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Review Article

A REVIEW ON MULTIPURPOSE MEDICINAL PROPERTIES OF TRADITIONALLY USED *PSIDIUM GUAJAVA* LEAVES

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ABSTRACT

Psidium guajava is an important food crop and medicinal plant available in tropical and subtropical countries. *P. guajava* (Guava), belonging to the family of *Myrtaceae. P. guajava* Linn. (Guava) is used not only as food but also as folk medicine in subtropical areas around the world because of its pharmacologic activities. 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. Conventionally, guava is used for the treatment of various ailments such as antioxidant, hepatoprotective, anti-allergy, antimicrobial, antigenotoxic, antiplasmodial, cytotoxic, antispasmodic, cardioactive, anti-cough, antidiabetic, anti-inflammatory, and antinociceptive activities, supporting its traditional uses.

Keywords: Phytoconstituents, Pharmacological and structural use, *Psidium guajava*, Traditional use

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INTRODUCTION

Nature has blessed *P. guajava* with many essential nutrients. *Psidium guajava* L., prevalently known as guava, is a small tree having a place with the myrtle family (*Myrtaceae*) [1]. Local to tropical regions from South Mexico to North South America, guava trees have been developed by numerous different nations having tropical and subtropical atmospheres, in this manner permitting creation around the globe [2]. Conventionally, arrangements of the leaves have been utilized in folk medicine in a few nations, mostly as an anti-diarrheal remedy [3]. Besides, a few uses have been portrayed somewhere else on all continents, except for Europe [4]. Fig. 1 outlines the principle of traditional uses of guava leaves in the primary producer countries. Depending on the disease, the use of the cure is either oral or topical. The consumption of decoction, infusion, and boiled preparation is the most widely recognized approach to overcome several disorders, for example, rheumatism, diarrhea, diabetes mellitus, and cough, in India, China, Pakistan, and Bangladesh [5]. While in Southeast Asia, the decoction is utilized as a gargle for mouth ulcers and as an antibacterial in Nigeria [4]. For skin and wound, application poultice is very utilized in Mexico, Brazil, the Philippines, and Nigeria; furthermore, biting stick is utilized for oral consideration in Nigeria [5].

P. guajava is a little tree up to 20 feet high, with spreading branches. Guava is anything but difficult to perceive due to its smooth, thin, copper-shaded bark which pieces off, demonstrating the greenish layer underneath and because of the appealing, "hard" part of its trunk which may in time achieve a width of 10 inches [6]. *P. guajava*, which is viewed as local to Mexico, reaches out all through South America, Europe, Africa, and Asia. It is principally found in tropical and subtropical locales. In India, it is cultivated in Uttar Pradesh, Bihar, Maharashtra, Assam, West Bengal, Haryana, and Andhra Pradesh [2]. The leaves are evergreen, inverse, short-petioles, oval, or elongated elliptic, to some degree unpredictable in layout; 7–15 cm long to 3–5 cm wide, rough, with obvious parallel veins, and pretty much down on the underside [3]. This popular guava leaf is a factory of nutrients which can be very well depicted from Table 1.

P. guajava species are available throughout the world and their traditional use

P. guajava species are found in a different country. Their parts have different traditional therapeutic uses mentioned in Table 2.

