International Journal of Humanities Social Science and Management (IJHSSM)
Volume 3, Issue 2, Mar.-Apr. 2023, pp: 298-309 www.ijhssm.org

A Review on Psidium Guajava, A Potential Phytopharmacological Source Of Natural Medicine For Better Health

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Date of Submission: 07-03-2023 Date of Acceptance: 19-03-2023

Abstract:
Psidium guajava (L.) belongs to the Myrtaceae family and it is an important fruit in tropical areas like India, Indonesia, Pakistan, Bangladesh, and South America. The leaves of the guava plant have been studied for their health benefits which are attributed to their plethora of phytochemicals, such as quercetin, avicularin, apigenin, guaijaverin, kaempferol, hyperin, myricetin, gallic acid, catechin, epicatechin, chlorogenic acid, epigallocatechin gallate, and caffeic acid. Extracts from guava leaves (GLs) have been studied for their biological activities, including anticancer, antidiabetic, antioxidant, antidiarrheal, antimicrobial, lipid-lowering, and hepatoprotection activities. In the present review, we comprehensively present the nutritional profile and phytochemical profile of GLs. Further, various bioactivities of the GL extracts are also discussed critically. Considering the phytochemical profile and beneficial effects of GLs, they can potentially be used as an ingredient in the development of functional foods and pharmaceuticals. More detailed clinical trialsneed to be conducted to establish the efficacy of the GL extracts.

I. Introduction :

Plants are a primary herbal supply of a mess of bioactive compounds.Since Foods 2021, 10, 752, numerous illnesses had been cured with numerous botanicalsin peoples remedies, and the nutraceutical enterprise has advanced each botanicalsand natural botanicals. We pay extra interest to chemicals.The natural complementmarketplace is projected to develop to approximately $86.seventy four billion through 2022, with the pharmaceutical zone having the most importantmarketplace share, observed through the nutritional complement enterprise. boom.Interestingly, the usage of natural dietary supplements in cosmetics, beverages, foods, and drugs broadly speaking is predicated at the leaves of the plant. Among all plant organs, leaves are the most important reservoirs of bioactive compounds which include: B. Secondary metabolites. Several current research have stated the phytochemical profiles and organic sports of numerous crop leaf extracts. Plant leaves are consequently taken into consideration agricultural waste, however are a wealthy supply of outstanding nutra-pharmaceutical compounds. The guava tree (Psidium guajava L.) (Figure 1), which belongs to the Myrtaceae family, is a totally specific and conventional plant cultivated for its a couple of medicinal and dietary residences. Guava has been grown and used as an critical fruit in tropical areas which include India, Indonesia, Pakistan, Bangladesh and South America. Various components of the guava tree, i. H. Roots, leaves, bark, stems, and end result had been utilized in many nations to deal with belly pain, diabetes, diarrhea,and different fitness illnesses. Guava leaves (Psidii guajavae folium; GL) are characterised through darkish green, oval, elliptical, with blunt tips. Guava leaves, along side the pulp and seeds, are used to deal with sure breathing and gastrointestinal situations and to boom platelet counts in dengue patients. GL is likewise generally used for its antispasmodic, antitussive, anti-inflammatory, antidiarrheal, antihypertensive, antiobesity, and antidiabetic residences . Animal version research have additionally confirmed the function of GL isolates as mighty antitumor,

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Volume 3, Issue 2, Mar.-Apr. 2023, pp: 298-309 www.ijhssm.org

anticancer, and cytotoxic agents. GLs are broadly hired for treating diarrhea and digestive illnesses, even as the fruit pulp is applied to beautify the platelet rely for treating dengue fever. The ability of guava leaf extracts for diarrhea remedy became additionally studied . The flavonoids found in guava leaf extract mainly decide their antibacterial hobby, even as quercetin, that's the maximum essential flavonoid of guava leaves, well-knownshows robust antidiarrheal sports. The antidiarrheal hobby of quercetin is ascribed to its enjoyable impact at the intestinal muscle lining which prevents bowel contractions. Guava leaf polysaccharides (GLPs) may be applied as an antioxidantadditive in meals and for diabetes remedy. The presence of a completely unique form of bioactive polyphenolic compounds, like quercetin and different flavonoids, and ferulic, caffeic, and gallic acids, found in guava leaves broadly speaking decide their bioactive and healing residences. These phenolic compounds are called secondary metabolites which show off robust antioxidant and immunostimulant sports. This overview targets to talk about the numerous dietary and bioactive compounds found in guava leaves and decipher the molecular foundation in their pharmacological and medicinal residences regarding human fitness, nutrition, and as complementary medicine.

Fig 1. Guajava fruit and leaf imag

1.Chemical CompositionProximate Composition
Guava leaves (GLs) are a rich source of various health-promoting micro- and macronutrients as well as bioactive compounds. They contain 82.47% moisture, 3.64% ash, 0.62% fat, 18.53% protein, 12.74% carbohydrates, 103 mg ascorbic acid, and 1717 mg gallic acid equivalents (GAE)/g total phenolic compounds . The overall proximate profile of GLs is presented.

