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PHYTOCHEMISTRY AND PHARMACOLOGICAL ACTIVITIES OF *PSIDIUM GUAJAVA*: A REVIEW

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ABSTRACT

Keywords:

Guava,
Psidium guajava,
Phytochemistry,
Pharmacology

Guava (*Psidium guajava* Linn.) Family Myrtaceae is important plant used traditionally for medicinal purposes. Guava is rich in antioxidants compounds and contains a high level of ascorbic acid. The pharmacological actions and the medicinal uses of aqueous extracts of guava leaves in folk medicine include the treatment of various type of gastrointestinal disturbances such as vomiting, diarrhea, inhibition of the peristaltic reflex, gastroenteritis, spasmolytic activity, dysentery, abdominal distention, flatulence and gastric pain. The important active constituents are essential oils, flavonoids, carotenoids, polyphenolic compounds, pentacyclic triterpenoids, esters, and aldehydes etc. This paper explains the Evidence-based information regarding the phytochemistry and pharmacological activity of this plant.

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INTRODUCTION: Guava (*Psidium guajava* Linn.), belonging to the Family Myrtaceae, is originated in the tropical South America¹ and grows wild in Bangladesh, India, Thailand, Brazil, Florida, West Indies, California and also in several other countries². Guava is rich in antioxidants compounds and contains a high level of ascorbic acid ranging from 174.2 to 396.7 mg/100 g fresh fruit³. Myricetin and apigenin were reported to be 549.5 and 579.0 mg/kg dry weight, respectively⁴. It plays a vital role in fulfilling the vitamin C deficiency among the people of the country since 100 g of fruit contains about 260 mg of vitam⁵, which is 2–5 times higher than the fresh orange. The wood is hard and tough⁶, used as posts for rural house buildings.

The pharmacological actions and the medicinal uses of aqueous extracts of guava leaves in folk medicine include the treatment of various types of gastrointestinal disturbances such as vomiting, diarrhea, inhibition of the peristaltic reflex, gastroenteritis, spasmolytic activity, dysentery, abdominal distention, flatulence and gastric pain⁷. These extracts have also been indicated to cause disturbances of the central nervous system: insomnia, convulsions and epilepsy⁸. Bronchitis, asthma attacks, cough, pulmonary diseases could be also treated with guava teas⁹ and could also be useful as anti-inflammatory and hemostatic agent¹⁰. Moreover, aqueous extracts of guava leaves were described to be effective against a number of microbial strains¹¹ and anti-rotavirus activity¹².

Traditional uses: *Psidium guajava*, is an important food crop and medicinal plant in tropical and subtropical countries is widely used like food and in folk medicine around of the world. A survey of the literature shows *P. guajava* is mainly known for its antispasmodic and antimicrobial properties in the treatment of diarrhoea and dysentery. It has also been used

extensively as a hypo-glycaemic agent. Many pharmacological studies have demonstrated the ability of this plant to exhibit antioxidant, hepato-protective, anti-allergy, antimicrobial, antigenotoxic, antiplasmodial, cytotoxic, antispasmodic, cardioactive, anticough, antidiabetic, anti-inflammatory and antinociceptive activities, supporting its traditional uses¹³.

Chemical constituents:

