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AN UPDATE OF PHARMACOLOGICAL ACTIVITY OF *PSIDIUM GUAJAVA* IN THE TREATMENT OF VARIOUS DISEASES

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ABSTRACT: *Psidium guajava* is a small medicinal tree that is native to South America and Brazil is among the world's top producers and most of the country's production is destined for the food industry. It is popularly known as guava and has been used traditionally as a medicinal plant throughout the world for a number of diseases. It contains important phytoconstituents such as tannins, triterpenes, flavonoid: quercetin, pentacyclic triterpenoid, guajanoic acid, saponins, carotenoids, lectins, leucocyanidin, ellagic acid, amritoside, beta-sitosterol, uvaol, oleanolic acid and ursolic acid. It is one of the valuable plant in the Myrtaceae family. *Psidium guajava* which was reported the antibacterial, anti-diarrhoeal, antihyperglycemic, anti-malarial, anti-inflammatory, anti-cancer, antioxidant activity etc. The present review is an attempt to generate interest among the masses regarding its immense potential in preventing and treating several common diseases.

INTRODUCTION: The use of plants as medicines predates written human history. Ethno botany (the study of traditional human uses of plants) is recognized as an effective way to discover future medicines¹. The World Health Organisation (WHO) estimates that 80% of the population of some Asian and African countries presently uses herbal medicine for some aspect of primary health care. Studies in the United States and Europe have shown that their use is less common in clinical setting but has become increasingly more in recent years as scientific evidence about the effectiveness of herbal medicine has become more widely available².

Guava is a small tropical tree that grows up to 35 feet tall; it is widely grown for its fruit in tropics. It is a member of the Myrtaceae family, with about 133 genera and more than 3,800 species. The leaves and bark of *P. guajava* tree have a long history of medicinal uses that are still employed today³. *Psidium Guajava* (*P. guajava*) is a plant native to tropical America and belongs to the family Myrtaceae. *P. guajava* is called "guayaba" in Spanish speaking countries and "goiaba" in Brazil. It is an important tropical fruit widely grown in Taiwan, Hawaii, Thailand, Philippines and Malaysia.

All parts, including the fruits, leaves and barks have been traditionally used as the folkloric herbal medicines and exhibit many therapeutic uses including⁴. This plant is available in the South America, European, Africa and Asia. The common names of *Psidium Guajava* are guava (English), jambu batu (Malay), mansala (India) and gwaaba (Africa)⁵.

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Guava is a tree commonly used for shade or can be a shrub in dooryard gardens in the tropics⁶. Brazil is among the world's top producers of guava and most of the country's production is destined for the food industry to produce different products, like candies, juices, jams and frozen pulp.

Various evidences depict that the leaves and bark of *P. guajava* tree possess a long history of medicinal uses⁷. The aqueous extract of guava leaves has been reported to be efficacious in the treatment of various types of gastrointestinal (GIT) disturbances such as diarrhoea, inhibition of the peristaltic reflex and gastroenteritis⁸. Moreover the whole plant is used as skin tonic and is employed in the treatment of female related disease like dysmenorrhoea, miscarriages, uterine bleeding and premature labour.

Classification:¹⁰

Kingdom: Plantae
 Division: Magnolioph
 Class: Magnoliopsida
 Subclass: Rosidae
 Order: Myrtales
 Family: Myrtaceae
 Subfamily: Myrtoide
 Tribe: Myrteae
 Genus: Psidium
 Species: guajava

Guava's main plant chemicals include: alanine, alpha-humulene, alpha-hydroxyursolic acid, alpha-linolenic acid, alpha-selinene, amritoside, araban, arabinose, arabopyranosides, arjunolic acid, aromadendrene, ascorbic acid, ascorbigen, asiatic acid, aspartic acid, avicularin, benzaldehyde, butanal, carotenoids, caryophyllene, catechol-tannins, crataegolic acid, D-galactose, D-galacturonic acid, ellagic acid, ethyl octanoate, essential oils, flavonoids, gallic acid, glutamic acid, goreishic acid, guafine, guavacoumaric acid, guaijavarin, guajiverine, guajivolic acid, guajavolide, guavenoic acid, guajavanoic acid, histidine, hyperin, ilelatifol D, isoneriucoumaric acid, isoquercetin, jacoumaric acid, lectins, leucocyanidins, limonene, linoleic acid, linolenic acid, lysine, mecocyanin, myricetin, myristic acid, nerolidiol, obtusin, octanol, oleanolic acid, oleic acid, oxalic acid, palmitic acid, palmitoleic acid, pectin, polyphenols, psidiolic acid, quercetin, quercitrin, serine, sesquiguavene,