Polysaccharides
Polysaccharides ar macromolecules that ar ubiquitously gift in nature. they're manufactured from long compound chains, that ar composed of sugar units. These polysaccharides demonstrate varied chemistry, biological, and medicine properties, like inhibitor, medicinal drug, medicinal drug, immunomodulatory, and anticancer activities. Guava leaf polysaccharides (GLPs) are often isolated victimization ultrasound-assisted extraction (UAE) (time: twenty min, power: 404 W, temperature: sixty two ◦C). These GLPs contain concerning nine.13% uronic acid and sixty four.42% total sugars, outof that a pair of.24% ar reducing sugars. GLPs ar soluble in water, whereas insoluble in organic solvents like alcohol, ethoxyethane, ester, acetone, and chloroform. Extracted GLP with a amount of a hundred μg/mL exhibits sensible inhibitor capability with fifty six.38% and 51.73% 2,2-diphenyl-1- picrylhydrazyl (DPPH) radical- and a pair of,20 -azino-bis(3- ethylbenzothiazoline-6-sulfonic acid (ABTS) radical cation-scavenging capability, severally . Similar results were conjointly rumored by Kong et al. They obtained up to zero.51% GLP victimization UAE that exhibited sensible DPPH• - and •OH-scavenging activity (72–86% and forty two.94–58.33%). GLPs are often classified into 2 groups: unsulfated and sulfated GLPs. SulfatedGLP contains concerning eighteen.58% sulphate content. Sulfated GLP exhibited sensible inhibitor activity in terms of DPPH, hydroxyl, and group radical-scavenging activity (0.10, 0.02, and 0.17 IC50, mg/mL, respectively). Studies showed that guava leaves extracts (GLE) effectively reduced the aerobic stress and toxicity caused by oxide in class cell lines (Vero cells) . GLPs are found to be useful in treating diabetes symptoms. Acarbose (an medicinal drug drug) is usually used for the treatment of sort a pair of polygenic disease . It acts as associate substance of organic compound hydrolases like α-glucosidase and α-amylase and so prevents speedy aldohexose unleash from advanced carbohydrates. This activity causes a number of the incompletely digestible advanced carbohydrates to stay within the gut and be transported to the colon. The internal organ microflora digests these advanced supermolecule fractions, inflicting channel issues like symptomand flatulence. A study rumored that GLP suppressed suppressed a lot of with efficiency than acarbose while not considerably block the α-amylase activity. Moreover, it conjointly caused a considerable call in fast glucose, total cholesterin,

International Journal of Humanities Social Science and Management (IJHSSM)
Volume 3, Issue 2, Mar.-Apr. 2023, pp: 298-309 www.ijhssm.org

total triglycerides, glycated humour supermolecule, creatinine, andmalonaldehyde Foods 2021, 10, 752 four of twenty in diabetic mice while not inflicting any major aspect impact. Therefore, GLP are often used as a replacement of acarbose for managing diabetes associated conjointly as an inhibitor additive in foods.

Proteins

Guava leaves contains nine.73% supermolecule on a dry weight basis. Proteins ar massive biomolecules composed of amino acids and act as building blocks of cells. Proteins play a serious role in growth and maintenance, accelerator regulation, and cell signal, and conjointly as biocatalysts. Recently, plant-based nutrients have gained potential due to the high demand for nutritionally wealthy food, significantly supermolecule. a good effort is currently being created to seek out extremely property nutritionally wealthy food sources. Thomas et al. reported sixteen.8 mg protein/100g eight|and eight} mg amino acids/100g in guava leaves as calculable in keeping with Lowry's and ninhydrin strategies, severally. Guava leaves will be used as a unique and property dietary supply as they're a chic supply of proteins, carbohydrates, and dietary fibers.

Minerals and Vitamins

Guava leaves area unit the made supply of minerals, like atomic number 20,potassium, sulfur, sodium, iron, boron, magnesium, manganese, and vitamins C and B. the upper concentrations of Mg, Na, S, Mn, ANd B in GLs makes them a extremely appropriate selection for human nutrition and conjointly as an animal feed to forestall substance deficiency . Thomas et al. according the concentration of minerals like Ca, P, K, Fe, and Mg as 1660, 360, 1602, 13.50, and 440 mg per 100g of guava leaf dry weight (DW), severally. The concentration of vitamins C and B was 103.0 and 14.80 mg per 100g DW, severally. Consumption of Ca- and P-rich GLs reduces the danger of deficiency-related diseases like hypocalcaemia, hypophosphatemia, and pathology. The study conjointly according that the concentration of Ca, P, Mg, Fe, and vitamin B complex in GLs was on top of that in guava fruit. the upper vitamin C content in GLs might facilitate in up the system and maintain the health of Foods 2021, 10, 752 five of twenty blood vessels, whereas vitamin B complex plays a crucial role in up blood circulation, nerve relaxation, and psychological feature perform stimulation