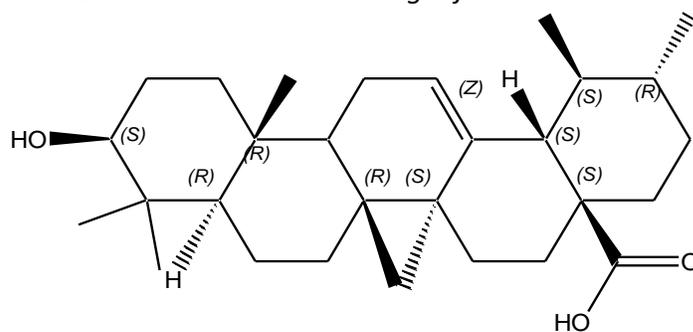
- **Leaves:** The constituents of essential oils from the leaves of *Psidium guajava* Linn were analyzed by GC-MS qualitatively and quantitatively. Sixty compounds of the essential oils were identified at rate 90.56%. The major components were caryophyllene (18.81%), copaene (11.80%), [1aR-(1a alpha, 4a alpha, 7 alpha, 7a beta, 7b alpha)]-decahydro-1, 1, 7-trimethyl-4-methylene-1H-cycloprop[e] azulene (10.27%), eucalyptol ()¹⁴ One new pentacyclic triterpenoid psidiumoic acid along with four known compounds beta-sitosterol, obtusol, oleanolic acid, and ursolic acid have been isolated from the leaves of *Psidium guajava*.

The new constituent has been characterized as 2 alpha-glycolyl-3beta-hydroxyolean-12-en-28-oic acid through 2D NMR techniques¹⁵. Five constituents including one new pentacyclic triterpenoid guajanoic acid and four known compounds beta-sitosterol, uvaol, oleanolic acid, and ursolic acid have been isolated from the leaves of *Psidium guajava*. The new constituent has been characterized as 3beta-p-E-coumaroyloxy-2alpha-methoxyurs-12-en-28-oic acid¹⁶. Guajadial, a novel caryophyllene-based meroterpenoid, was isolated from the Leaves of *Psidium guajava*¹⁷. Three novel sesquiterpenoid-based

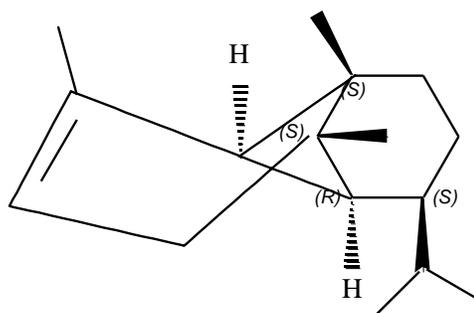
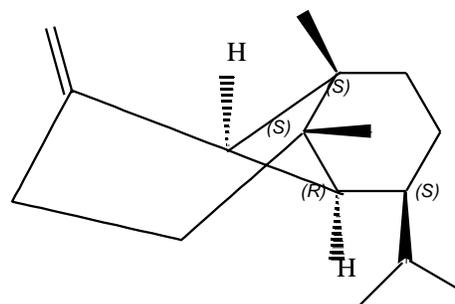
meroterpenoids of psidials A-C have been isolated from the leaves of *Psidium guajava* L. Their complete structures were elucidated by spectral and chemical methods, and that was confirmed by single-crystal X-ray diffraction analysis. Psidial B and C showed the new skeleton of the 3, 5-diformylbenzyl phloroglucinol-coupled sesquiterpenoid¹⁸. Four antibacterial compounds were isolated from leaves of guava (*Psidium guajava* L.), two new flavonoid glycosides, morin-3-O- α -L-lyxopyranoside and morin-3-O- α -L-arabopyranoside, and two known flavonoids, guajavarin and quercetin, were identified¹⁹. The methanolic extract of leaf contain a trace of quercetin aglycone together with five glycosides was isolated from this active fraction and identified as quercetin 3-O- α -L-arabinoside (guajavarin); quercetin 3-O- β -D-glucoside (isoquercetin); quercetin 3-O- β -D-galactoside (hyperin); quercetin 3-O- β -L-rhamnoside (quercitrin) and quercetin 3-O-gentobioside²⁰.