PHYTOCONSTITUENT PRESENT IN *PSIDIUM GUAJAVA* LEAF

The guava leaves contain a few substance constituents, for example, α-pinene, β-pinene, limonene, menthol, terphenyl acetic acid derivation, isopropyl liquor, longicyclene, caryophyllene, β-bisabolene, caryophyllene oxide, β-copaene, farnesene, humulene, selinene, sardine and curcumin, malic acids, nerolidol, β-sitosterol, ursolic, crategolic, and guayavolic acids, cineol, quercetin, 3-L-4-4-arabinofuranoside (avicularin) and its 3-L-4-pyranoside (fundamental oil), pitch, 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 corrosive (2 α-,3 β-,6 β-,23-tetrahydroxyurs-12,20(30)- dien-28-oic corrosive, triterpene oleanolic corrosive, triterpenoids, flavinone-2'-ene, prenol, dihydro-benzo-phenanthridine, and cryptonine [16]. Guavas contain carotenoids and polyphenols, the significant classes of giving them generally high potential against cancer prevention agent esteem among plant foods. As these shades deliver the natural product skin and tissue shading, guavas that are red-orange have greater color content as polyphenol, carotenoid, and Vitamin A, retinoid sources than yellow-green ones. Guavas contain the two carotenoids and polyphenols like (+) gallocatechin, guaijaverin, leucocyanidin, and amritoside [17]. It was accounted for that the leaves of *P. guajava* contain fundamental oil wealthy in cineol, tannins, and triterpenes. Three flavonoids (quercetin, avicularin, and guaijaverin) have been isolated from the leaves [17]. The leaves of guava are rich in flavonoids, especially quercetin. The bark of the guava tree contains considerable amounts of tannins (11–27%) and hence is used for tanning and dyeing purposes. Leucocyanidin, lactic acid, ellagic acid, and amritoside have been isolated from the stem bark. Five constituents, one new pentacyclic triterpenoid: Guajanoic acid, and another four known compounds beta-sitosterol, uvaol, oleanolic acid, and ursolic acid, have been recently isolated from the leaves of *P. guajava* by Begum *et al.* [17]. The essential oil contains alpha-

