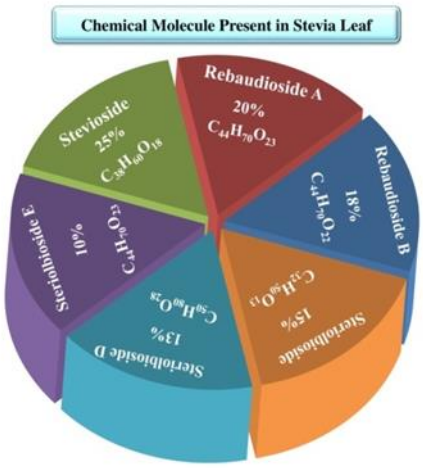

Fig.10 Chemical Molecule Present in Stevia

S. rebaudiana demonstrated its antimicrobial activity by inhibiting the growth of several other microorganisms, including Pseudomonas aeruginosa, Bacillus subtilis, Vibrio cholera, and Escherichia coli (2015, Naikwadi & Nadaf). [47]

When The stevia extract made from methanol showed an excellent region of resistance pertaining to the Epstein-Barr virus and bacteria such as S. aureus in an agar well diffusion technique when compared to the element parthenium, ginkgo trees azithromycin because of and cepaxim medications. (Fazal et al., 2011).[48] Leishmaniasis major, Styphylococcus aureus, and Escherichia coli were all positively affected by the green synthesised zinc oxide nanoparticles of stevia (Khatami et al., 2018).[49] Listeria innocua was effectively inhibited by the stevia extracts produced by convection and infrared drying techniques (Lemus-Mondaca et al., 2018).[50]The extracts of stevia leaves in water, methanol, ethyl acetate, acetone, chloroform, and hexane were examined for their antimicrobial properties and shown to be effective against a variety of microorganisms, including Bacillus megaterium, Proteus vulgaris, Yeast, Rhizopus oligoporus, Salmonella typhi, Serrstia marcenscens, Micrococcus luteus, Candida albicans, Aeromonas hydrophila, and Cryptococcus neoformans (Tadhani and Subhash, 2006b; Jayaraman et al., 2008).[51, 52] Ghosh et al. (2008) reported that The liquid form of petroleum ether, which is shown remarkable efficacy in opposition to 10 distinct microorganisms, encompassing specimens of harmful bacteria and fungi.[53] The antibacterial Stevia leaf methanol extracts' effectiveness was found below a range of (N) treatments, Ten, fifteen, twenty, plus 5 kg ha-1; however, no significant effect in antibacterial efficaciousness was seen at any of the concentrations (Atas et al., 2018).[54]

Stevia leaf extract was found to have antibacterial action against cariogenic bacteria of the species Streptococcus and Lactobacillus when it was produced in solvents such as Chloroform, hexane, alcohol, methanol, and ethyl acetate. Regarding extracts of ethyl acetate and chloroform, which the Compared to Streptococcus, the area of restriction over four Lactobacillus genus measured between 12.3 and seventeen percent mm. (Gamboa and Chaves, 2012).[55] Stevia can be utilised as a natural sweetener that is non-cariogenic since different dilutions of the plant decreased the production of S. mutans biofilms (Escobar & Associates, 2020; Chen & Associates, 2020).Furthermore, the Stevia leaf extracts in methanol, acetone, and ethanol showed concentration-dependent inhibition of S. mutans bacterial growth [56,57]. The concentrated forms of ethanol and acetone were used. of stevia had been demonstrated to possess significantly more inhibitory capability with relation to the extraction in water (Mohammadi-Sichani et al., 2012).[58]

Both the ethanol production and methanolic in chamomile compounds may be recognised as potent antibacterial agents as they both showed greatest inhibition against S. pneumonia and B. subtilis and the biggest concentration of bioactive components (Zohra, 2015).[59]Stevia has the potential to be a bactericidal agent due to the phytochemicals it contains. The least MBC, which is or antibacterial percentage gegen 49 prolonged- these enzymes in the spectrum (ESBL), which) that produce infectious agents of the urinary tract ranging from between 10 and 20 mg/mL of its aqueous & petroleum-based ether alcohol, methanol, and formaldehyde extractions from solvents (Raut and Aruna, 2017).[60] Aqueous extracts of stevia, hexane, ethanol, and carbon tetrachloride all showed inhibitory effects on cultures of Pseudomonas aeruginosa, S. aureus, and Staphylococcus epidermidi. Aqueous extracts (84.4%) had the greatest inhibitory effect against Styphylococcus epidermidi of all the

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preparations (Arámbula Pereira and others, the year 2017). [61] Stevia extraction from leaves and roots were reported to have strong antibacterial properties and to be effective gegen E. coli DM 4100 and B. subtilis strain NCIM 2708 at 500 mg/ml (Singh et al., 2012).[62] With the greatest and lowest antibacterial indexes of 11.89 ± 0.07mm and 7.24 ± 0.03mm, respectively, The raw extraction as well as the essential oil of stevia include naturally bactericidal against Pseudomonas paratyphi infection B. subtilis, bacteria such as E. coli, P. aureus, and Shigella burg boydii other bacteria (Siddique et al., 2014).[63] Enterobacter aerogenes was shown to be more sensitive to the activity of all preparations in an additional test of the antimicrobial properties of extracts from stevia leaves (Mali et al., 2015).[64] In By using an agar well diffused technique, desiccated foliage of stevia cultivated both species and in assays extract in chloroform and methanol shown promising antibacterial action against medically significant bacteria (Debnath, 2008).[65] Against harmful bacteria, such as B. subtilis, S. aureus, K. pneumonia, P. vulgaris, and S. pneumoniae, and P. florescence, natural stevia flower extracts were found to have more antibacterial compared to preparations from leaves (Preethi et al., 2011).[66] The stevia extracts in water-soluble, methanolic in, and alcohol-based forms have excellent antibacterial properties against a variety of microorganisms and can be utilised in medications and preservatives.

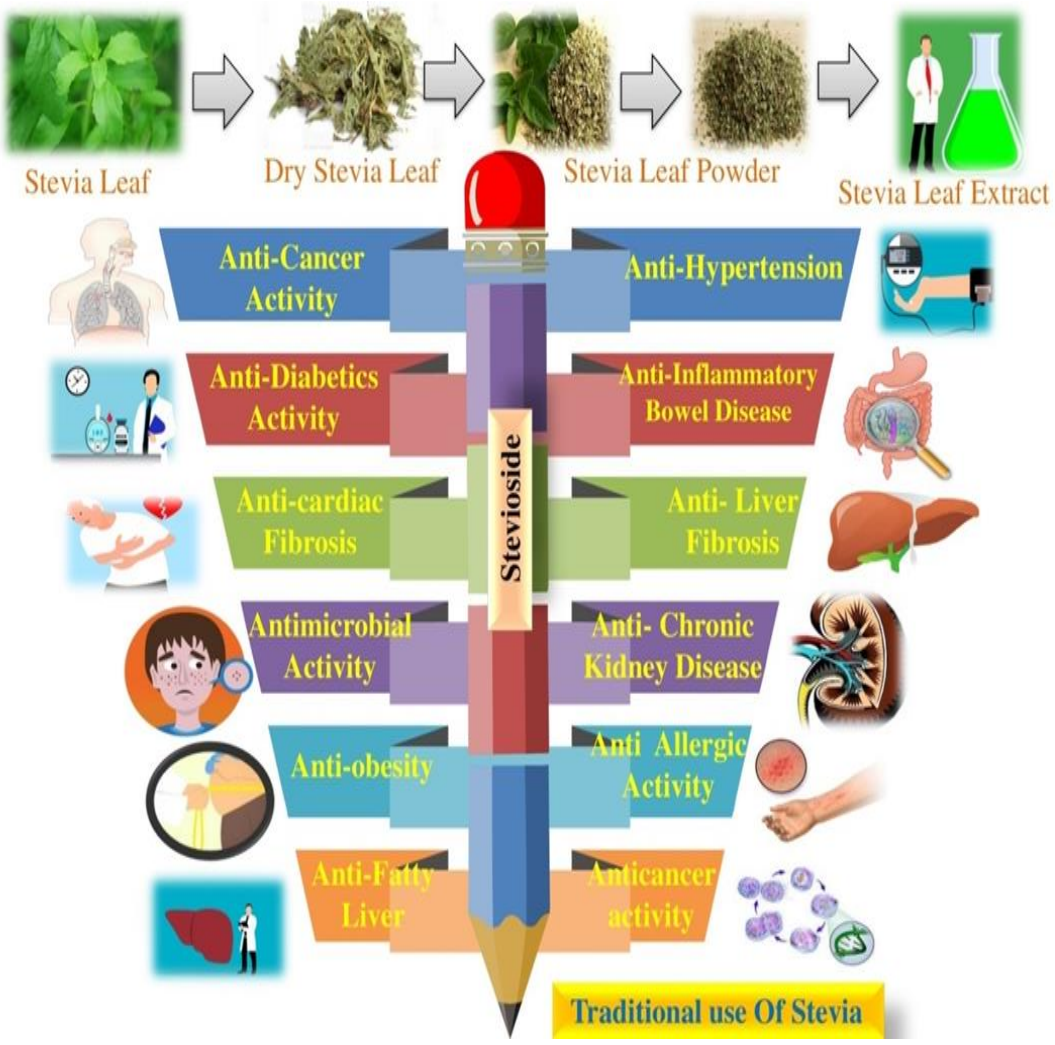

Fig.11 Traditional Use of Stevia

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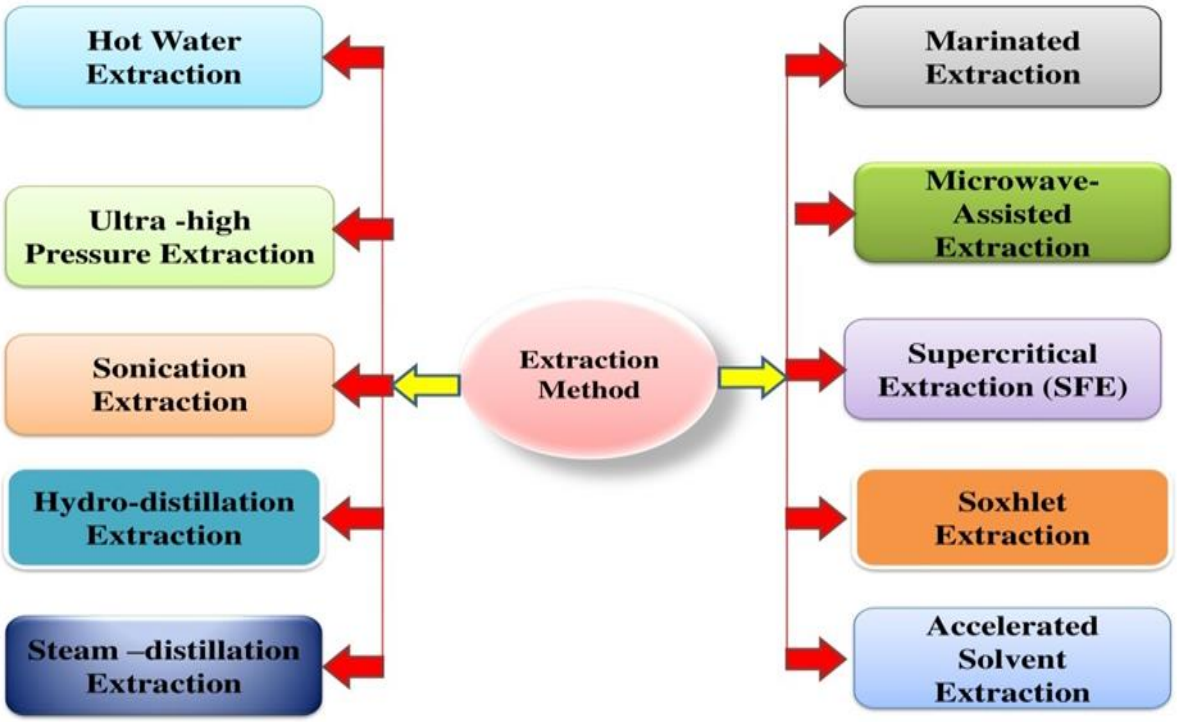