Two triterpenoids, 20 β -acetoxy-2 α , 3 β -dihydroxyurs-12-en-28-oic acid (guavanoic acid), and 2 α , 3 β -dihydroxy-24-*p*-z-coumaroyloxyurs-12-en-28-oic acid (guavacoumaric acid), along with six known compounds 2 α -hydroxyursolic acid, jacoumaric acid, isoneriuoumaric acid, asiatic acid, ilelatifol D and β -sitosterol-3-O- β -D-glucopyranoside, have been isolated from the leaves of *Psidium guajava*²¹. Two new triterpenoids, guajavolide (2 α , 3 β , 6 β , 23-tetrahydroxyurs-12-en-28, 20 β -olide) and guavenoic acid (2 α , 3 β , 6 β , 23-tetrahydroxyurs-12, 20 (30)-dien-28-oic acid) along with one known triterpene oleanolic acid were isolated from the fresh leaves of *Psidium guajava*²². Two

triterpenoids, 20 β -acetoxy-2 α , 3 β -dihydroxyurs-12-en-28-oic acid (guavanoic acid), and 2 α , 3 β -dihydroxy-24-*p*-z-coumaroyloxyurs-12-en-28-oic acid (guavacoumaric acid), along with six known compounds 2 α -hydroxyursolic acid, jacoumaric acid, isoneriuoumaric acid, asiatic acid, ilelatifol D and β -sitosterol-3-O- β -D-glucopyranoside, have been isolated from the leaves of *Psidium guajava*²³.



a. Ursolic acid

b. (i) α copaeneb. (ii) β copaene

- **Seeds:** Ten phenolic and flavonoid compounds including one new acylated flavonol glycoside were isolated from *Psidium guajava* seeds. The new compound isolated was quercetin-3-O-beta-D-(2''-O-galloyl glucoside)-4'-O-vinylpropionate²⁴. Diguajadial is a new meroterpenoid, which is symmetric homo dimeric ether with two guajadial units was isolated from *Psidium guajava* seeds²⁵. Guava seeds found to contain phenolic fraction with results varying from 0.380 to 1.738% (w/w)²⁶. The high-performance liquid chromatography chromatogram showed that the Guava 'Horana red' variety contained almost exclusively lycopene, with a small amount of lutein, beta-carotene and beta-cryptoxanthin²⁷.
- **Flesh:** Sixteen carotenoids were isolated from the flesh of Brazilian red guavas. Their structures were established by means of UV-visible, 400 and 500 MHz ¹H NMR, 120 and 125 MHz ¹³C NMR, mass spectra, and circular dichroism spectra. Thirteen of the carotenoids identified are reported as guava carotenoids for the first time²⁸.
- **Fruits:** The ripe edible fruits of *Psidium guajava* L. was phytochemically investigated, three benzophenone glycosides, 2, 6- dihydroxy- 3, 5- dimethyl- 4- O- beta- D- glucopyranosyl- benzophenone, 2, 6- dihydroxy- 3- methyl-4-O-(6''- O- galloyl- beta- D- glucopyranosyl)- benzophenone, 2, 6- dihydroxy- 3, 5- dimethyl- 4- O- (6''-O- galloyl- beta- D- glucopyranosyl)- benzophenone were isolated by means of chromatography²⁹. A water-soluble polysaccharide was isolated from hot

aqueous extracts of fruits of *Psidium guajava*. The polysaccharide was found to contain 2-O-methyl-l-arabinose, 2-O-acetyl-D-galactose, and D-methyl galacturonate in a molar ratio of approximately 1:1:1³⁰. Immature fruits and those in their intermediate stage of maturation, were predominantly the aldehydes such as (*E*)-2-hexenal and (*Z*)-3-hexenal. In mature fruits, esters like *Z*-3-hexenyl acetate and *E*-3-hexenyl acetate and sesquiterpenes caryophyllene, α -humulene and β -bisabolene are present³¹. Characterization of the aromatic profile in commercial guava essence and fresh fruit puree by GC-MS yielded a total of 51 components quantified. Commercial essence was characterized to present a volatile profile rich in components with low molecular weight, especially alcohols, esters, and aldehydes, whereas in the fresh fruit puree terpenic hydrocarbons and 3-hydroxy-2-butanone were the most abundant components.