tannins, terpenes, ursolic acid and some other compounds listed **Table 1**. Recent studies on the pharmacological properties of the bark, fruit and leaves depicts antibacterial, hypoglycaemic, anti-cancer, anti-inflammatory, anti-pyretic, spasmolytic and central nervous system depressant activities⁹. Thus, this review depicts the pharmacological activity on guava in the treatment of various disorders.

TABLE 1: CHEMICAL COMPOSITION OF VARIOUS PARTS OF GUAVA (*PSIDIUM GUAJAVA* LINN.)

Parts	Constituents
Fruit	Vitamin C, Vitamin A, iron, calcium, Manganese, phosphoric, oxalic and malic acids, saponin combined with oleanolic acid. Morin-3-O- α -L-lyxopyranoside and morin-3-O- α -L-arabopyranoside, flavonoids, guaijavarin, quercetin. Essential oil contains hexanal, -2-hexenal, 2,4-hexadienal, 3-hexenal, 2-hexenal, 3-hexenyl acetate and phenol, while β -caryophyllene, nerolidol, 3-phenylpropyl acetate, caryophyllene oxide, pentane-2-thiol, 3-penten-2-ol and 2-butenyl acetate, 3-hydroxy-2-butanoic acid, 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 (pink guava fruit) ^{12, 13, 14, 15, 16, 17}
Leaves	α -pinene, β -pinene, limonene, menthol, terpenyl acetate, isopropyl alcohol, longicyclene, caryophyllene, β -bisabolene, caryophyllene oxide, β -copanene, farnesene, humulene, selinene, cardinene and curcumene, mallic acids, nerolidiol, β -sitosterol, ursolic, crataegolic, and guayavolic acids, cineol, quercetin, 3-L-4- β -D-arabino-furanoside (avicularin) and its 3-L-4-pyranoside (Essential oil), resin, tannin, eugenol, caryophyllene (1a α -, 4a α -, 7 α -, 7a β -, 7b α -)]-decahydro-1H-cycloprop[e] azulene, guajavolide (2 α -, 3 β -, 6 β -, 23-tetrahydroxyurs-12-en-28,20 β -olide; 1) and guavenoic acid (2 α -, 3 β -, 6 β -, 23-tetrahydroxyurs-12,20(30)-dien-28-oic acid, triterpene oleanolic acid, triterpenoids, flavinone-2'-ene, prenol, dihydrobenzophenanthridine and cryptonine ^{13, 15, 18, 19, 20, 21}
Bark	polyphenols, resin and crystals of calcium oxalate ^{14, 15}
Root	Tannin, leucocyanidins, sterols, gallic acid, carbohydrates, salts, tannic acid ^{13, 21}
Seed	Proteins, starch, oils, phenolic, flavonoid compounds, flavonol glycoside, quercetin-3-O- β -D-(2''-Ogalloylglucoside)-4'-O-vinylpropionate ^{14, 22}
Twigs	Calcium, magnesium, phosphorous, potassium, sodium, fluoride, copper, iron, zinc manganese and lead ²³

Morphology: It's a low evergreen tree or shrub 6 to 25 feet high, with wide spreading branches and square, downy twigs, is a native of tropical America. It's a common vegetation cover by roads and in waste places in Hawaii. Guava is a tropical and semitropical plant. It is well known in the islands for its edible fruit. It is common in the backyards. The branches are crooked, bringing opposite leaves. The flowers are white, incurved petals, 2 or 3 in the leaf axils; they are fragrant, with four to six petals and yellow anthers. The fruit is small, 3 to 6 cm long, pearshaped, reddish-yellow when ripe¹¹.



FIG. 1: *PSIDIUM GUAJAVA*

Pharmacological Activity: Studies indicates that number of pharmacological active components are present in the *Psidium guajava* which are responsible for the various biological activities like antidiabetic, antidiarrhoeal, antimicrobial, antioxidant, cardioactive, hepatoprotective, antipyretic, spasmolytic, immunomodulatory and contractile effect, which are explained in latter part of review.