Fig.12 Type of Extraction Method

principal group	Individuals	Section	Reference
Polysaccharide	Glucopyranosaccharide	Take root and leaf	(De Oliveira and others, 2011)[67]
Terpene Glycosides	Steviolbioside, dulcoside A and C, astroinuline, jhanol, rebaudioside A, as well as C, D, E, and so on F, and M; steroids A.	Flowers, roots, stems, and leaves	(The works of Guleria and Yadav Prasad (2012), for instance, SakamOTO et al. (1977), Darise et al. (1983), Upadhyay Sharma and Kumar (2013) are cited.[70]

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These chemicals	Caryophyllene (β) and trnas β farnesene, α-humulene, nerolidol.	Leaves	(Marković et al., 2008)[71]
Alkaloids	Steviamine, stevioside	Leaves, stem , root	(Kumari and Chandra, 2015); [72] (Michalik and others, 2010). [73]
Anabolic steroids	cholesterol lipids, Glucocorticoid	stems, leaves, and root	(Kumari and Chandra, 2015)[74]
Saponins	Steroid saponins	Stem, root and leaf	(Kumari and Chandra, 2015)[75]
Tannins	Gallic and tannic acids	Leaves of grass	(Kovačević & colleagues, 2018)[76]
phenols	Apigenin, epicatechin, rutin catechin, and querciten.	stem, roots, and leaves	(Howlader and others, 2016). [77]
Carotene	The protein Lutein	Leaves	(Kovađević and others, 2018) [78]
phenolics	Gallic acid, cholorogenic acid, caffeineic acid, and protocatechuic acid acid, cinamic acid.	Leaves	(Howlader et al., 2016) [79]

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Sugars and Fats	Starch and glucose	root, stem, leaves	(Chandra and Kumari, 2015)[80]
Acidsa chlorogenic	Quinic acid with hydroxycinnamic acid	Root, stem, leaves	[81]

Table-03 Phytochemical constituents of Stevia

Pharmacological Activity of Stevioside (Stevia Leaf)

01-Antioxidant activity

Free radicals are very reactive and unstable molecular entities with unpaired electrons. They have little effect at low to moderate concentrations, but at higher concentrations, they induce oxidative stress [82], which is highly harmful to human health and accelerates the onset of conditions like illnesses of the nervous system, cancer, heart problems, inflammation bowel conditions, obesity, and osteoarthritis [83]. Antioxidants have become important because of this because of their ability to stop oxidative stress-related damage. By scavenging, chelating with catalytic metals, and neutralising free radicals, they halt the oxidative process [84]. since it is less harmful properties of edible plants, their potential as sources of antioxidant chemicals is being thoroughly investigated [85]. Numerous studies on stevia extracts have demonstrated the potential for dose-dependent antioxidant activity in both leaf and callus extracts [86]. Since the amount Numerous investigations have reported on the Stevia extract's inherent antioxidant capacity in the agricultural sector.Polyphenols, or as well as antioxidants in the ethanolic form of the extract showed eliminating properties against the compound ABTS, which and DPPH levels (1,1-diphenyl-2-picrylhydrazyl), which•+(2,2′ 3-ethylbenzothiazoline-6-sulfonic acid - azino-bis acidic solution) radicals. Moreover, extract and glycol aqueous extracts have considerably greater concentrations of these components [87]. A preclinical investigation revealed that the extract from stevia residue that is produced as an aftereffect of the substance glycoside synthesis has demonstrated defending impact in opposition to oxidant caused in old mice by the enhancement of the activity of enzymes such glutathione peroxidases, Both superoxide dismutase and peroxidase via D-galactose. Furthermore, it has been seen to enhance the overall antioxidant potential and reduce acetylcholinesterase activity and malondialdehyde levels in the brain's activity, blood, and liver. It is stated that this happens via turning on the Akt/Nrf2/HO-1 pathway., which provides a highly sought-after option for dietary supplementation to counteract Oxidative stress Disorder, which might potentially vary with age [88]. In an additional animal prototype In diabetic rodents, stevia leaf, wistar rats, and powdery extraction (4.0%) showed favourable changes in anti-oxidation markers and decreased lipid peroxidation [89]. Even when wheat bread with stevia extracts is produced, its potential as an antioxidant is preserved, making it a useful food [90]. Comparably, exotic fruit drinks with Drinks with 1.25, which is and 2.5 percent (w/v) glycosides included being an ingredient in sweeteners likewise regarded as useful beverages because research shows that they have superior antioxidant properties to non-stevia beverages [91].

Similarly, compared to the juices without stevia, the strawberry-based drinks with green stevia powder added exhibit higher overall content of flavonoids and phenols, as well as improved antioxidant potential. Furthermore, the sonication processing method used in strawberry juices made with stevia emphasises how crucial it is to preserve while also boosting the anti-oxidant and sweetness of the beverage [92]. On the other hand, compared to regular yoghurt, beneficial

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yoghurts that include 0.25–0.5% freeze-dried fruit stevia furthermore filter had higher overall content of phenolic compounds as well as greater antioxidant prospective supporting the preservation of intestinal health [93].

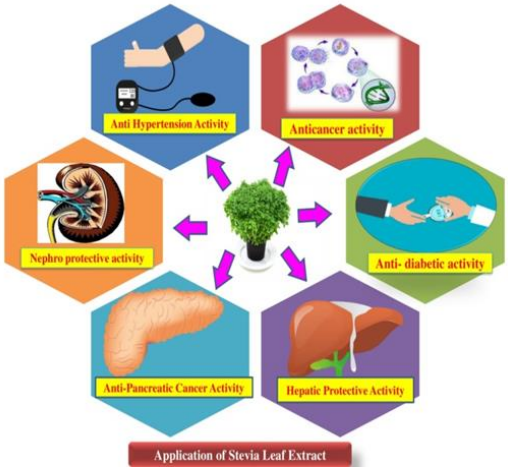

Fig.13 Application of Stevia

Free radicals are created by metabolic activities that take place in our bodies. Conditions related to the environment, pathogens, physical world, and chemistry can all greatly enhance the generation of free radicals. Free radicals are created when both internal and environmental influences, such as medications, tobacco, pollution, stress, and other things, have an adverse effect on our body and change the structure of DNA, lipids, and proteins. These deformities may accelerate ageing and have severe effects on a variety of human diseases (El-Beltagi, El-Salam, Omran, & Afify, the year 2012; [94]). Matus-, Moguel- and Segura-Campos Ruiz- and Basto (2015).[95] Free radicals most frequently damage lipids, producing peroxides and other unpleasant chemicals that give off an unpleasant odour. Once these free radicals assault proteins, enzymatic activity is disrupted. Free radical exposure can cause mutagenesis and carcinogenesis in nucleic acids. By estimating antioxidant assays such as Prior and after fermentation in the intestines and metabolism, DPPH as ABTS. This FRAP, the etc. antioxidant capacity resulting from phenolic compounds from various diets was evaluated (Tavarini & Angelini, 2013).[96] No cost Radicals participate in oxidative stress, which directly contributes to the pathophysiology of several illnesses. Oxidative stress occurs when the body's balance alters in favour of free radicals, causing an increase or decrease in anti-oxidative chemicals Nayak, Liu, and Tang (2015); Flores, Wu, Negrin, & Kennelly (2015). [97] By stabilising free radicals by hydrogen ion donation, DPPH is frequently used to assess the antioxidant capacity of dietary materials to remove free radicals(Benedict and others, Gaweł) .[98] The lipophilic The free molecule DPPH levels is the first step in the auto-oxidation of lipids. response. Because this radical is the least reactive, when it combines with the other, a stable molecule is created. Research indicates that consuming above 1 gramme of polyphenolic chemicals daily might have a protective impact prevent the onset of cancer and mutations (Shukla et al., 2009).

Fig.14 Application of Stevia

[99] According to Gasmalla et al. (2014) [100], The process of scavenge radicals that are harmful via stevia Extract from leaves was determined to be 3.38% and 10.15% at 10 µgm/mL and 100 µgm/100 mL, respectively. Numerous tests' findings demonstrated that stevia extract from leaves has left greater With the exception of 10 µg/mL, the The ability of DPPH to scavenge free radicals was assessed againsto the extract from The callus formation Stevia. Mehta, Shukla, Mehta, and In a study about the free radical elimination process of DPPH levels, Bajpai (2012)[101] discovered that 1 gramme of extract from stevia leaves produced Glycolic acid, often known as phenols, 56.74 milligrammes while 1 gramme of extract from ethanol produced 61.5 mg of gallic acid. The impact of several Periche, Koutsidis, and Escriche (2014) investigated the

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effects of heat treatments (50°C, 70°C, and 90°C) with different time durations (15, 20, and 40 minutes) on the anti-inflammatory properties of stevia extract of leaves. [102]. Different concentrations of stevia

Antioxidant activity at 200 µg/mL were 40%, 46.84%, 51.35%, 64.26%, and 72.37%, in that order. Using DPPH and ABTS tests, The antioxidant potential of methanolic extracts derived from the root, branches, stem, and flower of Stevia was evaluated by Singh et al. (2012) [103]. The DPPH test and the ABTS radical scavenging activity assay were used to assess total antioxidant activity. For the ABTS reactive oxygen species scavenging activity, the trolox equivalent of antioxidant activity (TEAC) was greatest in root extract (64.23 ± 8.35 mM); leaves, stem, and blossom exhibited 56.26 ± 16.87, 49.28 ± 12.87, and 46.49 +/- 13.13 MM, which is in that order. To ascertain the anti-oxidative capacity of The root extract exhibited the greatest activity of 4.84 ± 0.22, 8.6 ± 0.45, and 2.24 ± 0.05, respectively, in the Enzymatic assays for peroxidase, catalase, and superoxide dismutase (SOD) according to Shukla et al., 2012; Singh et al., 2012) have been published.[104]

02-S. Rebaudiana: As an ingredient in food

Because of its mild, refreshing, and agreeable flavour similar to liquorice, stevia is used in both industrial and therapeutic settings. It is added to foods to improve both flavour and scent. Stevia leaves are used to make sauces, salad dressings, herbal drinks, and coffee. Its leaves are occasionally used to give culinary preparations colour [105]. Its extract is also found in dairy goods including yoghurts, ice creams, and flavor-infused milk. When bioactive substances like carotenoids, tannins, polyphenols, and chlorophyll are present, they provide additional significance to the stevia for its uses in the manufacturing of nutraceuticals and functional foods [106].Insulin, a fructan-type polysaccharide derived from stevia roots, has been shown to have prebiotic benefits in the synthesis of functional foods [107].

03- As a sweetener without calories

The food sector is under pressure to eliminate artificial sweeteners and sucrose from food and beverage preparations due to increased health concerns, all while maintaining flavour integrity [108]. If the sweetener is natural and non-nutritive, replacement is welcomed much more [109]. The parts that follow emphasise this substitution.