In the olfactometric analyses totals of 43 and 48 aroma active components were detected by the panelists in commercial essence and fruit puree, respectively. New components were described for the first time as active aromatic constituents in pink guava fruit (3-penten-2-ol and 2-butenyl acetate). Principal differences between the aroma of the commercial guava essence and the fresh fruit puree could be related to acetic acid, 3-hydroxy-2-butanone, 3-methyl-1-butanol, 2,3-butanediol, 3-methylbutanoic acid, (*Z*)-3-hexen-1-ol, 6-methyl-5-hepten-2-one, limonene, octanol, ethyl octanoate, 3-phenylpropanol, cinnamyl alcohol, alpha-

copaene, and an unknown component. (E)-2-Hexenal seems to be more significant to the aroma of the commercial essence than of the fresh fruit puree³².

- **Whole plant:** An extract of whole guava, after TLC and GLC, showed the presence of two monoterpenes and nine sesquiterpenes. β -Caryophyllene comprised 95% of this fraction³³. Bioautography directed chromatographic fractionation, yield biologically active compound, quercetin- 3- O- alpha- l- arabinopyranoside (guaijaverin), from

crude methanol extract of *P. guajava*³⁴. Numerous tannins, polyphenolic compounds, flavonoids, pentacyclic triterpenoids, guaijaverin, quercetin, and other chemical compounds are present in the plant³⁵. Nine more compounds were isolated from this plant, and the structures of them were identified as ursolic acid, 2 alpha-hydroxyursolic acid, 2 alpha-hydroxyoleanolic acid, morin- 3- O- alpha- L- arabopyranoside, quercetin, hyperin, myricetin- 3- O- beta- D- glucoside, quercetin- 3- O- beta- D- glucuronopyranoside, 1- O- galloyl- beta- D- glucose³⁶.

Pharmacological Activity:

PHARMACOLOGICAL ACTIVITY	DETAILS	REFERENCE
Antioxidant activity	The extracts from distilled water, 65% ethanol and 95% ethanol respectively showed effects on scavenging hydroxyl radicals and inhibiting lipid peroxidation in the dose-dependent manner, had 50% effective concentration (EC50) on scavenging hydroxyl radicals of 0.63, 0.47 and 0.58g/L, had EC50 on inhibiting lipid peroxidation of 0.20, 0.035, 0.18g/L.	37
Treatment of cough	The water extract of the plant at doses of 2 and 5 g/kg, p.o. decreased the frequency of cough induced by capsaicin aerosol by 35 and 54%, respectively, as compared to the control, within 10 min after injection of the extract, (P < 0.01).	11
Anti-diabetic activity	The ethanolic stem bark extract exhibited statistically significant hypoglycaemic activity in alloxan-induced hyperglycaemic rats but was devoid of significant hypoglycaemic effect in normal and normal glucose loaded rats (OGTT). In both acute and sub-acute tests, the water extract, at an oral dose of 250 mg/kg, showed statistically significant hypoglycemic activity.	38, 39
Antimicrobial activity	<i>Psidium guajava</i> aqueous bark and methanolic extracts were found to possess anti-bacterial activity. Four antibacterial compounds were isolated from leaves of guava were identified. The minimum inhibition concentration of morin-3-O-alpha-L-lyxopyranoside and morin-3-O-alpha-L-arabopyranoside was 200 microg/ml for each against <i>Salmonella enteritidis</i> , and 250 microg/ml and 300 microg/ml against <i>Bacillus cereus</i> , respectively.	40, 19
Hepatoprotective activity	<i>P. guajava</i> aqueous leaf extracts (250 and 500mg/kg, po) possesses good hepatoprotective activity.	41