Phytochemical Profile.**Essential Oil Profile**

GL is a rich source of essential oils (Table 2). The main components of GL essential oils include 1,8-cineol and trans- caryophyllene. , α-pinene and 1,8- cineole are the most important. GL essential oils from the Philippines were found to contain different profiles of limonene, α-pinene, β-caryophyllene, and longicycles. Ecuadorian GL essential oil contained high levels of monoterpenes (limonene and α-pinene), while Tunisian guava leaf oil contained high levels of beryldiflorol and transcaryophyllene. In contrast to other studies where sesquiterpenes are the main compound in GL essential oils, monoterpene amounts are high. 4 α-serine-7(11)-enol, α-serine, β-caryophyllene, β-caryophyllene oxide are blended as the main components of GL essential oil. Another study identified 64 different compounds in essential oils extracted from GL by gas chromatography-mass spectrometry (GC-MS). Among them, caryophyllene (24.97%) was found to be predominant. It acts as an antioxidant, anticancer, anti- inflammatory, and antibacterial agent. In this study, the concentrations of non- oxygenated sesquiterpenes, oxygenated sesquiterpenes, and monoterpenes were reported to be 73.67%, 12.94%, and 8.55%, respectively. GL is a rich source of essential oils (Table 2). The main components of GL essential oils include 1,8-cineol and trans-caryophyllene. , α-pinene and 1,8- cineole are the most important. GL essential oils from the Philippines were found to contain different profiles of limonene, α-pinene, β- caryophyllene, and longicycles. Ecuadorian GL essential oil contained high levels of monoterpenes (limonene and α-pinene), while Tunisian guava leaf oil contained high levels of beryldiflorol and transcaryophyllene. In contrast to other studies where sesquiterpenes are the main compound in GL essential oils, monoterpene amounts are high. 4 α-serine- 7(11)-enol, α-serine, β-caryophyllene, β-caryophyllene oxide are blended as the main components of GL essential oil. Another study identified 64 different compounds in essential oils extracted from GL by gas chromatography-mass spectrometry (GC-MS). Among them, caryophyllene (24.97%) was found to be predominant. It acts as an antioxidant, anticancer, anti- inflammatory, and antibacterial agent. In this study, the concentrations of non- oxygenated sesquiterpenes, oxygenated sesquiterpenes, and monoterpenes were reported to be 73.67%, 12.94%, and 8.55%, respectively.

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Essential oil components of guava leaves.

Compounds References	Content/Composition
Essential oil components	
α-Pinene	1.53%
Benzaldehyde	0.83%
p-cymene	0.52%
Limonene	54.7%
1,8-Cineole	32.14%
β-cis-Ocimene	0.28%
+γ-Terpinene	0.38%
α-Terpineol	1.79%
β-Caryophyllene	2.91%
α-Humulene	0.77%
Total identified constituents	95.85%
Caryophyllene, copaene, nerolidol,	
caryophyllene oxide, humulene, limonene	
eucalyptol, beta-bisabolene, cadin-4-en-10-ol,	
trans-cadina-1,4-diene, sesquiterpenes,	
eugenol, isoeugenol, cevadine, emetine	
(extracted from guava leaves, Ludhiana,	
India using hydro-distillation by Clevenger-type apparatus)	

Phenolic Compounds:

GL is widely used as a traditional medicinal source in Asian countries dueto its hypoglycemic activity. As mentioned in the previous paragraph, they containhigh quality bioactive polysaccharides, proteins, lipids, essential oils, vitamins andminerals. Various secondary metabolites of GL include phenolic acids, flavonoids,triterpenoids, sesquiterpenes, glycosides, alkaloids, and saponins. Phenoliccompounds (PCs) serve as important bioactive compounds that impart antioxidant and hypoglycemic properties to GL. In general, these PCs play important roles in controlling various metabolic and physiological activities in the human body. Using high-performance liquid chromatography-diode array detector-quadrupole time-of-flight tandem mass spectrometry, approximately 72 different phenolic compounds were identified in the GL. In general, five quercetin glycosides are present in GL. The existence of two new benzophenone galloyl glycosides (guabinosides A and B) and quercetin galloyl glycoside (guabinoside C) has also been reported. 17 triterpenoids, 30 flavonoids and 19 sesquiterpenoids have also been reported in GL. In addition, diphenylmethane sesquiterpenoids diphenylmethane meroterpenoids (psiguadial A and B) and pseguanines A–D (1– 4) were also included in the GL. Epidemiological studies have demonstrated the role of polyphenolic compounds in chronic diseases such as diabetes, cancer, neurodegenerative diseases and cardiovascular disease. Phenolic compounds regulate numerous physiological processes such as cell proliferation, enzymatic activity, cellular redox potential, and signaling pathways to combat chronic disease. GLs are widely popular as a traditional source of medicine in Asian countries due to their antihyperglycemic effect. As mentioned in the previous sections, they contain superior quality bioactive polysaccharides, proteins, lipids, essential oils, vitamins, and minerals. The various secondary metabolites present in GLs include phenolic acids, flavonoids, triterpenoids, sesquiterpenes,