Anti-diabetic Activity: *Psidium guajava* has been reported to lower the blood glucose level. Guava fruit extract has been shown to significantly restore the loss of body weight and reduces the blood glucose level in the diabetic condition. In STZ induced diabetic's guava fruit extract, when administered at a dose of 125 and 250 mg/kg. Fruit extract of guava protects the pancreatic tissues, including islet beta cells, against lipid per oxidation and thus reduces the loss of insulin-positive beta cells and insulin secretion²⁴. The ethanolic stem bark extract exhibited significant hypoglycaemic activity in alloxan induced hyperglycaemic rats at an oral dose of 250 mg/kg²⁵.

Aqueous leaf extracts of guava at 0.01 - 0.625 mg/ml showed significant inhibition on low density

lipid (LDL) glycation in a dose dependent manner²⁶. Various investigations indicated that leaf extract of guava and its phenolic compounds inhibit the glycation process in an albumin/glucose model system. The guava leaf extracts also showed strong inhibitory effects on the production of Amadori products and advanced glycation end products (AGEs) from albumin in the presence of glucose²⁷.

P. guajava leaf aqueous extract (PGE, 50 - 800 mg/kg) in rat experimental paradigms. The hypoglycemic effect of the plant's extract was examined in normal and diabetic rats, using streptozotocin (STZ)-induced diabetes mellitus model. Hypertensive Dahl salt-sensitive rats were used to investigate the hypotensive (antihypertensive) effect of the plant's extract. Chlorpropamide (CPP; 250 mg/kg, p.o.) was used as the reference hypoglycemic agent for comparison. Acute oral administrations of the plant's extract (PGE; 50 - 800 mg/kg, p.o.) caused dose-related, significant ($p < 0.05-0.001$) hypoglycemia in normal (normoglycemic) and STZ-treated, diabetic rats.

Moreover, acute intravenous administrations of the plant's extract (PGE, 50 - 800 mg/kg i.v.) produced dose dependent, significant reductions ($p < 0.05-0.001$) in systemic arterial blood pressures and heart rates of hypertensive, Dahl salt-sensitive rats. Although the exact mechanisms of action of the plant's extract still remain speculative at present, it is unlikely that the extract causes hypotension in the mammalian experimental animal model used *via* cholinergic mechanisms, since its cardio depressant effects are resistant to atropine pretreatment.

The numerous tannins, polyphenolic compounds, flavonoids, pentacyclic triterpenoids, guaijaverin, quercetin, and other chemical compounds present in the plant are speculated to account for the observed hypoglycemic and hypotensive effects of the plant's leaf extract. However, the results of this experimental animal study indicate that the leaf aqueous extract of *Psidium guajava* possesses hypoglycemic and hypotensive properties, and thus lend pharmacological credence to the suggested folkloric, ethnomedical uses of the plant in the management or control of adult-onset, type 2 diabetes mellitus and hypertension in some rural African communities²⁸.

Anticancer Effect: Various studies showed that ¹⁷ Thai medicinal plants of *Psidium guajava* have anti-proliferative effects on human mouth epidermal carcinoma and murine leukemia cells ⁶¹. Further Studies showed that the acetone extracts of guava (*Psidium guajava* L.) branch (GBA) had cytotoxic effects on HT-29 cells. The GBA showed highly cytotoxic effects via the MTT reduction assay, LDH release assay, and colony formation assay. The extract showed inhibition against growth of HT-29 cells at 250 µg/ml. branch extract showed characteristic apoptotic effects in HT-29 cells, including chromatin condensation and sharking. It induces cytotoxicity and an increase in the sub-G1 phase of HT-29 cells ²⁹.

Studies showed that budding leaves of *psidium guajava* contain huge amounts of soluble polyphenolics (SP) including (in mg/g) gallic acid (348), catechin (102), epicatechin (60), rutin (100), quercetin (102), and rutin (100) and to exhibit potent anticancer activity ³⁰. It could be used as an anti-tumor chemo preventive in view of anti-angiogenesis and anti-migration, indicated that the IC₅₀ of *Psidium guajava* for DU145 cells was 0.57 mg ml⁻¹.