Antidiarrhoeal activity	<i>Psidium guajava</i> leaf aqueous extract (PGE) (50-400 mg/kg p.o.) produced dose-dependent and significant protection of rats and mice against castor oil-induced diarrhoea, inhibited intestinal transit, and delayed gastric emptying. Like atropine (1 mg/kg, p.o.), PGE produced dose-dependent and significant ant motility effect, and caused dose-related inhibition of castor oil-induced enteropooling in the animals. Like loperamide (10 mg/kg, p.o.), PGE dose-dependently and significantly delayed the onset of castor oil-induced diarrhoea, decreased the frequency of defaecation, and reduced the severity of diarrhoea in the rodents.	42
Treatment of plaque	The active flavonoid compound, quercetin-3-O-alpha-l-arabinopyranoside (guajaverin) isolated from <i>Psidium guajava</i> demonstrated high potential antiplaque agent by inhibiting the growth of the Strep. Mutans.	34
Spermatoprotective activity	The extracts of the leaves of <i>Psidium guajava</i> Linn. possess beneficial effects on sperm production and quality, and may thus improve the sperm parameters of infertile males with oligospermia and nonobstructive azoospermia.	43
Antimutagenic activity	The water extract of <i>P.guajava</i> was effective in inactivating the mutagenicity of direct-acting mutagens.	44
Inotropic effect	The extract from <i>P. guajava</i> leaves depress myocardial inotropism.	45
Spasmolytic effect	The spasmolytic activity of the <i>Psidium guajava</i> leaf remedy is mainly due to the aglycone quercetin, present in the leaf and in the extract mainly in the form of five flavonols, and whose effect is produced when these products are hydrolyzed by gastrointestinal fluid.	20
Treatment of infantile rotaviral enteritis	<i>Psidium guajava</i> showed good curative effect on infantile rotaviral enteritis.	46
Anti- cancer activity	Aqueous extract of <i>Psidium guajava</i> L. budding leaves has been shown to possess anti-prostate cancer activity in a cell line model. Treatment with <i>Psidium guajava</i> L. budding leaves (1.5 mg/mouse/day) significantly diminished both the prostate specific antigen (PSA) serum levels and tumor size in a xenograft mouse tumor model.	47
Antifungal activity	The hot water extract and the methanol extract of <i>Psidium guajava</i> showed high activity against <i>Arthrimum sacchari</i> and <i>Chaetomium funicola</i> strains.	48
Analgesic & anti-inflammatory activity	The aqueous extract of <i>P. guajava</i> leaves possesses analgesic and antiinflammatory properties. The hexane, ethyl acetate and methanol extracts of <i>Psidium guajava</i> leaves (20,100,500 and 1250 mg/kg) exhibited mostly dose-dependent antinociceptive effects in chemical and thermal tests of analgesia.	49,50
Immunomodulatory activity	Extracts derived from <i>Psidium guajava</i> revealed immunomodulatory activities.	51
Treatment of acne	<i>Psidium guajava</i> leaf extracts are used in treatment of acne.	52
Antiproliferative activity	Guava leaf extract has antiproliferative activity caused by inhibition of the catalytic activity of Prostaglandin endoperoxide H synthase (PGHS) isoforms.	53
Antipyretic	The methanol extract of the leaves of <i>Psidium guajava</i> exhibited an antipyretic effect.	54
Contractile effect	Aqueous leaves extract of <i>Psidium guajava</i> significantly and dose-dependently (0.25-2 mg/ml) contracted aorta rings. The effect of <i>P. guajava</i> was to a large extent mediated by activation of alpha-adrenoceptor and to a lesser extent by acting via calcium ion channel	55