glycosides, alkaloids, and saponins. Phenolic compounds (PCs) serve as key bioactive compounds which provide antioxidant and hypoglycemic properties to GLs. Generally, these PCs play a major role in managing various metabolic and physiological activities in the human body. About seventy-two different phenolic compounds have been determined in GLs using high-performance liquid chromatography– diode array detector–quadrupole time-of-flight tandem massspectrometry . Generally, five quercetin glycosides are present in GLs. The presence of two new benzophenone galloyl glycosides (guavinosides A and B) and one quercetin galloyl glycoside (guavinoside C) was also reported . Seventeentypes of triterpenoids, thirty types of flavonoids, and nineteen types of sesquiterpenoids in GLs have also been reported . Moreover, diphenylmethane sesquiterpenoid-diphenylmethane meroterpenoids (psiguadials A and B) and psiguanins A–D (1–4) were also found in GLs. Epidemiological studies have established the roles of polyphenolic compounds against chronic diseases, such as diabetes, cancer, and neurodegenerative and cardiovascular diseases . Phenolic compounds modulate numerous physiological processes like cell proliferation, enzymatic activity, cellular redox potential, and signal transduction pathways to fight against chronic pathologies .

Phenolic Compounds:

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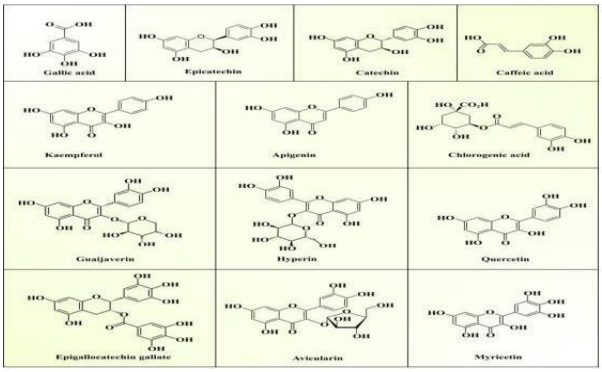
Phenolic compounds of guava leaves.

Origin of GuavaLeaves	Extract/Fraction	Bioactive Compounds
Leaves from Guangzhou (China)	Ethyl acetate- soluble fraction, n-butanol-soluble fraction, 75% ethanol extract, residual fraction, dichloromethane-	Quercetin, avicularin, apigenin, guaijaverin, kaempferol, hyperin, myricetin
	soluble fraction	
Leaves from Jing-cin Farm (Tianzhong Township, Changhua County, Taiwan)	Aqueous extract	Gallic acid, catechin, epicatechin, quercetin, chlorogenic acid, epigallocatechin gallate, caffeic acid
Leaves from Motril(Spain)	Acetone, water,andacetic acid extract	Proanthocyanidins(PAs)
Leaves from Jiangmen (China)	Methanol extract	Gallic acid, chlorogenic acid, epicatechin, mono-3- hydroxyethyl-quercetinglucuronide,rutin, isoquercitrin, quercetin-3-O-α-L-arabinofuranoside, quercetin-3-O-β-D- xylopyranoside, avicularin, quercitrin,kaempferol-3-arabofuranoside, quercetin, kaempferol

Among phenolic compounds, quercetin is an important bioactive phenolic compound of GL. A diet rich in bioactive compounds has received a lot of attention in recent years because it can reduce the risk of developing many chronic diseases. , and myricetin were separated and isolated from the ethyl acetate (EtOAc) soluble GL fraction using Sephadex LH-20 column chromatography and reversed-phase thin-layer chromatography (RP-TLC). The structure of the compound was elucidated using mass spectrometry and nuclear magnetic resonance spectroscopy. Phenolic compounds were isolated from non-fermented guava leaves (NFGL) and fermented guava leaves (FGL) using high- performance liquid chromatography coupled with electrospray ionization quadrupole time-of- flight mass spectrometry (HPLC-TOF-ESI/MS). extracted and analyzed. The authors reported the presence of gallic acid, rutin, chlorogenic acid, avicularin, isoquercitrin, quercitrin, and kaempferol in NFGL and FGL samples. Of these, quercetin, rutin, gallic acid, avicularin, and isoquercitrin accounted for approximately 65% of the total peak area in the chromatogram. Another study reported higher levels of catechin (2.25%) and epicatechin (1.45%), while gallic acid, chlorogenic acid, quercetin, caffeic acid and epigallocatechin gallate were low in GL extract. In addition, phenolic compounds (eugenol and isoeugenol) and alkaloids (sebazine and emetine) were detected. Optimized extraction ofproanthocyanidins as anti-diabetic and anti-obesity drugs from GL by HPLC- fluorescence detector (FLD)-ESI-MS and investigation of the degree of polymerization under different oxidation states. The phytochemical profile of GL extracts thus indicates the presence of numerous phytochemicals with varying medicinal efficacy, suggesting applications for treating human diseases.

