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AN UPDATE OF PHARMACOLOGICAL ACTIVITY OF *PSIDIUM GUAJAVA* IN THE MANAGEMENT OF VARIOUS DISORDERS

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ABSTRACT

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In the recent years, the use of herbal products has been increasing in developing countries. *Psidium guajava* Linn. (Guava) family Myrtaceae is an important dietary plant used traditionally for medicinal purpose around the world. The fruit part of the guava is used because of its food and nutritional value but other part of the guava plant are used in the traditional system due to their medicinal properties. Since each part of the guava tree possess the economic value. The pharmacological and medicinal use have demonstrated the ability of this plant to exhibit antioxidant, hepatoprotective, antiallergic, antimicrobial, anticancer, cardioprotective, antidiabetic, ant cough, antidote properties. This review delineate with intervention of *Psidium guajava* in the management of various disorders.

INTRODUCTION: Guava (*Psidium guajava* Linn.) belonging to family Myrtaceae is a traditionally used plant because of its food and nutrition value. Guava is widely grown in tropical and many areas like India, Bangladesh, Florida, and West Indies. Different parts of the *Psidium guajava* are reported to be used in folk medicine. Various parts of the plant like root, bark, leaves and fruits are found to possess many pharmacological properties as it is used in the treatment of various disorders¹.

Various evidences depict that the leaves and bark of *P. guajava* tree possess a long history of medicinal uses². 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 gastroenteritis³. 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.

Recent studies on the pharmacological properties of the bark, fruit and leaves depicts antibacterial, hypoglycaemic, anti-inflammatory, antipyretic, spasmolytic and central nervous system depressant activities¹. Thus, this review depicts the pharmacological, medicinal and nutritional value of guava in the management of various disorders.

Morphological Description:

Plant: Small tree to 20 feet in height with broad, spreading top, branching freely close to the ground. Trunk short, with a scaly bark, reddish-brown to light brown in colour. Leaves are opposite, oblong, 3 to 7 inches in length, with prominent veins below.



Finally pubescent below, especially when young. Flowers are of white colour and about 1 inch in diameter, borne singly or in small groups in axils of leaves of recent growth. Self-pollination is possible but crosspollination by insects results in higher yields⁴. Fruits of guava are in various shape ranges from round, ovoid to pear shaped. Weight from one ounce to as much as one pound. Skin colour usually yellow with flesh ranging from white, yellow, and pink to red. Fruit ranges from thin-shelled, with many seeds embedded in a firm pulp to thick-shelled with few seeds. Flavour from sweet to highly acid. The distinctive aroma ranges from strong and penetrating to mild and pleasant⁵.



Source; Botanical Garden Sarangpur (Chandigarh)

Phytochemical constituents: Guava is a rich source of dietary fibres, vitamin A, C, folic acid and various dietary minerals like potassium, copper and manganese. Reports indicates that a single guava (*Psidium guajava*) fruit contains about four times the amount of vitamin C as an orange⁶. Leaf extract of guava has been reported for their antibacterial activity because of the presence of flavonoid glycosides, morin-3-O-alpha-L-lyxopyranoside and morin-3-O-alpha-L-arabopyranoside⁷. About sixteen types of carotenoids have been reported in the flesh part of the red guava and thirteen of them have been reported as guava carotenoids which is responsible for antioxidant activity⁸.

Nutrient content varies according to the area and season of cultivation. It has been reported that one of the guava i.e. strawberry guava (*P. littoralevar. cattleianum*), notably containing 90 mg of vitamin C per serving, has about 25% of the amount found in more common varieties, its total vitamin C content in one serving still provides 100% of the Dietary intake⁹. Further, guava also contain both carotenoids and polyphenols – which are reported as major classes of antioxidant pigments, thus guava provide relatively high potential antioxidant value among plant foods¹⁰. The pulp and peel of the guava are a remarkable source of anti-oxidants and anti-oxidant dietary fibre (AODF)¹¹.

Guava is rich in tannins, phenols, triterpenes, flavonoids, essential oils, saponins, carotenoids, lectins, vitamins, fibre and fatty acids. Guava fruits are also a good source of pectin - a dietary fibre. However lot of pharmacological activity is attributed due to the presence of flavonoids, leutin, zeaxanthine and lycopene¹². The flavonoids have demonstrated to possess antibacterial activity. The active flavonoid compound quercetine-3-O-alpha-l-arabinopyranoside has been reported for the anti-plague activity¹³.