Hypotensive	<i>P. guajava</i> leaf aqueous extract (PGE, 50-800 mg/kg i.v.) produced dose-dependent, significant reductions in systemic arterial blood pressures and heart rates of hypertensive, Dahl salt-sensitive rats. The extract causes hypotension in the mammalian experimental animal model used via cholinergic mechanisms.	35
Malaria	The leaves are used as an ingredient in the preparation of fever "teas". They are also used as a part of the pot herb used in steam treatment for malaria. The stem bark extract contained anthraquinones, flavonoids, seccoirridoids and terpenoids and was found to be effective for the treatment and/or prophylaxis of malaria.	56
Oral care	In southern Nigeria the twigs are used as chew sticks and the presence of bioactive compounds comprised of saponins, tannins, flavonoids, alkaloids is responsible for their effectiveness. Chewing sticks when used without toothpaste are very efficient, effective, and reliable for cleaning teeth. The teeth of chewing sticks users are usually strong, clean, fresh, and devoid of dental plaques carries.	57
CNS Activity	The leaves of the guava tree in decoction are used for spasms, epiand even for cerebral affections.	58
Conjunctivitis	Flowers are also used as a poultice for conjunctivitis.	59
Vaginal Disorders	The leaves of the guava tree in decoction are recommended fouterine haemorrhage. The same decoction is used as a wash for vaginal and uterine problems, and especially where an astringent remedy is needed.	58
Rheumatism	The pounded leaves in India are used for rheumatism.	59

- 1. Antioxidant activity:** The extracts from distilled water, 65% ethanol and 95% ethanol respectively showed effects on scavenging hydroxyl radicals and inhibiting lipid peroxidation in the dose-dependent manner, had 50% effective concentration (EC50) on scavenging hydroxyl radicals of 0.63, 0.47 and 0.58g/L, had EC50 on inhibiting lipid peroxidation of 0.20, 0.035, 0.18g/L.³⁷
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16. **Immunomodulatory activity:** Extracts derived from *Psidium guajava* revealed immunomodulatory activities⁵¹.
17. **Treatment of acne:** *Psidium guajava* leaf extracts are used in treatment of acne⁵².
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inhibition of the catalytic activity of Prostaglandin endoperoxide H synthase (PGHS) isoforms⁵³.

19. Antipyretic: The methanol extract of the leaves of *Psidium guajava* exhibited an antipyretic effect⁵⁴.

20. Contractile effect: Aqueous leaves extract of *Psidium guajava* significantly and dose-dependently (0.25-2 mg/ml) contracted aorta rings. The effect of *P. guajava* was to a large extent mediated by activation of alpha-adrenoceptor and to a lesser extent by acting via calcium ion channel⁵⁵.

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22. Malaria: The leaves are used as an ingredient in the preparation of fever "teas". They are also used as a part of the pot herb used in steam treatment for malaria. The stem bark extract contained anthraquinones, flavonoids, secoirridoids and terpenoids and was found to be effective for the treatment and/or prophylaxis of malaria⁵⁶.

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24. CNS Activity: The leaves of the guava tree in decoction are used for spasms, epiand even for cerebral affections⁵⁸.

25. Conjunctivitis: Flowers are also used as a poultice for conjunctivitis⁵⁹.

26. Vaginal Disorders: The leaves of the guava tree in decoction are recommended for uterine haemorrhage. The same decoction is used as a wash for vaginal and uterine problems, and especially where an astringent remedy is needed⁵⁸.

27. Rheumatism: The pounded leaves in India are used for rheumatism⁵⁹.

Safety Data: The LD50 of the aqueous extract was >5 g/kg, p. o.⁶⁰.

CONCLUSION: Major thrust by whole of the pharmaceutical industry is focused towards design and development of new innovative/indigenous plant based drugs through investigation of leads from traditional system of medicine⁶¹. In recent years, ethno-botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. It is best classical approach in the search of new lead molecules for management of various diseases. Thorough screening of literature available on *Psidium guajava* depicted the fact that it is a popular remedy among the various ethnic groups, vaidhyas, hakims and Ayurvedic practitioners for cure of ailments. It is needed to explore this plant very thoroughly and researchers are exploring the therapeutic potential of this plant.

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