International Journal of Humanities Social Science and Management (IJHSSM)
Volume 3, Issue 2, Mar.-Apr. 2023, pp: 298-309 www.ijhssm.org

Structures of phenolic compounds present in guava leaf extracts. Fig 2



Biological Activities of Guava Leaf Extracts

Diets enriched with bioactive compounds are gaining a lot of attention in recent years because of their potential to lower the chance of the event of diversechronic diseases. Seven pure compounds, quercetin, avicularin, apigenin, guaijaverin, like inhibitor, antibacterial drug, and anticancer effects compared to unsulfated ones. The helpful bioactivities of GL extract square measure given within the following subsections

Anticancer/Antitumor Activity

Liferation or a decrease, inflicting apoptosis . It may be as a result of numerous exogenous and endogenous elements concerned withinside the immoderate manufacturing of reactive oxygen species (ROS). This can bring about single- or double-strand breaks in DNA or RNA, base mutations, chromosomal breaking and reorganization, DNA cross- linkage, nucleic acid degradation, harm to cellular membrane integrity because of lipid peroxidation, and tumor formation . GLs are an amazing supply of triterpenoids, sesquiterpenes,tannins, psiguadials, unstable oils, flavonoids, benzophenone glycosides, and miscellaneous quinones . Psiguadial D and psiguadial C act as inhibitors of human hepatoma cells (HepG2) and protein tyrosine phosphatase 1B (PTP1B). Terpenoids and flavonoids found in GLs show off antitumor consequences via way of means of regulating the immune system, suppression of sign switch and tumor cellular adhesion, and an obstacle to tumor angiogenesis and cellular proliferation . Studies advise that those leaves show off a amazing inhibitory impact towards most cancers cellular traces like MDAMB-231 and Michigan Cancer Foundation-7 (MCF-7) for breast most cancers, Henrietta Lacks (HeLa) for cervical most cancers, KB for nasopharyngeal most cancers, LNCaP, DU 145, and prostate most cancers-3 (PC-3) for prostate most cancers, and colorectal 320 double minutes (COLO320DM) for colon most cancers. The increase of colorectaltumors mainly is predicated on angiogenesis, a technique via way of means of which new blood vessels expand from pre-present ones. Prolonged angiogenesis iscrucial for the development of tumors closer to malignancy because the blood vessels effectively deliver the growing tumor cells with crucial metabolites and oxygen and it additionally capabilities as an green method for mobile waste disposal. A examine become carried out to research the anticancer and antiangiogenic capacity of GL extracts towards angiogenesis-based colorectalmost cancers . Guava leaf extracts wealthy in nutrition E, flavonoids (apigenin), and β-caryophyllene verified sturdy antiproliferative hobby towards human colon carcinoma cellular traces Caco-2, HT-29, and SW480. The antiangiogenic assets of β-caryophyllene is on account of its interplay with the transcription aspect HIF-1α that regulates the organic pathways associated with hypoxia, tumor metastasis, and tumor-mediated angiogenesis. HIF-1α additionally mediates the transcription of vascular endothelial increase aspect (VEGF) withinside the presence of β- caryophyllene, explaining the antiangiogenic and anticolorectal most cancers assets of guava leaf extract. A caryophyllene-primarily based totally meroterpenoid known as guajadial from GLs become studied for its antiproliferative and antiestrogenic sports towards human breast most cancers cellular traces MCF-7 BUS and MCF-7 . The authors recommended that guajadialexerts its anticancer hobby via way of means of performing on estrogenic receptors, induction of apoptosis via way of means of blockading DNA synthesis, and inhibition of the cellular cycle on the G1 phase . A comparable examine indicated that 3 benzophenones, guavinoside B, guavinoside E, and 3,5- dihydroxy-2,4-dimethyl-1-O-(60 - O-galloyl-β-D-glucopyranosyl)-benzophenone, remoted from guava leaves inhibited the increase of HCT116 human colon most cancers cells . These compounds strongly prompted most cancers cellular apoptosis and modulated the expression of key proteins like extracellular sign- associated kinases (p-ERK1/2), p53, c-Jun NH2-terminal kinases (p-JNK), and cleaved caspases eight and 9, which might be concerned in apoptotic signaling and cellular proliferation. Another examine indicated the inhibitor impact of guava leaf extracts on lung most cancers genes, on the whole concerned in signaling pathways like PI3K-Akt . The authors said that

daidzein, ursolic acid, apigenin, genistein, and quercetin withinside the leaf extract strongly inhibited cyclindependent kinase 2,6 (CDK2,6), nutrition D3 receptor (VDR), hepatocyte increase aspect receptor (MET), epidermal increase aspect receptor (EGFR), progesterone receptor (PGR), peroxisome proliferator-activated receptor gamma (PPARG) and interleukin-2 (IL-2) proteins and finally blocked tumor proliferationand migration, tumor angiogenesis, tumor adhesion, and degradation of the extracellular matrix.