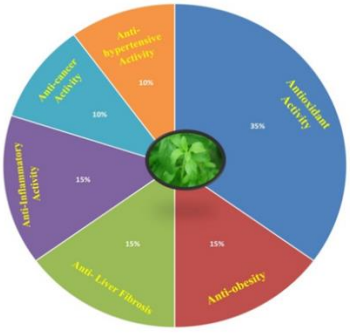

Fig.15 Application of Stevia

04- When used as a practical candy

In vitro experiments have shown that substituting stevia for sugar in bakery items including muffins, cakes, biscuits, and cookies considerably lowers the glycaemic index, improving its known nutritious worth [110]. However, Numerous authors have observed that the items made with stevia substitutes have an unpleasant aftertaste [111]. Thus, a study was carried out in which vanilla and cocoa powder were used together with 50% sucrose and stevia as a flavouring agent. The results were compared with those goods that included 100% stevia. According to the results of the sensory acceptability test, It was found that both the texture and sense of smell had been preserved with the 50% replacement. attributes. In a same vein, muesli Stevia extracts were added to cookies at 25%, 50%, 75%, and 100% sucrose. Additionally, according to the sensory acceptance test, cookies with Additions of twenty-five and fifty percent sucrose produce pleasant textures and senses. qualities [112]. Furthermore, dessert bread is being examined in a similar manner, with 50% and 100% of SGs added, respectively, and when all the factors are taken into account, In regard to physical as well as sensory aspects, the fifty per cent SGs that are and saccharine mixture has demonstrated Additional importance and acceptability characteristics [113].

Conversely, isomalt combined with rebausioside A is used to create functional whipped creams, which are then utilised in baked goods, cakes, sweets, and coffee in place of sucrose. This is an affordable way to create a low-calorie sweetener that is safe and healthful [114].

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Although Milk, yoghurt, cheese, and other foods frequently contain milk or milk derivatives daily life, they also contain huge amounts of sucrose. For this reason, flavorful yoghurts have been created that employ stevia in addition to sucrose to balance the sugar content. profile in addition to the health advantages [115]. Desserts like ice creams have also been made in a similar manner, keeping the texture and sweetness proportions the same [116]. Therefore, stevia has revolutionised the long-held notion that items containing sweeteners are unhealthy by finding widespread use in dairy and pastry goods.

05- As a practical replacement for drinks

Many drinks contain a significant quantity of sugar. One possible ingredient to substitute sugar in a variety of drinks is stevia. Peach juice, fruit juices, including apple cherry and numerous others have all been made with stevia as a beverage ingredient [117]. In one investigation, the authors found that substituting 160 mg/L of steviosides for −44% of the sucrose in a peach juice resulted in a 25% less calories without compromising the beverage's flavour [118]. More recently, peach juice has also been made by totally swapping out the sucrose, 20 mg of stevia per 100 mL, and preserves both its taste acceptability and physicochemical attributes [119]. On the other hand, juice made from passion fruits that has been enhanced using stevia has an unpleasant following flavour and is less well-liked overall [120]. But in certain situations, extra flavors—like lime flavor—are advised [121]. Similar to this, another research created mango nectar with all the required physicochemical and organoleptic properties by conditioning sucrose with 6% inulin and 3% w/w stevia. [122]. Chokeberry juice from yet another recent study has When stevia powdered leaves was added, the outcome was a beverage that retained the beverage's nutritional value by combining sufficient levels of carotenoids that polyphenols, chlorophyll as plus vitamin C are needed. [123]. Even the most well-known carbonated beverage companies, such as Drinks using stevia as an ingredient are now being sold by Pepsi, Atlanta, and Coca-Cola Co. [124]. Pepsi and Coca-Cola Companyin particular, have started selling low-calorie, stevia-sweetened drinks called Cane sugar and obstinate soda, correspondingly. In addition, stevia-infused iced tea has been created, and since 2010 over 300 stevia-infused teas that are designed to be low in calories have been created [125].06- Dairy: You may substitute stevia for sucrose.

The demand for dairy products made with stevia has increased significantly recently because of its antioxidant properties and ability to fend off a number of illnesses. Additionally, stevia decreases hunger and may help diabetics control their blood sugar levels. Dairy products that use stevia-based components may have less sugar added to them and have better cholesterol management. Stevia is a viable option for dairy-based goods given the prevalence of metabolic problems, weight gain, and obesity in today's society. Stevia is a potential becoming a star within the substance of sugar sector because it offers dairy farmers with A calorie-friendly labelling -free solution [126]. The Worldwide The National Milk Producers Association (NMPF) and the Cheese Associations (the Individuals with Dis) have petitioned the FDA to alter the definitions of milk and other dairy products. The use of stevia has been heavily promoted by the dairy industry as a means of reducing Infant adiposity and consumption of milk supplements. The dairy business will be revolutionised by this.

07- For use as a polymer in soluble and edible packaging

It is becoming more and more important to address the issue of the expanding plastic pollution caused by the disposal of food packaging. Thus, biodegradable polymers are periodically created, but the manufacturing process for these bioplastics requires specialised industrial handling [127]. Owing to its nutritional and antimicrobial qualities, stevia is becoming more and more important in the creation of sweetened edible films used in beverage packaging. Hence, stevia rebaudiana has been the subject of a recent study in which it was added to alginate as biofilm. This material's five homogeneities, great elasticity, flexibility, and power were transmitted. Due to stevia is a renewable plant, even little additions have consistent, environmentally beneficial benefits [128].

08- Sweeteners for the tablet

The food and nutraceutical industries' main goals are innovation, product enhancement, quality, and consumer pleasure. The demand for sugar consumption is rising steadily on a worldwide scale. Therefore,

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tabletop sweeteners have entered the market to cater to consumers who are always looking for a sweet flavour. These tabletop sweeteners are popular among consumers and are sold by food corporations. Depending on the company's formulations, These countertop sweeteners may contain bulking agents such as lactose, sorbitol, sucrose, polyethylene glycol, fructo-oligosaccharides, isomalto-oligosaccharides, fructose glycerol isomalte, dextrose, fructo-oligosaccharides, and isomalto-oligosaccharides. mannitol, maltitol, and maltodextrin, among others [129]. Tabletop offers low-calorie options for hot or cold beverages, as well as recipes fit for patients with a range of conditions and uses, including sprinkling. Along with colour, taste, scent, and consistency, other important aspects to take into account include sweetness, stability, and texture. All of these qualities are combined in stevia, meeting the demands of the producer.

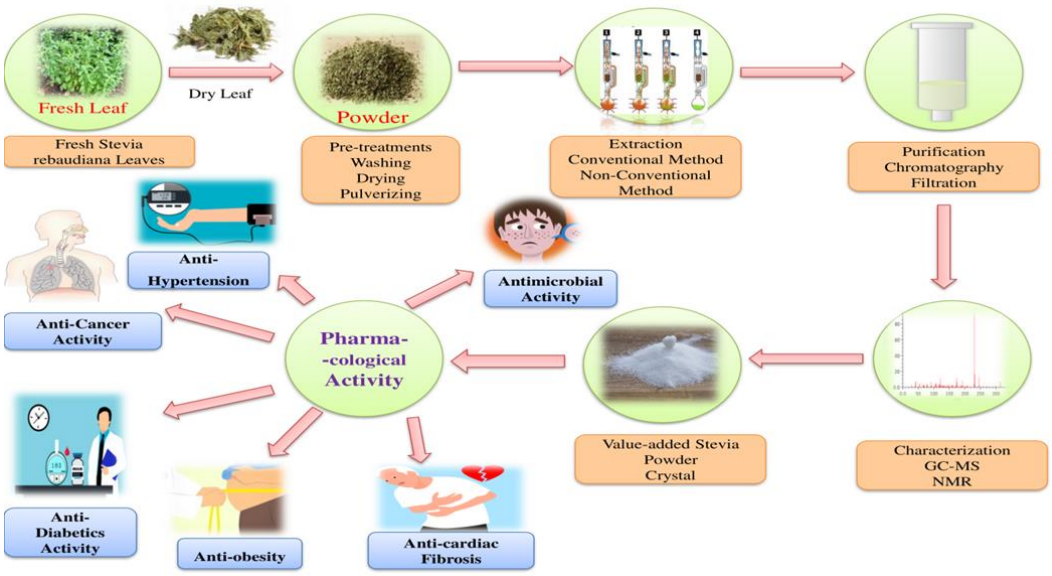

Fig.17 Extraction & Isolation and Identification of Stevioside and Pharmacological Activity

Fig.16 Use of Stevia

09- Chances arise from innovation.

The European market for stevia-containing food and beverages has grown by 26% in 2018. Numerous developments have been introduced in this regard. Better chances are presented to stevia exporters in emerging nations by new product releases in novel categories. Demand for more organic and healthful stevia-based goods, including beverages and meals fortified with stevia, is rising. As a result, innovation is crucial to meeting customer desires and offering natural sugar substitutes. Products made with stevia have been introduced by several well-known businesses, such as Nestle, PepsiCo, Danone Group, and Coca-Cola Co. Unilever and Ricola. Tate & Lyle, a well-known European sugar manufacturer, uses stevia to create Reb M stevia, a sweetener that was introduced as TASTEVA®. Therefore, creative thinking is a significant development for the stevia sector.

10-S. Rebaudiana: A medicinal sugar substitute

Given the period of rising illness prevalence, including diabetes and obesity, and the consequent rise in stevia-

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related product releases, the market value of stevia has even doubled. This is because stevia has a very excellent therapeutic index. describes the main pharmacological characteristics of stevia.

11- Diabetes

Insulin resistance and malfunction of the pancreatic beta cells are thought to be associated with diabetes. Stevia's scientific potential to improve impaired glucose metabolism and increase insulin sensitivity is supported by a number of preclinical research. The chemical components of stevia have a major protective effect against diabetes, according to animal research [130]. Additionally, the process explains how stevia lowers plasma glucose levels while postponing the onset of insulin resistance [131]. Stevia has been shown in several trials to increase insulin secretion and decrease islet inflammation [132]. The insulinomimetic action fructose and its compounds that are bioactive might affect immediately stimulation of the transporter for glucose molecule and improved absorption and uptake of fructose,as demonstrated by the molecular mechanism of anti-hyperglycemia [133]. Additionally, research from experiments indicates that stveia control the expression of proteins for Peripheral tissues absorb glucose and are crucial to the insulin-independent route. Furthermore, clinical research suggests that stevia has anti-diabetic properties [134]. Here are a few of the most recent studies in clinical practice:

• (I) - Sambra V. and colleagues (2021) study the association between appetite and both arbitrary and subjective parameters The resistance to insulin (IR) in femalesas well as the results of stevia or D-tagatose loads up front indicators of catabolism of carbohydrates following an oral carbohydrate intake. Randomised controlled crossover experiment. Women having IR lacking people with type 2 diabetes Three oral glucose loads were administered to (n = 32; age 23.4 per cent ± 3.8; Adiposity 28.1 ± 3.4 pounds × meters2). lasting three hours. The visits were spaced three days apart. Ten minutes before to the oral glucose load, participants ingested a

60 millilitres of water were preloaded with either D-tagatose (5000 mg), stevia (15.3 mg), or water (control). C-peptide and serum glucose levels were assessed at 10, 30, 60, 90, 120, and 180 minutes. A visual analogue scale was used to measure subjective hunger.

After 180 minutes, food consumption at the ad libitum buffet was recorded. In comparison to The Compared to D-tagatose (794 (366–1134) milligrammes × minute × The letter L−1; P = 0.0001), which or control (730 (516–1078) mg × min × The letter L−1; P = 0.012), stevia's C-peptide iAUC was substantially greater (the mean (IQR): 1033 (711–1293) ng × minute × The letter L−1).Serum glucose for stevia was greater at 30 and 60 minutes compared to further circumstances (P < 0.01). At 60 minutes, volunteers reported feeling fuller after eating d-tagatose particularly stevia in comparison to the control, and at 120 minutes, they were more eager to eat stevia (Everyone P < 0.05). P = 0.06 indicates that the target appetite was not condition-specific. There is life to these NNS, according to the findings. Stevia use raised blood glucose sooner while causing an immediate reaction on C-peptide release. NNS may influence hunger subjectively but not objectively [135]. (ii)- This 2-perpendicular, randomised, managed, open-label arm was studied by Stamataki Nm and colleagues (2020). experiment to see how daily stevia consumption affected glycaemic levels in healthy persons. Body mass index (BW) and energy intake (EI) were the same. secondary outcomes. A total of 28 individuals who were in good health (age 25 ± 5 years, with a body mass index of 21.2 ± 1.7 kg/m2) were randomly assigned to one of two groups: The population receiving stevia (n = 14), which had to take a daily stevia extract, or the 14-person control group. An oral glucose tolerance test was used to measure the glucose and insulin responses at weeks 0 and 12, and weeks 0 through 12 were used to evaluate BW and EI. The reactions to insulin and glucose did not differ significantly. • The stevia group maintained their weight in comparison to the control population (mean weight change at week 12: a value of 0. kg, 95% CI: [-0.96, 0.51] stevia group, +0.89 kg, 95% CI [0.16, 1.63] command the entire group). As a result, there was an important main effect of the the group on the BW shift (F (1,26) = 5.56, p = 0.026). The previously group stevia saw a substantial decrease in calorie consumption (p = 0.003) between weeks 0 and 12, whereas the control group experienced no change (p = 0.973). These results, which were not placebo-controlled, imply that regular Consuming stevia does not impact glycaemia in healthy people, however it might help with weight maintenance with the reduction of excessive intake of alcohol [136].