In addition, *Psidium guajava* effectively inhibited the expressions of VEGF, IL-6 and IL-8 cytokines, and MMP-2 and MMP-9, and simultaneously activated TIMP-2 and suppressed the cell migration and the angiogenesis. *Psidium guajava* potentially possesses a strong anti-DU145 effect. Thus, clinically it owns the potential to be used as an effective adjuvant anti-cancer chemo preventive ³¹. It has been reported that essential oil of *Psidium guajava* has the potent anti proliferative activity ³².

We used ferric-reducing antioxidant power (FRAP) and 2, 2-diphenyl-1-picryl hydrazil (DPPH) assays to estimate antioxidant activity of *P. guajava* leaf extracts (methanol, hexane and chloroform). Antitumor and *in-vivo* cytotoxic activities were determined using potato disc assay (PDA) and brine shrimp lethality assay, respectively. Three human carcinoma cell lines (KBM5, SCC4 and U266) were incubated with different doses (10 - 100 µg/mL) of extracts and the anticancer activity was estimated by MTT assay. NF-κB suppressing activity was determined using electrophoretic mobility shift assay (EMSA).

Chemical composition of the three extracts was identified by GC-MS. Total phenolic and flavonoid contents were measured by colorimetric assays. The order of antioxidant activity of three extracts was methanol > chloroform > hexane. The IC₅₀ values ranged from 22.73 to 51.65 µg/mL for KBM5; 22.82 to 70.25 µg/mL for SCC4 and 20.97 to 89.55 µg/mL for U266 cells.

The hexane extract exhibited potent antitumour IC₅₀ value = 65.02 µg/mL) and cytotoxic (LC₅₀ value = 32.18 µg/mL) activities. This extract also completely inhibited the TNF-α induced NF-κB activation in KBM5 cells. GC-MS results showed that pyrogallol, palmitic acid and Vitamin E were the major components of methanol, chloroform and hexane extracts. We observed significant (p < 0.05) difference in total phenolic and flavonoid contents of different solvent extracts. The present study demonstrates that *P. guajava* leaf extracts play a substantial role against cancer and down-modulate inflammatory nuclear factor κB ³³.

Anti-inflammatory Effect: The anti-inflammatory and analgesic activities of 70% ethanolic extract of *Psidium guajava* was investigated in rats using the carrageen induced hind paw oedema model. Extracts which exhibited anti-inflammatory activity were screened for analgesic activity using the Randall-Selitto method in rats. The extracts were administered at a dose of 300 mg/kg, p.o. Aspirin (300 mg/kg, p.o.) was employed as the reference drug. *Psidium guajava* leaves, showed significant anti-inflammatory activity with percentage inhibitions of 58.27% ³⁴.

Another modern study confirms many of the traditional uses. The methanol extract of guava leaves was found to inhibit paw oedema induced by carrageenan in rats, and pain induced by acetic acid in mice, and it exhibited an antipyretic effect in mice. The oral administration of the extract reduced intestinal transit time and prevented castor oil-induced diarrhoea in mice ³⁵.

The essential oil has also been proven to have anti-inflammatory effect. The essential oil, steam-distilled from leaves of *P. guajava* leaves, was given orally rats to study its effects on the exudative and proliferative phases of the inflammatory reaction (carrageenan-induced paw

oedema and cotton pellet-induced granuloma models). The essential oil (0.8 mg/kg) significantly reduced oedema formation induced by carrageenan. The essential oil (0.4 and 0.8 mg/kg) significantly reduced granuloma formation induced by cotton pellets. Another paper confirmed the anti-inflammatory activity and also showed significant antipyretic activity and potent anti-arthritic activity in rats. In Peru it is said to be good for oedema^{37, 38}. A decoction of *Psidium guajava* leaves is used for the treatment of various inflammatory ailments including rheumatism.

Anti-inflammatory and analgesic effects of the leaf extracts of *psidium guajava* was due to the presence of polyphenolics compound and triterpenoids. Aqueous extract of *Psidium guajava* at a dose of 50-800 mg/kg, i.p. produced dose-dependent and significant inhibition of fresh egg albumin-induced acute inflammation (oedema) in rats. Further, leaf extract (50 - 800 mg/kg, i.p.) also produced dose-dependent and significant analgesic effects against thermally and chemically induced nociceptive pain in mice³⁹.