Antidiabetic Activity

Diabetes is a serious chronic disease, with approximately 10% of the world's population suffering from a disorder of blood glucose metabolism, primarily characterized by hyperglycemia. This situation is characterized eitherby insufficient secretion of insulin from pancreatic islet β-cells (type 1 diabetes) or by the inability of cells to act in response to secreted insulin (type 2 diabetes). The International Diabetes Federation (IDF) estimates that diabetes affects 451 million people, will kill 5 million people in 2017, and the global prevalence of diabetes will reach 693 million by 2045. Sustained conditions of hyperglycemia increase ROS production and lead to dyslipidemia, leading to severe cell damage and complications. GL is widely used as an ethnic medicine for diabetes management. Flavonoids and polysaccharides in GL have been described in several studies for their anti- diabetic potential. Guaijaverin and avicularin flavonoids from GL extracts are associated with significant improvements in islet β-cell function and hepatocyte morphology in diabetic mice. Guaijavelin inhibits the activity of theglucose homeostasis enzyme dipeptidyl peptidase IV, and avicularin inhibits intracellular lipid aggregation by inhibiting GLUT-4- mediated glucose uptake in vitro, with significant effects on 3T3-L1 adipocytes. showed no significant toxicity. We further tested the antidiabetic effect of GL polysaccharide (GLP) in combination with a high-fat diet in streptozotocin-induced diabetic mice. The authors found that GLP was associated with significant reductions in total cholesterol, triglycerides, serum glycated proteins, creatinine, fasting blood glucose, and malonaldehyde levels, as well as increases in total superoxide dismutase and total enzyme activity, shown to be related to antioxidant capacity in vivo. Suboptimal glycemic control can lead to elevated postprandial glucose levels. Inhibitors of the enzymes α-amylase and α-glucosidase can reduce postprandial glucose absorption and thus are potential targets for diabetes management. Polysaccharides were isolated from GL by ultrasound-assisted extraction and the anti-glycation activity of the extracted polysaccharides was investigated. The authors found that GLP strongly inhibited α-glucosidase with 99.54% inhibition at a concentration of 100 µg/mL and less inhibition of α-amylase with 14.06% inhibition at the 1 mg/mLdose level. discovered. milliliter. This result suggests that bioactive compoundsfrom GL can effectively reduce the risk of diabetes.

Antioxidant Activity

Oxygen is an important factor for aerobic organisms as it serves as the terminal electron acceptor during the respiratory process, which is an important source of energy production. However, free radicals produced during metabolic processes are responsible for many diseases in the human body, including inflammatory diseases, ischemic diseases, neurological diseases, hemochromatosis, emphysema, and acquired immunodeficiency syndrome. The presence of phenolic compounds such as gallic acid, catechol, taxifolin, ellagic acid and ferulic acid are involved in the antioxidant effects of GL. High- performance liquid chromatography analysis of GL extracts showed the presence of seven major flavonoids. Other bioactive compounds such as quercetin, hesperetin, kaempferol, quercitrin, rutin, catchkin, apigenin, kaempfertin, isoquinoline, and corilaginoline alkaloids have also been identified. These compounds are the main compounds responsible for the antioxidant properties of GL. Numerous studies have demonstrated the importance of antioxidant compounds from GL in minimizing the harmful effects of free radicals. The essential oil extracted from GL was found to be a moderate antioxidant with an IC50 value of ~460.37 ± 1.33 µg/mL as shown by the DPPH assay. The reduction in linoleic acid oxidation and peroxyl radical scavenging effect has been demonstrated by other analyzes on GL extracts. This study also showed a linear relationship between antioxidant efficacy, ability to scavenge free radicals, and phenolic content of GL extracts. The protective effect of GL polysaccharide was studied in zebrafish. The authors demonstrated that GL polysaccharide exerts a protective effect against hydrogen peroxide-induced oxidative stress by inhibiting the formation of reactive oxygen species (ROS) that reduce lipid peroxidation and cell death. showed. Another study found that over 4000ppm of GL extract could prevent oxidation in fresh pork sausages, suggesting its use as a functional food ingredient. GL was observed to co-ferment with yeast and bacterial strains to release

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Volume 3, Issue 2, Mar.-Apr. 2023, pp: 298-309 www.ijhssm.org

insoluble bound polyphenolic components, and fermentation enhanced the antioxidant capacity of soluble guava leaf polyphenols. In advanced studies, silvernanoparticles were synthesized using crude polysaccharides of GL and showed high DPPH radical and ABTS radical cation scavenging activity. The results indicate that GL extract can be a useful antioxidant in the food preservation and cosmetic industries.