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- (iii)- Farhat G. and others (2019), for instance looked at how stevia affected hunger, food consumption, and postprandial glucose levels. In a three-arm crossover study, thirty individuals (20 females/10 males; ages 26.1 On three different days, the subjects The individual's Weight is 23.44 (3.42) kg/m2. obtained preloads including 1 g of stevia, 60 g of sugar, and water. which were followed by an unlimited pizza meal. Breakfast evolved became a norm.
- A diet on exam day journal for a single day was gathered. Subjective emotions of hunger were measured using visual analogue scales (VAS). Samples of blood glucose were taken every 30 minutes up to 120 minutes after lunch. The amount of energy consumed did not change significantly. Between the two preloads for the entire day ($p = 0.33$) With meals served at will ($p = 0.78$). After stevia preload, compared to water, the VAS values for the urge to eat and appetite (the DTE) were decreased. ($p < 0.05$). Consequently correction for the calorie content and sugar preload, There wasn't any discernible variation in postprandial glucose concentrations varying between them treatments.Stevia reduces the feeling of hunger without increasing meal intake or The amounts of subsequent hypoglycemia. It may be a helpful tactic in the management as well as defence of diabetes and obesity [137]. By increasing This insulin influenced by dose characteristic production and encouraging glucose utilisationblood glucose levels in diabetics rats with diabetes decreased (0.5 mg/kg) in a dose-dependent manner when SGs were administered. A a limitation enzyme in lactic acid production, phosphoenol Pyruvate carboxykinase (PEPCK) expression,is decreased in stevioside-administered groups in a dose-dependent manner [138]. The regulatory enzymes for the breakdown of carbohydrates, α-amylase and α-glucosidase, play a crucial role in regulating Sugar in the blood concentrations. In a recent investigation Within an in vitro method experiment, it was discovered that stevia leaf extract effectively inhibited the activities of α-glucosidase and α-amylase [139]. Recently, four other phenylethanolyl glycosides and a Steviophethanoside is a new glycoside containing a phenyl-ethanoid group. were found in stevia leaves. This glycoside has been shown to stimulate The islet the -cells (the Indian National Savings-1)suggesting that it may have hypoglycemic effects, though further research is required to determine its exact mechanism of action [140]. An essential metabolite of glucose that stimulates diabetes and Blood glucose levels fluctuate in a manner that fluctuates on dosage is streptoglucuronide as more recent research has shown [141]. a combination of both clinically as well as in animal research, stevia is generally considered a potentially effective treatment for hypertension -related pathophysiology. research; however, a more thorough understanding of the underlying mechanism is still required.

12- High blood pressure

A number of serious conditions, such as Although hypertension cannot be identified as a disease in and of itself, it can lead to a number of conditions, such is vascular disease of the peripheral nervous system, such as atrial fibrillation, pulmonary neuropathy, retinopathy, aneurysms, myocardial infarction, and cardiac failure with congestive left ventricle hypertrophy. Since it is capable oflast for a long period without causing any symptoms, hypertension is frequently called the "silent killer." If identified early, antihypertensive drugs and modifiable lifestyle modifications can lower hypertension and its associated consequences [142,143]. According to several research, stevia is used as a heart tonic to control heartbeats and restore unstable blood pressure to normal. In a clinical trial, 106 hypertensive women received 0.25 g of SGs three times a day, resulting in normal glucose and lipid levels and both systolic and diastolic blood pressure. In a similar vein, SGs have been shown to significantly lower systolic blood pressure while having no effect on diastolic blood pressure [144]. The blocking of entry of calcium ions into the cells of the smoothness cardiovascular muscle is part of the process that has been proposed [145].

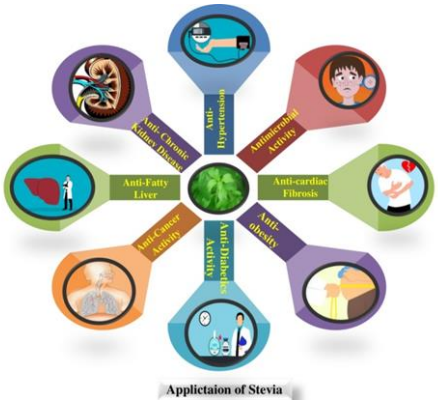

Fig.18 Application of Stevia

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An other method that has been suggested involves the suppression of the angiotensin converting enzyme, which is substantially inhibited by protein hydrosylates derived from stevia leaves [146].

13- Overweight

With a complex aetiology, obesity is a significant risk factor for health and the root cause of many health-related issues. This may be inherited or the result of unhealthy diet and living patterns. Its growth is also aided by a large consumption of sugar-based meals, thus it makes sense that avoiding high-calorie foods and beverages is crucial to managing weight. Compared to sweeteners like sucrose that are high in calories, stevia is a better non-caloric sweetener option. But compared to sucrose, stevia adds sweetness that is around 100–300 times more [147]. Even in actuality, a research has shown that rats given stevia, but individuals that are exposed to sucrose have the reverse pattern [148]. A more recent study found that rats fed an aqueous extract of stevia leaves had a better calorie profile, which eventually led to a drop in body weight from feed consumption [149]. However, encouraging outcomes in human subjects have not yet been observed. Furthermore, it has been discovered that stevia preload lowers self-reported hunger and dietary desire in healthy participants [150]. Artificial sweeteners, which are typically added to foods and beverages, are not caloric but are harmful to health since they can lead to weight gain, bladder and brain tumours, and other issues [151]. Therefore, it is vital to defend the use of sugar substitutes like splenda since they are safe and healthful.

Fig-19 Traditiona

l application of Stevia

14- Cavities In Teeth

Dental decay is an infectious disease that spreads slowly and may be brought on by the oral cavity's resident microbiota, dietary consumption of carbohydrates and fermented goods, and fluctuations in salivary flow rate [152]. Therefore, it's critical to locate a healthy alternative that can aid in caries prevention. In comparison to a 10% sucrose solution rinse, a research on dental plaque revealed a decrease in plaque following rinsing with 10% stevia extract. Furthermore, Research has shown that the active ingredient re and a substance called exhibit minimal S.mutans biofilm development upon washing and are naturally non-acidogenic [153]. Bacterial life is hampered by the non-fermentable nature of stevia solution [154]. In terms of dental cavities, stevia has demonstrated overall long-term safety.

15- Malignant

The World Health Assembly of the WHO states that cancer is the second most prevalent cause of death worldwide, accounting for almost 9.6 million deaths in 2018. It would be ideal to develop novel chemotherapy drugs that come from natural sources. Additionally, steviosides, which are naturally occurring phytochemicals derived from stevia, have demonstrated some potential both as a cancer-causing agent and an anti-tumor agent to acquire resistance [155]. Stevioside was administered to female rats with mammary gland adenomas in the initial investigation, and it was discovered that the drug had anti-tumor action. Studies conducted in vitro have shown this. Additionally, three Cancerous cell lines of text, including pancreatic (MiaPaCa-2) and colorectal (the condition116) cervical (HeLa)—have demonstrated an anti-tumor activity due to the stevia leaf ethanolic extract's diterpene inhibitors. Moreover, An erroneous gene produces the enzyme CDK4, which was inhibited by the extract that was used. associated with the formation of malignancies, confirming its anti-tumor action through CDK enzyme inhibition [156]. Conversely, stevia essential oil has demonstrated cytotoxicity against Chinese hamster ovary cells and rat glioma cells, which is analogous to vinblastine [157]. In gastric cancer cells, same results were seen [158]. Additionally, positive outcomes were seen in the cells from MCF which are breast cancer cells, and the proposed method showed that the impact

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is caused by the stimulation of apoptosis in MCF-7, suggesting that stevia and its bioactive components would be a good option for future research into the treatment of breast cancer [159]. Stevia has the capacity to stop or slow the formation of malignant cells by causing apoptosis and limiting the number of cells that divide on SKBR3 and The MDA-MB [160].Together with the onset of cell cycle arrest and death, the inactivation of the the PI3K mechanism is considered a further plausible explanation for this action [161]. This mechanism is explained by the steviosides' capacity to prevent ovarian cancer from spreading cells. All things considered, these investigations show that steviol-based drugs have beneficial effects; nevertheless, in order to prove their anti-tumor potential, more thorough clinical and pre-clinical trials are needed.

16- Kidney functioning

The kidneys carry out several vital bodily tasks, such as maintaining the body's homeostatic balance and electrolyte and fluid balance. When given to hypertensive rats, steviosides produced from S. Rebaudiana leaves have been demonstrated to increase both glomerular filtration rate and renal plasma flow. It directly prevents PAH-p-aminohippurate from being transported across epithelial cells [162]. Steviol derivatives block the CFTR-cystic fibrosis transcranial conductance regulator, which explains why they have an inhibitory impact on the Madin-Darby doggy organ (MDCK) epithelial cyst paradigm. Steviol analogues may thus be suitable options for the treatment of congenital kidney damage [163].

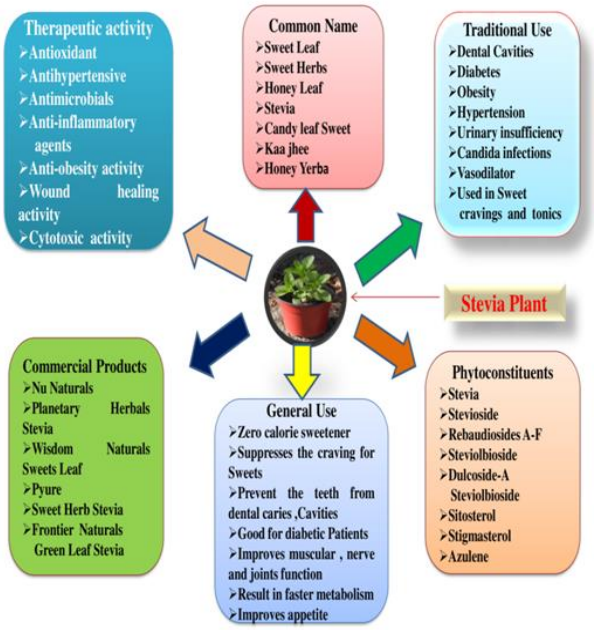

Fig.20- Pharmacological & Pharmacognostic Application of Stevia

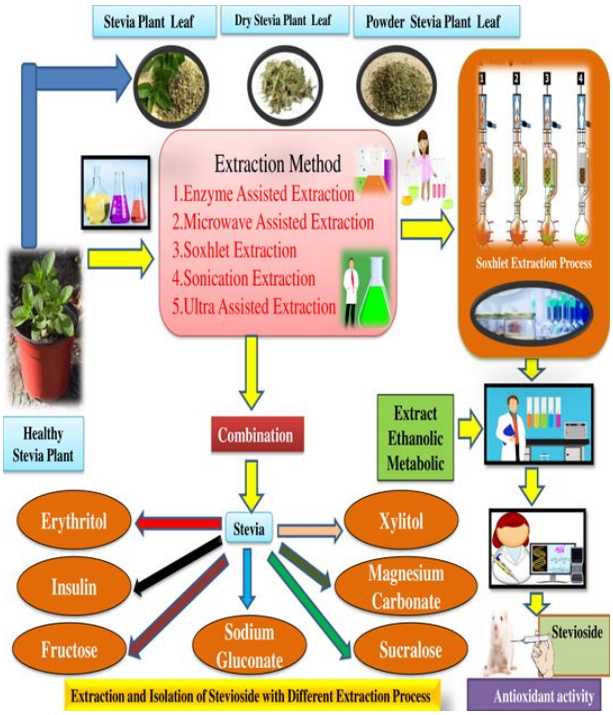

Fig.21 Extraction and Isolation of Stevioside

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Fig.22 Chemical Molecule

Table 04- varied extraction techniques, solvent composition, and yield values.