Antidiarrhoeal Activity: Diarrhoea is a major problem in the world. The ripe fruit of guava has been reported as laxative which is used to treat constipation. Studies indicate that guava fruit is more effective Antidiarrhoeal when it is used with the peel⁴⁸, but if taken unripe fruit in large quantity cause indigestion, vomiting⁴³. The leaf decoction of guava has been reported for the gastroenteritis and chronic diarrhoea, while the young leaves and shoots has been reported for dysentery and diarrhoea^{50, 51}.

Quercetine, the major component of the guava leaf extract is responsible for the inhibition of the intestinal movement and reduce capillary permeability in the abdominal cavity and inhibition of increased watery secretion that occur in the acute diarrhoeal disease^{44, 52}. Fresh leaf extract of the plant when administered at a dose of 0.2 ml/kg of morphine sulphate showed inhibition of propulsion^{53, 54}. Flower buds and leaf extraction of the *Psidium guajava* consist of Quercetin and quercetin-3-arabinoside which are used in the treatment of diarrhoea in the Costa Rica⁴². This extract at concentrations of 1.6 ug/ml showed a morphine-like inhibition of acetylcholine release in

the coaxially stimulated ileum, as well as an initial increase in muscular tone, followed by a gradual decrease⁵¹. Various studies indicates that a galactose specific lectin in guava was shown to bind to *Escherichia coli* preventing its adhesion to the intestinal wall and thus preventing its adhesion to the intestinal wall and thus preventing infection resulting diarrhoea⁵⁵. It is also reported that the asiatic acid, which is present in the leaf extraction, showed dose-dependent (10-500 µg/ml) spasmolytic activity in spontaneously contracting isolated rabbit jejunum preparations³⁹. Methanol extract from leaves (8 µg/ml) of *Psidium guajava* showed activity against simian (SA-11) rotavirus (93.8% inhibition)⁴¹.

Antimicrobial Activity: 4 antibacterial flavonoids (morin-3-*O*-lyxoside, morin-3-*O*-arabinoside, quercetin and quercetin-3-*O*-arabinoside) of the leaf extract of *Psidium guajava* are found to be effective against the pathogenic bacteria including *Bacillus stearothermophilus*, *Brochothrix thermosphacta*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Pseudomonas fluorescens*, *Salmonella enterica*, *Staphylococcus aureus* and *Vibrio cholera*⁵⁷. Studies showed that *P. guajava* leaf extract has trypanocidal properties which could be attributed in parts to the broad antimicrobial and iron chelating activity of flavonoids and tannins respectively. Iron chelation has been suggested by several reports as an effective way of killing trypanosomes.

The methanolic root extract of *Psidium guajava* has been found to possess fungicidal effect because of the quercetin which is present in the root extract⁴¹. Bark tincture showed fungicidal activity at different concentrations but exhibit only fungistatic property in case of *Candida albicans*^{59, 60}. Leaf extract of *psidium guajava* also reported for the anti-bacterial activity on *staphylococcus aureus* due to the protein degrading activity of the leaf extract⁶¹. The aqueous extract was more potent in inhibiting the growth of *E. coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* than the organic extracts.

The gram negative bacteria were less susceptible to the effect of crude drugs⁶². Due to the presence of tannins the leaf extract of guava has been reported for antimicrobial activity against gram-positive and gram-negative organisms (*Sarcina lutea* and

Staphylococcus aureus) and *Mycobacterium phlei*⁴⁷. Studies indicate that leaf extract of *Psidium guajava* has potent anti-microbial activity against Propionibacterium acnes and is beneficial for the treatment of acne⁴⁶. The leaf extract of guava is effective against the agents which cause the infection in the human intestine like *Streptococcus mutatis*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Bacillus cereus*, *proteus sp.* *Shigella sp.*^{58, 64}. The aqueous and methanolic extract is effective against the spore formation and production of *Clostridium prefringens* type A⁶⁵. Further, four antibacterial compounds have been reported from the methanolic root extract which were further separated by column Chromatography. Three antibacterial substances have been detected in the leaves which are derivatives of quercetin^{57, 66}.