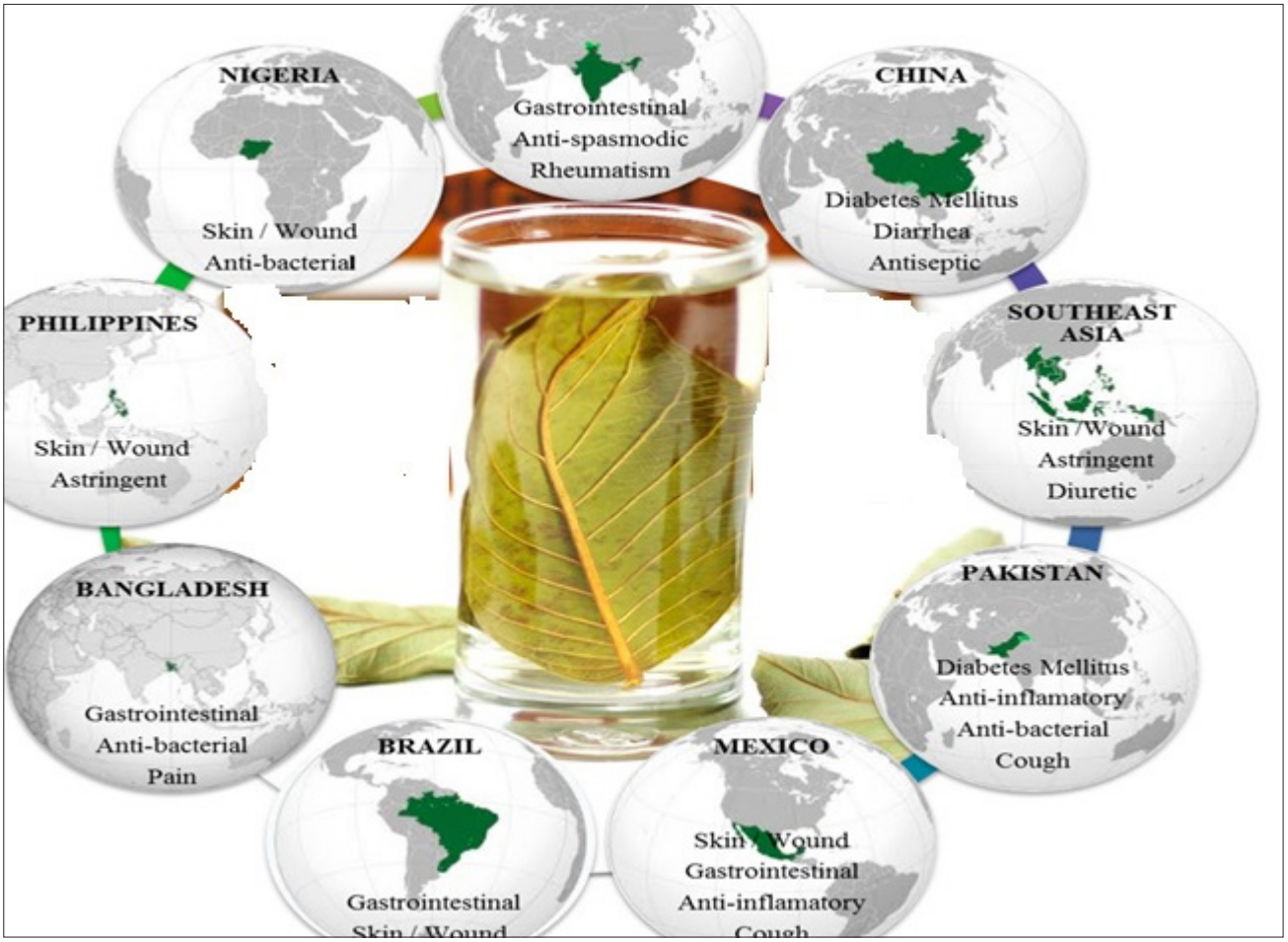


Fig. 1: Main traditional uses of guava leaves in the principal producer countries

Table 1: Botanical classification of *Psidium guajava*

Kingdom	***Plantae***	**Order**	**Myrtales**
Subkingdom	*Tracheobionta*	Family	*Myrtaceae*
Superdivision	*Spermatophyta*	Subfamily	*Myrtoideae*
Division	*Magnoliophyta*	Tribe	*Myrteae*
Class	*Magnoliopsida*	Genus	*Psidium*
Subclass	*Rosidae*	Species	*P. guajava*

P. guajava: *Psidium guajava*

pinene, caryophyllene, cineol, D-limonene, eugenol, and myrcene. The significant constituents of the unstable acids incorporate (E)-cinnamic acid and (Z)-3-hexenoic acid [18].

Traditional use of different parts of *P. guajava*

P. guajava have different traditional use of different parts. Their parts are used in a different country for their different therapeutic activity, which is mentioned in Table 3.

Structure and pharmacological activity of some chemical constituents of *Psidium guajava* leave

Based on structures and their pharmacological activity mentioned in Table 4.

PHARMACOLOGICAL ACTIVITIES OF *PSIDIUM GUAJAVA* SPECIES

- Anti-inflammatory
- Anti-amebic
- Antimalarial
- Antibacterial
- Anticestodal
- Anti-diarrheal
- Anti-rotavirus
- Antihyperglycemic
- Anti-stress
- Cardiovascular system effects
- Infectious and parasitic diseases
- The pharmacological effect of guava.

ANTI-INFLAMMATORY ACTIVITY

The inflammatory reaction happens when cells and body tissues are harmed by natural, compound, or physical challenges, for example, microorganisms, injury, poisons, or heat. It is a champion among the most imperative barrier components, which is gone for the expulsion of the harmful boosts and commencement of the recuperating procedure. Macrophages play an important role against different incendiary maladies and in the reaction where they discharge pro-inflammatory mediator and proteins, including interleukin-6 (IL-6), tumor necrosis factor-a (TNF-a), cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS) (Grip, Janciauskiene, and Lindgren, 2003). The RAW264.7 mouse macrophage cell line, when actuated by lipopolysaccharide (LPS), produces pro-inflammatory cytokines and other inflammatory intermediates including nitric oxide (NO) and prostaglandin E2 (PGE2), which are incorporated by iNOS and COX-2, separately [40]. Among the various conventional restorative herbs, *P. guajava* L. (*Myrtaceae*), ordinarily known as guava, has for sometimes been utilized as a part of prescriptions as a helpful actor for the treatment of various sicknesses, for example, as a calming, for diabetes, rheumatic disease, hypertension, wounds, ulcers, etc. [41]. Guava leaf extract (GLE) altogether hindered LPS-induced generation of NO and

Table 2: *Psidium guajava* **species found throughout the world and their traditional use**