S. No.	Steviol These compounds	Procedures and conditions for extraction	Chemicals	Productivity	Citation
1.	Steviosside	Warm extraction (leaf material)	hot water (65 °C)	7.53%	[164]
		Ratio of drug to solvent: 1:15-2:75			
		Hot Extraction (leaf material)	methanol	94.90%	
		Ratio of drug solvent: (1:15–1:75)4:1			
		Hot Separation (leaf material)	Methanol and water (4:1)	92.34%	
		Drug solvent ratio:4:1			
2.	Rebaudioside A	For extraction, high power (300–480 W) and warming (to 30 °C) are employed.	Liquor isopropyl	35.61 g of leaf per one hundred grammes	[165]
		Solvent: 60 percent v/v isopropyl alcohol, mixture duration: 6–24 minutes			
3.	Reb A and Steviosside	2L of methanol was refluxed with leaf material for one hour. Methanol was used to dissolve the extracted residue.	Methanolic	57.50 kilogramme	[166]
4.	The Steviosside	The extraction process: with the aid of enzymes Pectinase,	Pectinase, cellulase, and hemicellulose enzymes at five distinct	At 60 °C, the maximum stevioside recovery was accompli	[167]

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		cellulase, and hemicellulase are three distinct proteins.	concentrations (w/v) 0.5%, 1%, 2%, 3%, and 4%	shed in one hour utilising Hemicellulase	
		Five distinct weight-to-volume ratios of 0.5 percent, one percent, two percent, 3%, and four percent			
		35, 45, and 55 degrees Fahrenheit for pectinase; forty degrees Celsius, fifty degrees Celsius, and 60 degrees Celsius for cellulase; and 50, sixty, and seventy °C for hemicellulase are the extraction temperatures.			
		Time: (15, 30 and 45 min).			
5.	Reb A and Stevioside	Extracting cold:	water, ethanol, and methanol	One twentieth of Reb-A and six quarters of stevioside	[168]
		Time: 12 h			
		The temperature at which ultrasound extraction was performed was 35 ± 5 °C.	water, ethanol, and methanol	1.98% of Reb-A and 4.20% of stevioside	
		Time:30 min			
		extraction with microwave assistance (MAE) Power level: 80 W at 50 °C for one minute.	methanol, ethanol and water	2.34 percent of Reb-A and 8.64 percent of the chemical	

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6.	Rebaudioside D	Rebaudioside D of Bertoni's rebaudiana plant is cleaned up.	alcohol-water mixture	8.8 g, 98.4% of which is Reb D	[169]
		Alcohol-water solution is the solvent.			
7.	Reb M	Hot extraction	Aqua	High-performance liquid chromatography (HPLC) yielded 1.1 grammes of >98% genuine Reb M.	[170]
		40 degrees Celsius is the temperature.			
		Time: 2 h			
8.	Steviol glycosides	Hot extraction	Water	A dark brown priming juice, 650 ml.	[171]
		Increased temperature			
		Autoclaving was utilised for excellent juice.			
9.	Reb A and Stevioside	Warm Extractions	Water	Reb A (12.1%) and steviosid	[172]
		Procedure: lower pressure rotary evaporator, followed by lyophilization.		e (16.4%)	
10.	Rebaudioside A	The use of ultrasound as an extraction method	water	32.79 grammes per hundred grammes	[173]
		ultrasonication: 360 W of power			
		Duration: 12 minutes			
		Water is the solvent.			
		Ultrasonication as an extraction method	bioethanol	33.85 grammes per 100 grammes	
		ultra-sonication: power 360 W			
		Duration: 12 minutes			
		bioethanol			
		Ultrasonic sound	Alcohol isoprop	37.10 grammes	

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	as an extraction method	yl	per 100 grammes	
	supersonication: 360 watts			
	Duration: 12 minutes			
	Isopropyl alcohol as a solvent			

06.Conclusion & Discussion

The need for novel low- or no-calorie sweeteners has surged recently due to the rise in the incidence of various metabolic diseases globally. There are several artificial sweeteners available on the market, but their usage is restricted because of potential negative side effects. Consequently, the quest for naturally occurring sugar alternatives has yielded some compounds with highly sweet tastes or taste-altering qualities. S. rebaudiana is a crop that is grown and harvested for its high intensity natural sweetening properties. It is an important source of phytochemical elements as a raw material that supports health and creates functional meals. components. Diterpene glycosides are a natural sweetener that is used extensively in foods and beverages. They are now available on the market. Compared to other artificial sweeteners now on the market, it is 200–300 times sweeter. Its low calorie index and non-toxic nature, as demonstrated by clinical and preclinical evidence, support its application in the food and beverage business. Harvesting practices, extraction methods, yield value, purification, and other business-related factors need to be given more attention. With better blending methods, the more recent stevia-based product version may have better flavour profiles and fewer or no adverse effects.

Reference

[1] Lemus-Mondaca, R., Vega-Gálvez, A., Zura-Bravo, L., & Ah-Hen, K. (2012). SteviarebaudianaBertoni, source of a high-potency natural sweetener: A comprehensive review on thebiochemical, nutritional and functional aspects. Food Chemistry, 132(3), 1121–1132.https://doi.org/10.1016/j.foodchem.2011.11.140.

[2] Shivanna, N., Naika, M., Khanum, F., & Kaul, V. K. (2013). Antioxidant, anti-diabetic andrenal protective properties of Stevia rebaudiana. Journal of Diabetes and Its Complications,27(2),103–113. https://doi.org/10.1016/j.jdiacomp.2012.10.001.

[3] -Lemus-Mondaca, R., Vega-Gálvez, A., Zura-Bravo, L., & Ah-Hen, K. (2012). SteviarebaudianaBertoni, source of a high-potency natural sweetener: A comprehensive review on thebiochemical, nutritional and functional aspects. Food Chemistry, 132(3), 1121–1132.https://doi.org/10.1016/j.foodchem.2011.11.140.

[4] -Wolwer-Rieck, U. (2012). The leaves of Stevia rebaudiana (Bertoni), their constituents andthe analyses thereof: a review. Journal of Agricultural and Food Chemistry, 60(4), 886–895.https://doi.org/10.1021/jf2044907.

[5] 05-Abbas Momtazi-Borojeni, A., Esmaeili, S.-A., Abdollahi, E., & Sahebkar, A. (2017). Areview on the pharmacology and toxicology of steviol glycosides extracted from Steviarebaudiana. Current Pharmaceutical Design, 23(11), 1616–1622.

[6] 06-Goyal, S. K., Samsher, & Goyal, R. K. (2010). Stevia (Stevia rebaudiana) a bio-sweetener: areview. International Journal of Food Sciences & Nutrition, 61(1), 1–10. https://doi.org/10.3109/09637480903193049.

[7] 07-Abbas Momtazi-Borojeni, A., Esmaeili, S.-A., Abdollahi, E., & Sahebkar, A. (2017). Areview on the pharmacology and toxicology of steviol glycosides extracted from Steviarebaudiana. Current Pharmaceutical Design, 23(11), 1616–1622.

[8] 08-Ruiz-Ruiz, J. C., Moguel-Ordoñez, Y. B., Matus-Basto, A. J., & Segura-Campos, M. R.(2015). Nutritional, amylolytic enzymes

inhibition and antioxidant properties of breadincorporated with Stevia rebaudiana. International Journal of Food Sciences & Nutrition, 66(6),649–656.https://doi.org/10.3109/09637486.2015.1077785.

[9] 09-Abbas Momtazi-Borojeni, A., Esmaeili, S.-A., Abdollahi, E., & Sahebkar, A. (2017). Areview on the pharmacology and toxicology of steviol glycosides extracted from Steviarebaudiana. Current Pharmaceutical Design, 23(11), 1616–1622.

[10] 10--Carrera-Lanestosa, A., Moguel-Ordóñez, Y., & Segura-Campos, M. (2017). SteviarebaudianaBertoni: a natural alternative for treating diseases associated with metabolic syndrome. Journal of Medicinal Food, 20(10), 933–943. https://doi.org/10.1089/jmf. 2016.0171.

[11] 11-Gantait, S., Das, A., & Mandal, N. (2014). Stevia: a comprehensive review onethnopharmacological properties and in vitro regeneration. Sugar Tech, 17(2), 95–106.https://doi.org/10.1007/s12355-014-0316-3.

[12] 12-Goyal, S. K., Samsher, & Goyal, R. K. (2010). Stevia (Stevia rebaudiana) a bio-sweetener: areview. International Journal of Food Sciences & Nutrition, 61(1), 1–10. https://doi.org/10.3109/09637480903193049.

[13] 13-Kobus-Moryson, M., & Gramza-Michałowska, A. (2015). Directions on the use of stevialeaves (Stevia rebaudiana) as an additive food products. ActaScientiarumPolonorumTechnologiaAlimentaria, 14(1), 5–13.

[14] Lemus-Mondaca, R., Vega-Gálvez, A., Zura-Bravo, L., & Ah-Hen, K. (2012). SteviarebaudianaBertoni, source of a high-potency natural sweetener: A comprehensive review on thebiochemical, nutritional and functional aspects. Food Chemistry, 132(3), 1121–1132.https://doi.org/10.1016/j.foodchem.2011.11.140.

[15] 15-Marcinek, K., & Krejpcio, Z. (2015). Stevia rebaudianaBertoni: health promoting propertiesand therapeutic applications. Journal fürVerbraucherschutz und Lebensmittelsicherheit, 11(1),3–8.

[16] 16-Panpatil, V. V., & Polasa, K. (2008). Assessment of stevia (Stevia rebaudiana)–naturalsweetener: A review. Journal of Food Science & Technology, 45(6), 467–473.

[17] 17-Rojas, E., Bermudez, V., Motlaghzadeh, Y., Mathew, J., Fidilio, E., Faria, J., ...Kuzmar, I.(2018). Stevia rebaudianaBertoni and its effects in human disease: emphasizing its role ininflammation, atherosclerosis and metabolic syndrome. Current Nutrition Reports, 7(3),161–170. https://doi.org/10.1007/s13668-018-0228-z.

[18] 18-Ruiz-Ruiz, J. C., Moguel-Ordoñez, Y. B., Matus-Basto, A. J., & Segura-Campos, M. R.(2015). Nutritional, amylolytic enzymes inhibition and antioxidant properties of breadincorporated with Stevia rebaudiana. International Journal of Food Sciences & Nutrition, 66(6),649–656. https://doi.org/10.3109/09637486.2015.1077785.

[19] 19-Yadav, S. K., & Guleria, P. (2012). Steviol glycosides from Stevia: biosynthesis pathwayreview and their application in foods and medicine. Critical Reviews in Food Science and Nutrition, 52(11), 988–998.

[20] 20-Šic Žlabur, J., Voća, S., Dobričević, N., Ježek, D., Bosiljkov, T., & Brnčić, M. (2013). SteviarebaudianaBertoni-A review of nutritional and biochemical properties of natural sweetener.Agriculturae Conspectus Scientificus, 78(1), 25–30.