Further, it has been showed that the Guava's main plant contain various chemicals like alanine, alpha-linolenic acid, ascorbic acid, Asiatic acid, aspartic acid, benzaldehyde, carotenoids, catechol-tannins, D-galactose, D-galacturonic acid, ellagic acid, essential oils, flavonoids, gallic acid, glutamic acid, guaijavarin, guajiverine, guajivolic acid, histidine, hyperin, isoquercetin, lectins, limonene, linoleic acid, linolenic acid, lysine, myricetin, oxalic acid, pectin, polyphenols, quercetin, serine, tannins, terpenes¹⁴. Leaves of the guava tree are a rich source of flavonoids, especially quercetin, which is mainly responsible for the antibacterial activity¹⁴.

Anti-diarrhoea effect is also contributed due to the quercetin. Among the major effect of the plant extract are antibacterial and trypanocidal activities which may be attributed mainly to the broad antimicrobial property of the flavonoids and iron chelating property of tannins¹⁵. Aqueous extract of guava leaves were reported to be effective against a number of microbial strains¹⁶ and anti-rotavirus activity¹⁷.

In the pink fruit, commercial essence was characterized to present a volatile profile rich in components with low molecular weight, especially alcohols, esters aldehydes, whereas in the fresh fruit puree terpenic hydrocarbons and 3-hydroxy-2-butanone were the most abundant components. 3-penten-2-ol and 2-butenyl acetate are the new active aromatic constituents found in the pink guava fruit¹⁴.

Traditional Use: Guava (*Psidium guajava*) is a well-known plant. Traditionally it is used to treat the various conditions. Fruit is a rich source of dietary fibres, vitamin A and C, thiamine, folic acid, riboflavin, niacin, vitamin B₃ and G₄⁶. Every part of the plant like leaves, root, bark, fruits is used for the medicinal use¹⁸. The traditional uses are explained according to the plant parts.

Root: In the Fiji and Senegal, root of plant is used in the treatment of Diarrhoea, coughs, stomach-ache, dysentery, toothaches, indigestion, constipation¹⁹. The aqueous extract of root is used in the treatment of diarrhoea and dysentery. The roots of the plant have been reported for their astringent property at a dose of 30-40 grams for 1 liter or 4-5 cups a day²⁰. In the Philippines the Decoction and poultice of the root are used astringent, ulcers, wounds, diarrhoea²¹.

Bark: The bark of the *Psidium guajava* has been reported for their astringent, febrifuge, antiseptic properties. The decoction form of the bark is used in the treatment of ulcer,²². In the Tahiti, Samoa the decoction and poultice form of plant is used to expel the placenta after child birth and in infection of the skin, caries, vaginal haemorrhage wounds and respiratory disturbances (World Health Organization, 1998)¹⁹. In Kinshasa the decoction form is also used to treat the diarrhoea and antiameobic²³.

Leaf: The leaves of the plant have been implicated in management of diarrhoea, wounds, ulcer, toothache, and stomach-ache and in the diabetes²⁴. Further, the infusion and decoction of leaves are used in the leucorrhoea like condition²². The decoction of the leaves are used as gargles or the sore throats, swelling of the mouth, laryngitis, external ulcer on the skin and vaginal irritations in the Latin America, Central and West Africa and South East Asia^{25,26}. *Psidium guajava* leaves have to possess the anti-inflammatory property

and is also used in various lung problems. In addition to this, leaves are used in various bacterial infection, diarrhoea, blood cleansing²⁶. Leaf extract of the *Psidium guajava* has been reported for the strong anti-microbial properties²⁷.

Fruit: Various evidence indicates that the ripe fruit of guava has laxative action, whereas the unripe fruit decoction is used as astringent, anti-diarrhoeic²¹, and has medicinal use²⁸. It has been shown that fruit of *psidium guajava* is used for the treatment of diabetes²⁹.

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 anti-diabetic, anti-diarrhoeal, anti-microbial, anti-oxidant, cardio active, hepatoprotective, antipyretic, spasmolytic, immunomodulatory, and contractile effect, which are explained in latter part of review.

1. 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 250mg/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 secretion²⁹. The ethanolic stem bark extract exhibited significant hypoglycaemic activity in alloxan-induced hyperglycaemic rats at an oral dose of 250mg/kg³⁰.

Aqueous leaf extract of guava at 0.01–0.625 mg/ml showed significant inhibition on low density lipid (LDL) glycation in a dose dependent manner³¹. 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 glucose³².

2. 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 peel²⁸, but if taken unripe fruit in large quantity cause indigestion, vomiting²². 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^{33, 34}.

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^{23, 35}. Fresh leaf extract of the plant when administered at a dose of 0.2 ml/kg of morphine sulphate showed inhibition of propulsion^{36, 37}. Flower buds and leaf extraction of the *Psidium guajava* consist of Quercetin and quercetin-3-arabioside which are used in the treatment of diarrhoea in the Costa Rica²⁰. 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 decrease³⁴.