Antidiarrhea ActivityAntimicrobial Activity

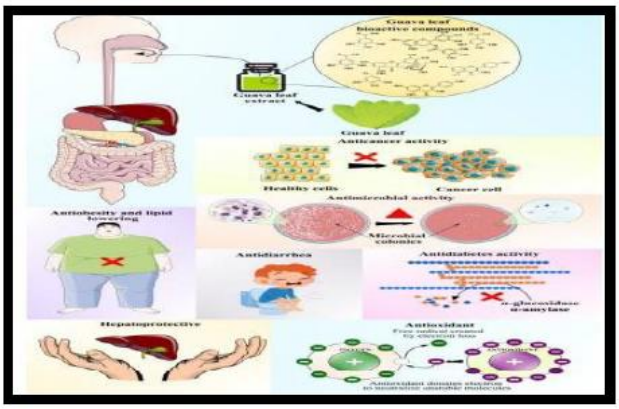
The evolution of novel disease-causing strains and resistance of microbes toclassical antibiotics are currently serious concerns. Diarrhea is currently one of theleading causes of death in children aged 0-5. Attempts have been made to find new drugs with minimal side effects on other organs of the body. In developing countries, attention has been focused on identifying new phytochemicals from medicinal plants to develop new drugs with minimal side effects. Most of the pharmaceutical industry is busy developing a range of potential treatments to combat the disease. Many treatments are available to treat diarrhea in the form of synthetic drugs that have many side effects on the human body, including constipation, intestinal obstruction, inducing bronchospasm, and vomiting.Combatting these side effects requires a focus on researching and isolating potent bioactive compounds from medicinal plants. GL has antidiarrheal properties, as reported by many researchers. The authors reported that administration of the extract at concentrations of 750 and 500 mg/kg could reduce diarrhea in castor oil-fed rats. Separately, similar activity in aqueous extracts of rodent GL has been used. They reported that oral administration of GL extract at doses of 52- 410 mg/kg suppressed diarrhea and resulted in decreased intestinal transit and extended elimination of unwanted gastric products. Furthermore, loperamide (13 mg/kg, p.o.) reduced stool development with diarrhea severity in the same animal model. GL extract dose-dependently decreased diarrhea symptoms. Various concentrations of GL in rabbits showed concentration-dependent pulsations and pendulum contractions in the duodenum.

Biological activities of guava leaf (GL) extracts.

Origin ofLeaves	Type ofExtract	Bioactive Compounds	Type of Cell Lines, Type of Study	Results
Antidiabetic activity				
Leaves from Bangladesh	Ethanolicextract	.	Wistar rats with alloxan-induced diabetes	Administration of guavaleaf extract significantly reduced($p < 0.05$) BGL at doses of 1.00 and 0.50 g/kg, as well as 0.75 g/kg in alloxan- induced diabetic Wistarrats ($p < 0.001$)
Leaves from Guangdong (China)	Ultrasound-assisted ethanolic extract	Polysaccharides	In vitro	Inhibited α- glucosidase activity and reduced the breakdown of glucoseand prevented
				flatulence by not attenuating α-amylaseactivity
-	65% ethanol and ethyl acetate extract	Flavonoids (guaijaverin and avicularin)	Kunming mice with high-fat dietand streptozotocin-induced diabetes	GLF (200 mg/kg/day) not able to prevent loss of body weight, which indicated the inability to remove the damage induced by streptozotocin

International Journal of Humanities Social Science and Management (IJHSSM)
Volume 3, Issue 2, Mar.-Apr. 2023, pp: 298-309 www.ijhssm.org

Various bioactivities of guava leaf extracts. Fig 3



Hepatoprotective Properties

Hepatic lipid metabolism requires the activity of adenosine monophosphate-activated protein kinase (AMPK) and PPARα, and rats treated with guava leaf extract showed enhanced activity of both parameters. In addition, guava leaf extract may improve hepatic insulin resistance.Alanine transaminase (ALT) and aspartate aminotransferase (AST) are associated with liver function. Elevated values are a sign of fatty liver and may be reduced by administration of guava leaf extract.In addition, diabetics may experience liver enlargement, fat, as the main function of the liver is to stabilize blood sugar levels. It has been foundto be closely associated with liver dysfunction such as liver disease and fibrosis. Abnormalities in glucose, lipid, and insulin metabolism are considered the classic condition of type 2 diabetes. The bioactive compounds guaijaverin and avicularin in guava leaves are potent inhibitors of glucose uptake mediated by dipeptidyl peptidase IV and glucose transporter 4 (GLUT4), respectively, and have been implicated in elevated blood glucose levels. increase. Treatment with guava leaf extract with increased flavonoid levels promoted insulin resistance and limited increases in glucose and lipid levels in rats with type 2 diabetes mellitus.

Antiobesity and Lipid-Lowering Activity

GL is known to have antidiabetic effects and is used in the treatment of diabetes. Treatment of diabetic rats with 200 mg/kg body weight (bw) of GL reduced blood glucose levels and promoted oral glucose tolerance, which is essential to prevent weight loss due to impaired glucose metabolism. Improved activity of hexokinase and his G6PDH and decreased activity of gluconeogenic enzymes and glucose-6-phosphatase stabilized insulin levels. Hypercholesterolemia, or high levels of cholesterol in the blood, occurs as a resultof improper dietary habits, genetic predisposition, or improper lifestyle.GL has antioxidant properties with health-promoting functions. It contains many bioactivecompounds with kings. Guava leaf extracts have been reported to contain flavonoids such as quercetin, kaempferol, guaijaverin, avicularin, myricetin, hyperin, and apigenin. Furthermore, these flavonoids contributed inhibitory effects on α-glucosidase and α-amylase. From this study, we could conclude that the presence of the -OH group in his third position of the flavonoid is responsible for the inhibitory effect. Although the inhibitory effects of myricetin, quercetin and kaempferol on α-glucosidase and α-amylase were the highest, the synergistic effect was very evident.The presence of glycosides is essential to perform their inhibitory function. Administration of ethanol extracts from guava leaves to rabbit diets significantly decreased serum triglyceride levels and low-density lipoproteins, and reduced high-density lipoprotein levels. Similar findings have been reported in rats suffering from chronic diabetes along with hyperlipidemia.