[21] Rodríguez-Cravero, J.; Gutiérrez, D. Stevia Cav. In Plantas Cultivadas de la Argentina: Asteráceas-Compuestas, 1st ed.; Hurrell, J.A., Bayón, N.D., Delucchi, G., Eds.; Hemisferio Sur: Buenos Aires, Argentina, 2017; pp. 273–278.

[22] Cantero, J.J.; Núñez, C.O.; Bernardello, G.; Amuchastegui, A.; Mulko, J.; Brandolin, P.; Palchetti, M.V.; Iparraguirre, J.; Virginil, N.; y Ariza Espinar, L. Las Plantas de Importancia Económica en Argentina, 1st ed.; UniRío Editora: Rio Cuarto, Argentina, 2019.

[23] Soejarto, D.D.; Compadre, C.M.; Kinghorn, A.D. Ethnobotanical notes on Stevia. Bot. Mus. Leafl. Harv. Univ. 1983, 29, 1–25.

[24] Soejarto, D.D. Ethnobotany of Stevia and Stevia rebaudiana. In Stevia. The Genus Stevia; Kinghorn, A.D., Ed.; Taylor and Francis: London, UK, 2002; Chapter 3; pp. 40–67.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

[25] 14. 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. Characterization of the antinociceptive activity from Stevia serrata Cav. Biomedicines 2020, 8, 79. [CrossRef]

[26] 11. Cariño-Cortés, R.; Hernández-Ceruelos, A.; Torres-Valencia, J.M.; González-Avila, M.; Arriaga-Alba, M.; Madrigal-Bujaidar, E. Antimutagenicity of Stevia pilosa and Stevia eupatoria evaluated with the Ames test. Toxicol. Vitro 2007, 21, 691–697. [CrossRef]

[27] Perez-Perez, I.; Valencia, J.M.T. Metabolitos secundarios aislados de las raíces y las hojas de Stevia jorullensis H.B.K. Bachelor's Thesis, Universidad Autónoma del Estado de Hidalgo, Pachuca de Soto, Mexico, 2016.

[28] Brown, A.E.; Moritán, M.G.; Ventura, B.; Hilgert, N.I.; Malizia, L.R. Plantas silvestres, ámbito doméstico y subsistencia. In Finca San Andrés. Un Espacio de Cambios Ambientales y Sociales en el Alto Bermejo; Brown, A.E., Moritán, M.G., Ventura, B., Hilgert, N.I., Malizia, L.R., Eds.; Subtrópico: Tucumán, Argentina, 2007; Chapter 7; p. 210.

[29] 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. Characterization of the antinociceptive activity from Stevia serrata Cav. Biomedicines 2020, 8, 79. [CrossRef]

[30] Joint FAO/WHO Expert Committee on Food Additives (JECFA). Steviol glycosides. In Compendium of Food Addditive Specifiations, 73th Meeting, FAO JECFA Monographs 10; FAO: Rome, 2010; pp 17−22.

[31] Starratt, A. N.; Kirby, C. W.; Pocs, R.; Brandle, J. E. Rebaudioside F, a diterpene glycoside from Stevia rebaudiana. Phytochemistry 2002, 59, 367−370.

[32] Ohta, M.; Sasa, S.; et al. Characterization of Novel Steviol Glycosides from Leaves of Stevia rebaudiana Morita. J. Appl. Glycosci. 2010, 57, 199−209.

[33] Charturvedula, V. S. P.; Clos, J. F.; Rhea, J.; Milanowski, D.; Mocek, U.; DuBois, G. E.; Prakash, I. Minor diterpenoid glycosides from the leaves of Stevia rebaudiana. Phytochem. Lett. 2011, 6, 175− 178.

[34] Charturvedula, V. S. P.; Rhea, J.; Milanowski, D.; Mocek, U.; Prakash, I. Two Minor Diterpene Glycosides from Leaves of Stevia rebaudiana. Nat. Prod. Commun. 2011, 6, 175−178.

[35] Charturvedula, V. S. P.; Prakash, I. Structures of the novel diterpene glycoside from Stevia rebaudiana. Carbohydr. Res. 2011, 346, 1057−1060.

[36] Charturvedula, V. S. P.; Upreti, M.; Prakash, I. Structures of the novel α-glycosyl linked diterpene glycoside from Stevia rebaudiana. Carbohydr. Res. 2011, 346, 2034−2038.

[37] Charturvedula, V. S. P.; Clos, J. F.; Rhea, J.; Milanowski, D.; Mocek, U.; DuBois, G. E.; Prakash, I. Minor diterpenoid glycosides from the leaves of Stevia rebaudiana. Phytochem. Lett. 2011, 6, 175− 178.

[38] Charturvedula, V. S. P.; Upreti, M.; Prakash, I. Diterpene Glycosides from Stevia rebaudiana. Molecules 2011, 16, 3552−3562.

[39] Debnath. (2008). Clonal propagation and antimicrobial activity of anendemic medicinal plant Stevia rebaudiana. Journal of Medicinal Plants Research. Vol.2(2), pp. 045-051

[40] Faizi, S., Rasool, N., Rashid, M., Khan, R. A., Ahmed, S., Khan, S.A., Ahmad, A., Bibi, N., Ahmed, S. A. (2003). Evaluation of the antimicrobial property of Polyalthia longifolia var. Pendula: isolation of a lactone as the active antibacterial agent from the ethanol extract of the stem. Phytother., Res. 17(10): 1177 - 1181.

[41] Adebolu, T.T, Oladimeji, S.A. (2005). Antimicrobial activity of leaf extracts of Ocimum gratissimum on selected diarrhea causing bacteria in south-western Nigeria.Afr. J. Biotechnol.,4 (7): 682-684.

[42] Parekh, J, Jadeja, D., Chanda, S. (2005). Efficacy of aqueous and methanol extracts of some medicinal Plants for potential antibacterial activity. Turk.J. Biol. 29: 203- 210.

[43] Tomita, T., Sato, N., Arai, T., Shiraishi, H., Sato, M, Takeuchi M, Kamio Y (1997). Bactericidal activity of a fermented hot-water extract from Stevia rebaudiana Bertoni and other food-borne pathogenic bacteria. Microbiol. Immunol. 41(12): 1005-1009.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

[44] Parekh, J, Jadeja, D., Chanda, S. (2005). Efficacy of aqueous and methanol extracts of some medicinal Plants for potential antibacterial activity. Turk.J. Biol. 29: 203- 210.

[45] Meireles MAA, Wang G-M, Hao Z-B, Shima K (2006). Stevia (Stevia rebaudiana Bertoni): futuristic view of the sweeter side of life.

[46] Escobar E, Piedrahita M, Gregory R (2020). Growth and viability of Streptococcus mutans in sucrose with different concentrations of Stevia rebaudiana Bertoni. Clinical oral investigations: 1-6.

[47] Nadaf SJ, Naikwadi HS (2015). A glance on sweet shrub Stevia rebaudiana Bertoni. Egyp Pharmaceut J., 14(3): 139.

[48] Fazal H, Ahmad N, Ullah I, Inayat H, Khan L, Abbasi BH (2011). Antibacterial potential in Parthenium hysterophorus, Stevia rebaudiana and Ginkgo biloba. Pak J Bot., 43(2): 1307-1313.

[50] Lemus-Mondaca R, Vega-Gálvez A, Rojas P, Stucken K, Delporte C, Valenzuela-Barra G, Jagus RJ, Agüero MV, Pasten A (2018). Antioxidant, antimicrobial and antiinflammatory potential of Stevia rebaudiana leaves: effect of different drying methods. J Appl Res Med Aroma Plant., 11: 37-46.

[51] Tadhani MB, Subhash R (2006b). In vitro antimicrobial activity of Stevia rebaudiana Bertoni leaves. Trop J Pharmaceut Res., 5(1): 557-560.

[52] Jayaraman S, Manoharan MS, Illanchezian S (2008). In-vitro antimicrobial and antitumor activities of Stevia rebaudiana (Asteraceae) leaf extracts. Trop J. Pharmaceut Res., 7(4): 1143-1149.

[53] Ghosh S, Subudhi E, Nayak S (2008). Antimicrobial assay of Stevia rebaudiana Bertoni leaf extracts against 10 pathogens. Int J Integr Biol., 2(1): 27-31.

[54] Atas M, Eruygur N, Ucar E, Ozyigit Y, Turgut K (2018). The Effects of different nitrogen doses on antioxidant and antimicrobial activity of Stevia (Stevia rebaudiana Bert.). Cell Mol Biol., (Noisy le Grand). 64(2).

[55] Gamboa F, Chaves M (2012). Antimicrobial potential of extracts from Stevia rebaudiana leaves against bacteria of importance in dental caries. Acta Odontológica Latinoamericana., 25(2): 171.

[56] Escobar E, Piedrahita M, Gregory R (2020). Growth and viability of Streptococcus mutans in sucrose with different concentrations of Stevia rebaudiana Bertoni. Clinical oral investigations: 1-6.

[57] Chen X, Daliri EB-M, Kim N, Kim J-R, Yoo D, Oh D-H (2020). Microbial Etiology and Prevention of Dental Caries: Exploiting Natural Products to Inhibit Cariogenic Biofilms. Pathogens., 9(7): 569.

[58] Mohammadi-Sichani M, Karbasizadeh V, Aghai F, Mofid MR (2012). Effect of different extracts of Stevia rebaudiana leaves on Streptococcus mutans growth. J Med Plant Res., 6(32): 4731-4734.

[59] Zohra FT (2015). Extraction of secondary metabolites, phytochemical screening and the analysis of antibacterial activity in Stevia rebaudiana. BRAC University.

[60] Raut D, Aruna K (2017). Antimicrobial activity of Stevia rebaudiana against antibiotic resistant ESBL producing uropathogens and evaluation of its antioxidant activity. Int J Adv Res Biol Sci., 4(3): 110-118.

[61] Miranda-Arámbula M, Olvera-Alvarado M, Lobo-Sánchez M, Pérez-Xochipa I, Ríos-Cortés AM, Cabrera-Hilerio SL (2017). Antibacterial activity of extracts of Stevia rebaudiana Bertoni against Staphylococcus aureus, Staphylococcus epidermidis and Pseudomonas aeruginosa.

[62] Singh S, Garg V, Yadav D, Beg MN, Sharma N (2012). In vitro antioxidative and antibacterial activities of various parts of Stevia rebaudiana (Bertoni). Int J Pharmac Pharmaceut Sci., 4(3): 468-473.

[63] Siddique AB, Rahman SMM, Hossain MA, Rashid MA (2014). Phytochemical screening and comparative antimicrobial potential of different extracts of Stevia rebaudiana Bertoni leaves. Asian Pac J Trop Diseas., 4(4): 275-280.

[64] Mali AB, Joshi M, Kulkarni V (2015). Phytochemical screening and antimicrobial activity of Stevia rebaudiana leaves. Int J Curr Microbiol App Sci., 4(10): 678-685.

[65] Debnath M (2008). Clonal propagation and antimicrobial activity of an endemic medicinal plant Stevia rebaudiana. J Med Plant Res., 2(2): 45-51.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

[66] Preethi D, Sridhar T, Josthna P, Naidu C (2011). Studies on antibacterial activity, phytochemical analysis of Stevia rebaudiana (Bert.)-An important calorie free biosweetner. J Ecobiotechnol.

[67] De Oliveira AJB, Gonçalves RAC, Chierrito TPC, dos Santos MM, de Souza LM, Gorin PAJ, Sassaki GL, Iacomini M (2011). Structure and degree of polymerisation of fructooligosaccharides present in roots and leaves of Stevia rebaudiana (Bert.) Bertoni. Food chem., 129(2): 305-311.

[67] Upadhyay S, Sharma S, Kumar R (2013). In vitro morphological, biochemical and microbial studies on elite clones of Stevia rebaudiana for enhanced production of Stevioside. Int J Tradition Herb Med., 1(1): 6-12.

[68] Yadav AK, Singh S, Dhyani D, Ahuja PS (2011). A review on the improvement of stevia [Stevia rebaudiana (Bertoni)]. Canad J Plant Sci., 91(1): 1-27.