In another study, fungicidal action against *Arthrinium sacchari* M001 and *Chaetomium funicola* M002 strains was observed from the methanolic extract of ripe fruit⁶⁷.

Antioxidant Activity: Oxidative stress occurs when free radical production exceeds the antioxidant capacity of a cell which can damage crucial cellular compounds, such as lipids, carbohydrates, proteins, and DNA^{68, 69}. Many studies have reported significant alterations in plasma antioxidant enzyme systems, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), and in lipid peroxidation⁴⁹. It has been well reported that *Psidium guajava* (PG) exhibits its antioxidant effect through the inhibition of Nuclear factor-kappa B (NF- κ B) activation and restoration of enzymatic antioxidants⁴⁹.

Studies have been reported that guava fruits with a red-coloured pulp flesh contained a significant amount of carotenoids, especially lycopene, and a high concentration of phenolic compounds. These compounds were largely responsible for the antioxidant activity⁷⁰. *Psidium guajava* contains phenolic phytochemicals which inhibit peroxidation reactions in the living body and thus prevent various types of chronic diseases such as diabetes, cancer and heart disease⁷¹. These antioxidant properties are associated with its phenolic compounds such as protocatechuic acid, ferulic acid, quercetin, gallic acid, ascorbic acid, gallic acid and caffeic acid⁷².

Guava leaf extracts and fruits are a potential source of natural antioxidants⁴⁶. Studies indicate that guava fruit also exerts antioxidant action, collagen formation and radio-protective activity in the assay with technetium-99m⁴⁶.

Antitussive Activity: It has been reported that water infusion from *Psidium guajava* leaf extract decreases the frequency of coughing induced by capsaicin aerosol⁷³. In Senegal and Peru *Psidium guajava* leaves boiled together to make a decoction is very effective for cough and treatment of trachea bronchitis⁴⁸. **Hepatoprotective Activity:** The aqueous leaf extract of *Psidium guajava* has been reported for its hepatoprotective action at a dose of 500 mg kg⁻¹⁷⁴.

Studies indicate that the Asiatic acid which is present in the leaves and fruit of *Psidium guajava* is responsible for the hepatoprotection⁷⁵. *Psidium guajava* leaf extracts (500 mg/kg, po) significantly reduced the elevated serum levels of aspartate aminotransferase, alanine aminotransferase (AAT), alkaline phosphatase, protein and bilirubin, some antioxidant enzymes, reduced glutathione (GSH), GPx, SOD and CAT activities, were also evaluated in the rat liver homogenate. The higher dose of the extract (500 mg/kg, p.o) prevented and showed an increase in liver weight while the lower dose was ineffective in the paracetamol-induced liver damage. In the acute liver injury induced by paracetamol the higher dose (500 mg/kg, p.o.) of *P. guajava* leaf extract was found to be more effective than the lower dose (250 mg/kg, p.o.)⁷⁶. Studies showed that the unripe fruit of *Psidium guajava* has a potent hepatoprotective agent⁷⁷.

Cardiovascular Effects: Studies showed that the aqueous leaf extract of *Psidium guajava* exhibited cardioprotective effects against myocardial ischemia-reperfusion injury in isolated rat heart⁷⁸. Augmentation of endogenous antioxidants, maintenance of the myocardial antioxidant status and significant restoration of most of the altered hemodynamic parameters may have contributed to its cardioprotective effect⁷⁸. Further investigation showed that aqueous fractions obtained from the acetic extract of *Psidium guajava* leaf exhibit a negative inotropic effect by decreasing the atrial contractility by reducing the calcium (Ca²⁺) entry in myocardial cells and also by opening potassium

channels of cardiac tissue ⁷⁹. Moreover various reports showed that the cardio-inhibitory actions in rats and guinea pigs of the aqueous leaf extract of *Psidium guajava* also appeared to be due to cholinergic involvement ⁴⁵.

Miscellaneous Activity: Leaf extract of *psidium guajava* is reported in the *Acne vulgaris*, a chronic inflammatory disease involving colonization of *Propionibacterium acnes*, plus activation of neutrophils and lymphocytes. *Psidium guajava* leaf extracts have potent antimicrobial activities against *Propionibacterium acnes* and may be beneficial in

treating acne especially when they are known to have anti-inflammatory activities ⁶³. Further, the aqueous leaf extract of *Psidium guajava* has been reported to be effective against dental caries and helpful in reducing dental plaque caused by *Staphylococcus sanguinis*, *Staphylococcus mitis* and *Actinomyces sp.* at a dose of 1 mg/ml ⁸⁰.