GLs as a Functional Food Ingredient

GL is known to have antidiabetic effects and is used in the treatment of diabetes. Treatment of diabetic rats with 200 mg/kg body weight (bw) of GL reduced blood glucose levels and promoted oral glucose tolerance, which is essential to prevent weight loss due to impaired glucose metabolism. Improved activity of hexokinase and his G6PDH and decreased activity of gluconeogenic enzymes and glucose-6-phosphatase stabilized insulin levels. Hypercholesterolemia, or high blood cholesterol levels, occurs as a result ofimproper diet, genetic predisposition, or improper lifestyle. GL contains

many bioactive compounds with antioxidant properties that have health-promoting properties. Wang et al reported the presence of flavonoids such as quercetin, kaempferol, guaijaverin, avicularin, myricetin, hype Recent articles have shown that plant byproducts, such as fruit or vegetable pomace, seeds, husk/bran/seed coat, peel, and leaves, are important source of bioactive compounds and can be utilized as functional food ingredients. Numerous reports suggest the beneficial effects of the inclusion of GL extract in food as a functional food ingredient, because of the presence of a myriad of compounds like rutin, naringenin, gallic acid, catechin, epicatechin, kaempferol, isoflavonoids, vitamins, citric acid, and flavonoids such as quercetin and guaijaverin, which are well known for their antimicrobial, antioxidant, and anti-inflammatory actions . A study on the hypoglycemic effects of GL extract, due to the presence of its phenolic compounds, were shown to improve vascular dysfunction in mice with diet-induced obesity . Recently, GL extract has been used in the preparation of jelly with pectin and was subjected to mass spectrometry analysis, which verified the presence of quercetin, gallocatechin, esculin, 3-sinapoylquinic acid, ellagic acid, gallic acid, and citric acid that are responsible for antioxidant and antimicrobial properties. Additionally, the addition of GL did not cause any change in the texture properties of the jelly . The potential of GL as a functional immunostimulatory component of foods fortified with high levels of antioxidants and phenolic compounds has also been investigated in detail. Another study evaluating the food-drug interactions of guava leaf tea (GLT), a functional food and beverage marketed in Japan, showed no possible interactions between GLT and drugs, suggesting that food-drug The results suggested the safety of GLT withrespect to the interaction of People with pre-diabetes, who are at high riskof developing diabetes, take GLT to reduce the rapid rise in blood sugar levels after meals. known to contribute to health through malabsorption of sugars or lipids. In addition, a recent report examining herbal teas also found that guava tea showed no drug interactions. Another study that added yellow strawberry GL, which is rich in phenolic and flavonoid compounds, to the diet of laying hens showed antibacterial and antioxidant effects that could improve egg quality through an inhibitory mechanism of the enzyme cyclooxygenase (COX) pathway. rice field. Fundamental role as an inflammatory mediator. Furthermore, we found that the natural antioxidants present in GL after fortification of fresh pork sausage effectively retarded the lipid oxidation process in fresh pork sausage. These examples demonstrate that GL is an excellent active ingredient source for functional additives in food without altering rheological or sensory properties.Essential to perform the suppression function.

II. Conclusions and Future Perspectives

GLs are documented as a supply of herbal compounds which might be effortlessly available. GL extracts were appreciably studied for his or her excessive degrees of antioxidant, anticancer, hypoglycemic, and different organic activities. The wealthy presence of minerals and proteins, in addition to vitamins, in GLs sell their usage as an instantaneous supply of nutrients. The presence of severa bioactive chemical substances in GLs were stated to beautify and stabilize unique physiological and metabolic features withinside the human body. GL additionally includes many secondary metabolites, along with flavonoids,triterpenoids, sesquiterpenes, glycosides, alkaloids, saponins, and different phenolic compounds. These compounds play a key position as immunestimulators and modulators of continual illnesses such as diabetes, cancer, and gastrointestinal, neurodegenerative, and cardiovascular illnesses. GL critical oil additionally has antioxidant, antimicrobial, and antiproliferative interest. GL extracts that include excessive concentrations of nutrition E, flavone (apigenin), or β-caryophyllene display widespread antiproliferative interest in opposition to colon carcinoma and diverse kinds of human cancer. GL consequently has bizarre traits and pharmaceutical and medicinal profiles that sell numerous packages as an critical plant aspect in medicinal studies and a low-fee aspect in foodstuffs. Furthermore, as an aspect of plant origin, GL can also additionally assist in mitigate drug resistance, that's a primary hassle for the pharmaceutical enterprise and additionally may be applied as a useful meals aspect, which might be in excessive demand. Thus, guava extract with its more than one medicinal houses wishes to be in addition evolved for wider applicability. In destiny studies, the identity and isolation of latest chemical additives for the improvement of precise merchandise can be the important thing studies area.

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