[69] Darise M, Kohda H, Mizutani K, Tanaka O (1983). Chemical constituents of flowers of Stevia rebaudiana Bertoni. Agric Biol Chem., 47(1): 133-135.

[70] SAKAMOTO I, YAMASAKI K, TANAKA O (1977). Application of 13C NMR spectroscopy to chemistry of plant glycosides: rebaudiosides-D and-E, new sweet diterpene-glucosides of Stevia rebaudiana Bertoni. Chemical and Pharmaceutical Bulletin., 25(12): 3437-3439.

[71] Marković IS, Đarmati ZA, Abramović BF (2008). Chemical composition of leaf extracts of Stevia rebaudiana Bertoni grown experimentally in Vojvodina. J Serbian Chem Societ., 73(3): 283-297.

[72] Kumari M, Chandra S (2015). Phytochemical studies and estimation of major steviol glycosides in varied parts of Stevia rebaudiana. J Pharmacol., 7(7): 62-65.

[73] Michalik A, Hollinshead J, Jones L, Fleet GW, Yu C-Y, Hu X-G, van Well R, Horne G, Wilson FX, Kato A (2010). Steviamine, a new indolizidine alkaloid from Stevia rebaudiana. Phytochemistry Letters., 3(3): 136-138.

[74] Kumari M, Chandra S (2015). Phytochemical studies and estimation of major steviol glycosides in varied parts of Stevia rebaudiana. J Pharmacol., 7(7): 62-65.

[75] Kumari M, Chandra S (2015). Phytochemical studies and estimation of major steviol glycosides in varied parts of Stevia rebaudiana. J Pharmacol., 7(7): 62-65.

[76] Kovačević DB, Maras M, Barba FJ, Granato D, Roohinejad S, Mallikarjunan K, Montesano D, Lorenzo JM, Putnik P (2018). Innovative technologies for the recovery of phytochemicals from Stevia rebaudiana Bertoni leaves: A review. Food Chem., 268: 513-521.

[77] Howlader MMS, Ahmed SR, Kubra K, Bhuiyan MKH (2016). Biochemical and phytochemical evaluation of Stevia rebaudiana. Asian J Med Biologic Res., 2 (1): 121-130.

[78] Kovačević DB, Maras M, Barba FJ, Granato D, Roohinejad S, Mallikarjunan K, Montesano D, Lorenzo JM, Putnik P (2018). Innovative technologies for the recovery of phytochemicals from Stevia rebaudiana Bertoni leaves: A review. Food Chem., 268: 513-521.

[79] Howlader MMS, Ahmed SR, Kubra K, Bhuiyan MKH (2016). Biochemical and phytochemical evaluation of Stevia rebaudiana. Asian J Med Biologic Res., 2 (1): 121-130.

[80] Kumari M, Chandra S (2015). Phytochemical studies and estimation of major steviol glycosides in varied parts of Stevia rebaudiana. J Pharmacol., 7(7): 62-65.

[81] Myint KZ, Wu K, Xia Y, Fan Y, Shen J, Zhang P, Gu J (2020). Polyphenols from Stevia rebaudiana (Bertoni) leaves and their functional properties. J Food Sci., 85(2): 240- 248.

[82] A. Phaniendra, D.B. Jestadi, L. Periyasamy, Free radicals: properties, sources, targets, and their implication in various diseases, Indian J. Clin. Biochem. 30 (1) (2015) 11–26.

[83] S. Saeidnia, M. Abdollahi, Toxicological and pharmacological concerns on oxidative stress and related diseases, Toxicol. Appl. Pharmacol. 273 (3) (2013) 442–455.

[84] V. Lobo, et al., Free radicals, antioxidants and functional foods: impact on human health, Phcog. Rev. 4 (8) (2010) 118.

[85] S.-S. Han, et al., Antioxidant activity of crude extract and pure compounds of Acer ginnala Max, Bull. Kor. Chem. Soc. 25 (3) (2004) 389–391.

[86] E.A. Abou-Arab, A.A. Abou-Arab, F.M. Abu-Salem, PHYSICO-CHEMICAL ASSESSMENT

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

OF NATURAL SWEETENERS STEVIOSIDES PRODUCED FROM STEVIA Rebudiana bertoni PLANT, J. Food Dairy Sci. 34 (12) (2009) 11037–11057.

[87] K. Gaweł-Bęben, et al., Stevia rebaudiana Bert. leaf extracts as a multifunctional source of natural antioxidants, Molecules 20 (4) (2015) 5468–5486.

[88] Q. Zhang, et al., Toxicological evaluation of ethanolic extract from Stevia rebaudiana Bertoni leaves: genotoxicity and subchronic oral toxicity, Regul. Toxicol. Pharmacol. 86 (2017) 253–259.

[89] F.J. Barba, et al., Stevia rebaudiana Bertoni as a natural antioxidant/ antimicrobial for high pressure processed fruit extract: processing parameter optimization, Food Chem. 148 (2014) 261–267.

[90]J.C. Ruiz-Ruiz, Y.B. Moguel-Ordonez, ˜ M.R. Segura-Campos, Biological activity of Stevia rebaudiana Bertoni and their relationship to health, Crit. Rev. Food Sci. Nutr. 57 (12) (2017) 2680–2690.

[91]J. Carbonell-Capella, et al., Study of the interactions of bioactive compounds and antioxidant capacity of an exotic fruits beverage that sweetened with stevia, MOJ Process. Technol. 7 (3) (2019) 79–86.

[92] J. Sic ˇ Zlabur, ˇ et al., Antioxidant potential of fruit juice with added chokeberry powder (Aronia melanocarpa), Molecules 22 (12) (2017) 2158.

[93]A. Oliveira, M. Pintado, Stability of polyphenols and carotenoids in strawberry and peach yoghurt throughout in vitro gastrointestinal digestion, Food Funct. 6 (5) (2015) 1611–1619.

[94] Afify, A. E.-M.-M., El-Beltagi, H. S., El-Salam, S. M. A., & Omran, A. A. (2012). Biochemical changes in phenols, flavonoids, tannins, vitamin E, β-carotene and antioxidant activity during soaking of three white sorghum varieties. Asian Pacific Journal of Tropical Biomedicine, 2(3), 203. doi:10.1016/S2221-1691(12)60042-2

[95] Segura-Campos, M., Barbosa-Martín, E., Matus-Basto, Á., Cabrera-Amaro, D., Murguía-Olmedo, M., Moguel-Ordoñez, Y., & Betancur-Ancona, D. (2014). Comparison of chemical and functional properties of Stevia rebaudiana (Bertoni) varieties cultivated in Mexican Southeast. American Journal of Plant Sciences, 5(03), 286. doi:10.4236/ajps.2014.53039

[96] Tavarini, S., & Angelini, L. G. (2013). Stevia rebaudiana Bertoni as a source of bioactive compounds: The effect of harvest time, experimental site and crop age on steviol glycoside content and antioxidant properties. Journal of the Science of Food and Agriculture, 93(9), 2121–2129. doi:10.1002/jsfa.2013.93.issue-9

[97] Nayak, B., Liu, R. H., & Tang, J. (2015). Effect of processing on phenolic antioxidants of fruits, vegetables, and grains—a review. Critical Reviews in Food Science and Nutrition, 55(7), 887–918. doi:10.1080/ 10408398.2011.654142

[98] Gaweł-Bęben, K., Bujak, T., Nizioł-Łukaszewska, Z., Antosiewicz, B., Jakubczyk, A., Karaś, M., & Rybczyńska, K. (2015). Stevia rebaudiana Bert. leaf extracts as a multifunctional source of natural antioxidants. Molecules, 20(4), 5468–5486. doi:10.3390/molecules20045468

[99] Shukla, S., Mehta, A., Bajpai, V. K., & Shukla, S. (2009). In vitro antioxidant activity and total phenolic content of ethanolic leaf extract of Stevia rebaudiana Bert. Food and Chemical Toxicology, 47(9), 2338–2343. doi:10.1016/j.fct.2009.06.024

[100] Gasmalla, M. A. A., Yang, R., Amadou, I., & Hua, X. (2014). Nutritional composition of Stevia rebaudiana Bertoni leaf: Effect of drying method. Tropical Journal of Pharmaceutical Research, 13(1), 61–65. doi:10.4314/tjpr.v13i1.9

[101] Shukla, S., Mehta, A., Bajpai, V. K., & Shukla, S. (2009). In vitro antioxidant activity and total phenolic content of ethanolic leaf extract of Stevia rebaudiana Bert. Food and Chemical Toxicology, 47(9), 2338–2343. doi:10.1016/j.fct.2009.06.024

[102] Periche, A., Koutsidis, G., & Escriche, I. (2014). Composition of antioxidants and amino acids in Stevia leaf infusions. Plant Foods for Human Nutrition, 69(1), 1–7. doi:10.1007/s11130-013-0398-1

[103] Singh, S., Garg, V., Yadav, D., Beg, M. N., & Sharma, N. (2012). In vitro antioxidative and antibacterial activities of various parts of Stevia rebaudiana (Bertoni). International Journal of Pharmacy and Pharmaceutical Sciences, 4(3), 468–473.

[104] Shukla, S., Mehta, A., Bajpai, V. K., & Shukla, S. (2009). In vitro antioxidant activity and total phenolic content of ethanolic leaf extract of Stevia

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

rebaudiana Bert. Food and Chemical Toxicology, 47(9), 2338–2343. doi:10.1016/j.fct.2009.06.024

[105] Singh, S., Garg, V., Yadav, D., Beg, M. N., & Sharma, N. (2012). In vitro antioxidative and antibacterial activities of various parts of Stevia rebaudiana (Bertoni). International Journal of Pharmacy and Pharmaceutical Sciences, 4(3), 468–473.

[106] M. Hossain, *et al.* Cultivation and uses of stevia (Stevia rebaudiana Bertoni): a reviewAfr. J. Food Nutr. Sci., 17 (4) (2017), pp. 12745-12757

[107]D.B. Kovačević, *et al.*Innovative technologies for the recovery of phytochemicals from Stevia rebaudiana Bertoni leaves: a review Food Chem., 268 (2018), pp. 513-521

[108]S.M.S. Lopes, *et al.* Chemical characterization and prebiotic activity of fructo-oligosaccharides from Stevia rebaudiana (Bertoni) roots and in vitro adventitious root cultures Carbohydr. Polym., 152 (2016), pp. 718-725

[109]S.C. Hutchings, J.Y. Low, R.S. Keast Sugar reduction without compromising sensory perception. An impossible dream? Crit. Rev. Food Sci. Nutr., 59 (14) (2019), pp. 2287-2307

[110]J. Gao, *et al.* Effect of sugar replacement with stevianna and inulin on the texture and predictive glycaemic response of muffins Int. J. Food Sci. Technol., 51 (9) (2016), pp. 1979-1987

[111]X. Luo, *et al.* A review of food reformulation of baked products to reduce added sugar intakeTrends Food Sci. Technol., 86 (2019), pp. 412-425

[112]V.A.G. Salazar, *et al.* Stevia rebaudiana: a sweetener and potential bioactive ingredient in the development of functional cookies J. Funct.Foods, 44 (2018), pp. 183-190

[113]M. Vatankhah, *et al.* Quality attributes of reduced-sugar Iranian traditional sweet bread containing stevioside J. Food Meas. Char., 11 (3) (2017), pp. 1233-1239

[114]M.H. Ahouei, R. Pourahmad, A.A. Moghari Improvement of physical and sensory properties of whipping cream by replacing sucrose with rebaudioside A, isomalt and maltodextrinFood Sci. Technol., 39 (2018), pp. 170-175

[115]G. Sukhmani, *et al.*Natural sweeteners: health benefits of stevia Food Raw Mater., 6 (2) (2018), pp. 392-402