Moreover Guava stem bark and leaf stem extract has been found to possess anti-giardiasis activity and inhibit growth of *Entamoeba histolytica* respectively **Table 2** ^{44, 81, 82}.

TABLE 2: PHARMACOLOGICAL EFFECT OF GUAVA

Pharmacological effect	Details
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 (EC ₅₀) on scavenging hydroxyl radicals of 0.63, 0.47 and 0.58g/L, had EC ₅₀ on inhibiting lipid peroxidation of 0.20, 0.035, 0.18g/L ⁸³
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) ⁸⁴
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 ^{85, 86}
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.
Hepatoprotective activity	<i>P. guajava</i> aqueous leaf extracts (250 and 500mg/kg, po) possesses good hepatoprotective activity ⁸⁷
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 antimotility 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 ⁸⁸
Treatment of plaque	The active flavonoid compound, quercetin-3-O-alpha-larabinopyranoside (guaijaverin) isolated from <i>Psidium guajava</i> demonstrated high potential antiplaque agent by inhibiting the growth of the Strep. Mutans ⁸⁹
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 ⁹⁰
Antimutagenic activity	The water extract of <i>P. guajava</i> was effective in inactivating the mutagenicity of direct-acting mutagens ⁹¹
Inotropic effect	The extract from <i>P. guajava</i> leaves depress myocardial inotropism.
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 ⁹²
Treatment of infantile rotaviral enteritis	<i>Psidium guajava</i> showed good curative effect on infantile rotaviral enteritis ⁹³
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

Analgesic and antiinflammatory activity	mg/mouse/day) significantly diminished both the prostate specific antigen (PSA) serum levels and tumor size in a xenograft mouse tumor model. Guava leaf essential oil has been shown to possess cytotoxic effect on Human cervical cancer cell lines ⁹⁴ The aqueous extract of <i>P. guajava</i> leaves possesses analgesic and anti-inflammatory 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 ^{95,96}
Immunomodulatory activity	Extracts derived from <i>Psidium guajava</i> revealed immunomodulatory activities ⁹⁷
Treatment of acne	<i>Psidium guajava</i> leaf extracts are used in treatment of acne. Qadan <i>et al.</i> , 2005 Antiproliferative activity. Guava leaf extract has antiproliferative activity caused by inhibition of the catalytic activity of Prostaglandin endoperoxide H synthase (PGHS) isoforms ⁹⁸
Antipyretic	The methanol extract of the leaves of <i>Psidium guajava</i> exhibited an antipyretic effect ⁹⁹
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 <i>via</i> calcium ion channel ¹⁰⁰
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 ⁸⁸
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 malaria ¹⁰¹
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 ²³
CNS Activity	The leaves of the guava tree in decoction are used for spasms, even for cerebral affections ¹⁰²
Conjunctivitis	Flowers are also used as a poultice for conjunctivitis ¹⁰³
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 needed ¹⁰²
Rheumatism	The pounded leaves in India are used for rheumatism ¹⁰³

CONCLUSION: The plant is show different type of chemical constituents like araban, arabinose, arabopyranosides, arjunolic acid, ascorbigen, asiatic acid, aspartic acid, D-galactose, D-galacturonic acid, ellagic acid, guaijavarin, guajiverine, guajavanoic acid, linoleic acid, myristic acid, octanol, oleanolic acid, palmitoleic acid, pectin, polyphenols, psidiolic acid, quercetin, quercitrin, serine, sesquiguavene, tannins, terpenes, ursolic acid The plant has been extensively studied in terms of pharmacological activity of its major components, and the results indicate potent anti-diarrheal, antihypertensive, hepatoprotective, antioxidant, antimicrobial, hypoglycaemic and antimutagenic activities. In recent years, emphasis of research has been on utilizing traditional medicines that have a long and proven history of treating various ailments. In this regard, further studies need to be carried out to explore *P.guajava* Linn. for its potential in preventing and treating diseases.

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