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 diarrhoea³⁸. It is also reported that the asiatic acid, which is present in the leaf extraction, showed dose-dependent (10–500 ug/ml) spasmolytic activity in spontaneously contracting isolated rabbit jejunum preparations³⁹. Methanol extract from leaves (8ug/ml) of *Psidium guajava* showed activity against simian (SA-11) rotavirus (93.8% inhibition)¹⁷.

3. Antimicrobial Activity: Four antibacterial flavonoids (morin-3-*O*-lyxoside, morin-3-*O*-arabioside, quercetin, and quercetin-3-*O*-arabioside) 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*⁴⁰. 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 trypanosomes¹⁵.

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*^{42, 43}. Leaf extract of *psidium guajava* also reported for the anti-bacterial activity on *staphylococcus aureus* due to the protein degrading activity of the leaf extract⁴⁴. 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 drugs⁴⁵.

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*²⁷. Studies indicates that leaf extract of *psidium guajava* has potent anti-microbial activity against *Propioni bacterium acnes* and 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* spp. *Shigella* spp^{47, 41}.

The aqueous and methanolic extract is effective against the spore formation and production of *Clostridium prefringens* type A⁴⁸. Further, four antibacterial compound has been reported from the methanolic root extract which was further separated by column Chromatograph. Three antibacterial substances have been detected in the leaves which are derivatives of quercetin^{49, 7}.

In another study, fungicidal action against *Arthrinium sacchari* M001 and *Chaetomium funicola* M002 strains was observed from the methanolic extract of ripe fruit⁵⁰.

4. 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^{51, 52}. Many studies have reported significant alterations in plasma antioxidant enzyme systems, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), and in lipid peroxidation²⁹. It has been well reported that *Psidium guajava* (PG) exhibit its antioxidant effect through the inhibition of Nuclear factor-kappa B (NF-kB) activation and restoration of enzymatic antioxidants²⁹.

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 activity⁵³. *Psidium guajava* contains phenolic phytochemical which inhibit peroxidation reaction in the living body and thus prevent various types of chronic disease such as diabetes, cancer and heart disease⁵⁴. These antioxidant properties are associated with its phenolic compounds such as protocatechonic acid, ferulic acid, quercetin, guavin, ascorbic acid, gallic acid and caffeic acid⁵⁵.

Guava leaf extracts and fruits are a potential source of natural antioxidants²⁶. Studies indicated that guava fruit also exert antioxidant action, collagen formation and radio protective activity in the assay with technetium-99m²⁶.

5. Antitussive Activity: It has been reported that water infusion from *Psidium guajava* leaf extract decreases the frequency of coughing induced by capsaicin aerosol⁵⁶. In senegal and Peru *Psidium guajava* leaves boiled together to make decoction is very effective for cough and treatment of trachea bronchitis²⁸. **Hepatoprotective Activity:** The aqueous leaf extract of *psidium guajava* has been reported for their hepatoprotective action at a dose of 500mg kg⁻¹⁵⁷.

Studies indicate that the Asiatic acid which is present in the leaves and fruit of *Psidium guajava* is responsible for the hepatoprotection⁵⁸. *P. guajava* leaf extracts (500mg/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 rats liver homogenate.

The higher dose of the extract (500mg/kg, p.o) prevented and showed 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 (500mg/kg, p.o.) of *P. guajava* leaf extract was found to be more effective than the lower dose (250mg/kg, p.o.)⁵⁹. Studies showed that the unripe fruit of *psidium guajava* has a potent hepatoprotective agent⁶⁰.

6. 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 cells⁶¹. 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-29cells⁶².

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 activity⁶³. 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 preventive⁶⁴. It has been reported that essential oil of *Psidium guajava* has the potent anti proliferative activity⁶⁵.

7. Anti-Inflammatory Activity: 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 50-800mg/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 mice⁶⁶.

8. Cardiovascular Effects: Studies showed that the aqueous leaf extract of *Psidium guajava* exhibited cardioprotective effects against myocardial ischemia-reperfusion injury in isolated rat heart⁶⁷. 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 effect⁶⁷. Further investigation showed that aqueous fractions obtained from the acetic extract of *Psidium guajava* leaf exhibit the negative inotropic effect by decrease the atrial contractile by reducing the calcium (Ca²⁺) entry in myocardial cells and also by openenig potassium channels of cardiac tissue⁶⁸.

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 involvement²⁵.

9. 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 activities⁴⁶. 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 1mg/ml⁶⁹. Moreover Guava stem bark and leaf stem extract has been found to possess anti giardiasis activity and inhibit growth of *Entamoeba histolytica* respectively^{70, 23, 71}.

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