[116]A. Giri, H. Rao Effect of partial replacement of sugar with stevia on the quality of kulfi J. Food Sci. Technol., 51 (8) (2014), pp. 1612-1616

[117]K. Balaswamy, *et al.* Production of low calorie ready-to-serve fruit beverages using a natural sweetener, stevia (Stevia rebaudiana L.) Focus. Modern Food Indus., 3 (2014), pp. 59-65

[118]G.P. Parpinello, *et al.* Stevioside as a replacement of sucrose in peach juice: sensory evaluationJ. Sensory Stud., 16 (5) (2001), pp. 471-484

[119]U. Ahmad, *et al.* Antihyperlipidemic efficacy of aqueous extract of Stevia rebaudiana Bertoni in albino rats Lipids Health Dis., 17 (1) (2018), pp. 1-8

[120]I.F.d.O. Rocha, H.M.A. Bolini Passion fruit juice with different sweeteners: sensory profile by descriptive analysis and acceptance Food Sci. Nutr., 3 (2) (2015), pp. 129-139

[121]L.H. Mielby, *et al.* Changes in sensory characteristics and their relation with consumers' liking, wanting and sensory satisfaction: using dietary fibre and lime flavour in Stevia rebaudiana sweetened fruit beverages Food Res. Int., 82 (2016), pp. 14-21

[122]A. Alizadeh, A.S. Oskuyi, S. Amjadi The optimization of prebiotic sucrose-free mango nectar by response surface methodology: the effect of stevia and inulin on physicochemical and rheological properties Food Sci. Technol. Int., 25 (3) (2019), pp. 243-251

[123]J. Šic Žlabur, *et al.* Antioxidant potential of fruit juice with added chokeberry powder (Aronia melanocarpa) Molecules, 22 (12) (2017), p. 2158

[124]S. Tey, *et al.* Effects of aspartame-, monk fruit-, stevia-and sucrose-sweetened beverages on postprandial glucose, insulin and energy intake Int. J. Obes., 41 (3) (2017), pp. 450-457

[125]Y. Shevchenko, *et al.* Influence of Stevia—additives on antioxidant properties of different green teas Agro Food Ind. Hi-Tech, 24 (2013), pp. 22-26

[126]K. Lisak, *et al.*Influence of sweetener stevia on the quality of strawberry flavoured fresh yoghurt Mljekarstvo: časopis za unaprjeđenje proizvodnje i prerade mlijeka, 61 (3) (2011), pp. 220-225

[127]H. Karan, *et al.*Green bioplastics as part of a circular bioeconomy Trends Plant Sci., 24 (3) (2019), pp. 237-249

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

[128]R. Puscaselu, G. Gutt, S. Amariei Biopolymer-based films enriched with stevia rebaudiana used for the development of edible and soluble packaging Coatings, 9 (6) (2019), p. 360

[129] Arumugam, A. Subramaniam, P. Alagaraj Stevia as a natural sweetener: a reviewCardiovasc. Hematol. Agents Med. Chem., 18 (2) (2020), pp. 94-103

[130]V. Ilić, *et al.* Insight into anti-diabetic effect of low dose of stevioside Biomed. Pharmacother., 90 (2017), pp. 216-221

[131]G. Wilcox Insulin and insulin resistance Clin. Biochem. Rev., 26 (2) (2005), p. 19

[132]J. Ray, *et al.* Effects of Stevia rebaudiana on glucose homeostasis, blood pressure and inflammation: a critical review of past and current research evidenceInt. J. Clin. Res. Trials (2020), p. 5

[133]B. Salehi, *et al.* Antidiabetic potential of medicinal plants and their active componentsBiomolecules, 9 (10) (2019), p. 551

[134]B. Rizzo, *et al.* Steviol glycosides modulate glucose transport in different cell typesOxidative Medicine and Cellular Longevity, 2013 (2013)

[135]P. Jutabha, C. Toskulkao, V. Chatsudthipong Effect of stevioside on PAH transport by isolated perfused rabbit renal proximal tubule Can. J. Physiol. Pharmacol., 78 (9) (2000), pp. 737-744

[136]C. Yuajit, *et al.* Steviol reduces MDCK Cyst formation and growth by inhibiting CFTR channel activity and promoting proteasome-mediated CFTR degradation PLoS One, 8 (3) (2013), Article e58871

[137] M.A.A. Gasmalla, R. Yang, X. Hua Extraction of rebaudioside-A by sonication from Stevia rebaudiana Bertoni leaf and decolorization of the extract by polymers J. Food Sci. Technol., 52 (9) (2015), pp. 5946-5953

[138]T.-H. Chen, *et al.*Mechanism of the hypoglycemic effect of stevioside, a glycoside of Stevia rebaudiana Planta Med., 71 (2) (2005), pp. 108-113

[139]L. Garcia-Mier, *et al.* Polyphenol content and antioxidant activity of stevia and peppermint as a result of organic and conventional fertilizationJ. Food Qual. (2021), p. 2021

[140] J. He, *et al.* A newly discovered phenylethanoid glycoside from Stevia rebaudiana Bertoni affects insulin secretion in rat INS-1 islet β cells Molecules, 24 (22) (2019), p. 4178

[141]S.D. Anton, *et al.* Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels Appetite, 55 (1) (2010), pp. 37-43

[142] C.L. Rock, *et al.* Effects of diet composition on weight loss, metabolic factors and biomarkers in a 1-year weight loss intervention in obese women examined by baseline insulin resistance statusMetabolism, 65 (11) (2016), pp. 1605-1613

[143]S. Oparil, M.A. Weber Hypertension: a Companion to Brenner & Rector's the Kidney(2000)

[144]C.C.B. Anker, S. Rafiq, P.B. Jeppesen Effect of steviol glycosides on human health with emphasis on type 2 diabetic biomarkers: a systematic review and meta-analysis of randomized controlled trials Nutrients, 11 (9) (2019), p. 1965

[145]M. Melis Stevioside effect on renal function of normal and hypertensive ratsJ. Ethnopharmacol., 36 (3) (1992), pp. 213-217

[146]L. Wang, W. Wu Angiotensin-converting enzyme inhibiting ability of ethanol extracts, steviol glycosides and protein hydrolysates from stevia leaves Food Funct., 10 (12) (2019), pp. 7967-7972

[147]M. Ashwell Stevia, nature's zero-calorie sustainable sweetener: a new player in the fight against obesity Nutr. Today, 50 (3) (2015), p. 129

[148]N.A. Elnaga, *et al.* Effect of stevia sweetener consumption as non-caloric sweetening on body weight gain and biochemical's parameters in overweight female rats Ann. Agric. Sci. (Cairo), 61 (1) (2016), pp. 155-163

[149]U. Ahmad, R.S. Ahmad Anti diabetic property of aqueous extract of Stevia rebaudiana Bertoni leaves in Streptozotocin-induced diabetes in albino rats BMC Compl. Alternative Med., 18 (1) (2018), pp. 1-11

[150]G. Farhat, V. Berset, L. Moore Effects of stevia extract on postprandial glucose response, satiety and energy intake: a three-arm crossover trial Nutrients, 11 (12) (2019), p. 3036

[151]E. Gupta, *et al.* Anticancer potential of steviol in MCF-7 human breast cancer cellsPhcog. Mag., 13 (51) (2017), p. 345

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 715-746 | ISSN:2251-6727

[152]W.J. Loesche Microbiology of dental decay and periodontal disease Medical Microbiology (fourth ed.) (1996)

[153]E. Brambilla, *et al.* An in vitro and in vivo comparison of the effect of Stevia rebaudiana extracts on different caries-related variables: a randomized controlled trial pilot study Caries Res., 48 (1) (2014), pp. 19-23

[154]E.S. Siraj, K. Pushpanjali, B. Manoranjitha fficacy of stevioside sweetener on pH of plaque among young adults Dent. Res. J., 16 (2) (2019), p. 104

[155]W. Wen, *et al.* Pterostilbene suppresses ovarian cancer growth via induction of apoptosis and blockade of cell cycle progression involving inhibition of the STAT3 pathway Int. J. Mol. Sci., 19 (7) (2018), p. 1983

[156]S.M.S. Lopes, *et al.* Chemical characterization and prebiotic activity of fructo-oligosaccharides from Stevia rebaudiana (Bertoni) roots and in vitro adventitious root cultures Carbohydr. Polym., 152 (2016), pp. 718-725

[157]T.S. Mann, *et al.* In vitro cytotoxic activity guided essential oil composition of flowering twigs of Stevia rebaudiana Nat. Prod. Commun., 9 (5) (2014)

]158]J. Chen, *et al.* Steviol, a natural product inhibits proliferation of the gastrointestinal cancer cells intensively Oncotarget, 9 (41) (2018), Article 26299

]159]E. Gupta, *et al.* Anticancer potential of steviol in MCF-7 human breast cancer cells Phcog. Mag., 13 (51) (2017), p. 345

[160]N. Khare, S. Chandra Stevioside mediated chemosensitization studies and cytotoxicity assay on breast cancer cell lines MDA-MB-231 and SKBR3 Saudi J. Biol. Sci., 26 (7) (2019), pp. 1596-1601

[161]W. Wen, *et al.* Pterostilbene suppresses ovarian cancer growth via induction of apoptosis and blockade of cell cycle progression involving inhibition of the STAT3 pathway Int. J. Mol. Sci., 19 (7) (2018), p. 1983

[162]P. Jutabha, C. Toskulkao, V. Chatsudthipong Effect of stevioside on PAH transport by isolated perfused rabbit renal proximal tubule Can. J. Physiol. Pharmacol., 78 (9) (2000), pp. 737-744

[163]C. Yuajit, *et al.* Steviol reduces MDCK Cyst formation and growth by inhibiting CFTR channel activity and promoting proteasome-mediated CFTR degradation PLoS One, 8 (3) (2013), Article e58871

[164]A.E. Abou-Arab, A.A. Abou-Arab, M.F. Abu-Salem Physico-chemical assessment of natural sweeteners steviosides produced from Stevia rebaudiana Bertoni plant Afr. J. Food Sci., 4 (5) (2010), pp. 269-281

[165]M.A.A. Gasmalla, R. Yang, X. Hua Extraction of rebaudioside-A by sonication from Stevia rebaudiana Bertoni leaf and decolorization of the extract by polymers J. Food Sci. Technol., 52 (9) (2015), pp. 5946-5953

[166]N. Kumari, *et al.* Extraction, purification and analysis of sweet compounds in Stevia rebaudiana Bertoni using chromatographic techniques Indian J. Pharmaceut. Sci., 79 (4) (2017), pp. 617-624

[167]A.B. Rao, *et al.* Enzyme-assisted Extraction of Steviol Glycosides from the Leaves of Stevia rebaudiana Bertoni Google Patents (2019)

[168]V. Jaitak, B.S. Bandna, y.V. Kaul An efficient microwave-assisted extraction process of stevioside and rebaudioside-A from Stevia rebaudiana (Bertoni) Phytochem. Anal., 20 (3) (2009), pp. 240-245

[169]J.C. Evans, *et al.* Method of Producing Purified Rebaudioside A Compositions Using Solvent/antisolvent Crystallization Google Patents (2015)

[170]I. Prakash, A. Markosyan, C. Bunders evelopment of next generation stevia sweetener: rebaudioside M Foods, 3 (1) (2014), pp. 162-175

[171]V. López-Carbón, *et al.* Simple and efficient green extraction of steviol glycosides from Stevia rebaudiana leaves Foods, 8 (9) (2019), p. 402

[172]J. Liu, J.-w. Li, J. Tang Ultrasonically assisted extraction of total carbohydrates from Stevia rebaudiana Bertoni and identification of extracts Food Bioprod. Process., 88 (2–3) (2010), pp. 215-221

[173]M.A.A. Gasmalla, *et al.* Influence of sonication process parameters to the state of liquid concentration of extracted rebaudioside A from Stevia (Stevia rebaudiana bertoni) leaves Arab. J. Chem., 10 (5) (2017), pp. 726-731