Place, country	Part (s) used	Traditional use	Preparation (s)	Reference (s)
Colombia, Mexico	Leaves	Gastroenteritis, diarrhea, dysentery, rheumatic pain, wounds, ulcers, and toothache	Decoction and poultice	[4]
Indigenous Maya, Nahuatl, Zapoteco, and Popoluca of the region Tuxtlas, Veracruz, Mexico	Leaves	Cough, diarrhea	Decoction or infusion	[5]
Latin America, Mozambique	Leaves	Diarrhea, stomachache	Infusion or decoction	[6]
Mexico	Shoots, leaves, bark, and leaves mixed, rip fruits	Febrifuge, expel the placenta after childbirth, cold, cough hypoglycemic, affections of the skin, caries, vaginal hemorrhage, wounds, fever, dehydration, respiratory disturbances	Decoction, poultice	[2], [5]
Panama, Cuba, Costa Rica, México, Nicaragua, Panamá, Perú, Venezuela, Mozambique, Guatemala, Argentina	Leaves	Anti-inflammatory	Externally applied hot on inflammations	[3]
South Africa	Leaves	Diabetes mellitus, hypertension	Infusion or decoction	[4], [5]
Caribbean	Leaves	Diabetes mellitus	Infusion or decoction	[6]
China	Leaves	Diarrhea, antiseptic, Diabetes mellitus	Infusion or decoction	[7]
Philippines	Leaf, bark, unripe fruit, roots	Astringent, ulcers, wounds, diarrhea	Decoction and poultice	[8]
Peru	Flower buds, leaves	Heart and constipation, conjunctivitis, cough, diarrhea, digestive problems, dysentery, edema, gout, hemorrhages, gastroenteritis, gastritis, lung problems, shock, vaginal discharge, vertigo, vomiting, worms	Infusion or decoction	[9]
Kinshasa, Congo	Leaves, bark	Diarrhea, anti-amebic	Infusion or decoction, tisane	[10]
Senegal	Shoots, roots	Diarrhea, dysentery	Infusion or decoction	[10]
Fiji	Leaves, roots, ripe fruit	Diarrhea, coughs, stomachache, dysentery, toothaches, indigestion, constipation	Juice, the leaves are pounded, squeezed in salt water	[11]
Tahiti, Samoa	The whole plant, shoots	Skin tonic, painful menstruation, miscarriages, uterine bleeding, premature labor in women, wounds	Infusion or decoction, paste	[11]
New Guinea, Samoa, Tonga, Niue, Futuna, Tahiti	Leaves	Itchy rashes caused by scabies	Boiled preparation	[11]
Cook Islands	Leaves	Sores, boils, cuts, sprains	Infusion or decoction	[12]
Trinidad	Leaves	Bacterial infections, blood cleansing, diarrhea, dysentery	Infusion or decoction	[11]
Latin America, Central, and West Africa, and Southeast Asia	Leaves	Gargle for sore throats, laryngitis, and swelling of the mouth, and it is used externally for skin ulcers, vaginal irritation, and discharge	Decoction	[6]
Panama, Bolivia, and Venezuela	Bark and leaves	Dysentery, astringent, used as a bath to treat skin ailments	Decoction	[13]
Brazil	Ripe fruit, flowers, and leaves	Anorexia, cholera, diarrhea, digestive problems, dysentery, gastric insufficiency, inflamed mucous membranes, laryngitis, mouth (swelling), skin problems, sore throat, ulcers, vaginal discharge	Mashed, decoction	[14], [15]
USA	Leaf	Antibiotic and diarrhea	Decoction	[8]

PGE2 in a dose-dependent manner. GLE reduced the effects of both inducible NO synthase and cyclooxygenase-2 to a limited extent through the downregulation of ERK1/2 initiation in RAW264.7 macrophages. Moreover, GLE showed huge mitigating movement in two distinctive animal models – Freund's whole adjuvant-induced hyperalgesia in the rodent and LPS-induced endotoxic shock in mice [42]. The methanolic extract of the leaves of *P. guajava* was found to repress paw edema induce through carrageenan in rats and pain actuated by acidic corrosive in mice and displayed an antipyretic impact [43]. Irritation is a pathophysiological reaction to damage, contamination, or devastation portrayed by warm, redness, pain, swelling, and aggravated capacities. Inflammation is an ordinary defensive reaction to tissue damage caused by physical injury, harmful synthetic or microbial operators. It is the body's foreign reaction to inactivate or kill the attacking living beings, expel the antibodies, and set the phase for tissue repair. It is activated by the arrival of synthetic mediators from damaged tissue and moving cells [44]. The present examination builds up the movement of *P. guajava* leaf extricates in tentatively prompted inflammation in Wistar rats. The fiery reaction is promptly delivered as paw edema with the inflammation or phlogistic operators. Such specialists such as carrageenan, formalin, bradykinin, histamine, serotonin, and so on when injected into the dorsum of the foot of the rats they deliver intense paw edema inside a couple of minutes of infusion. Carrageenan-induced rodent paw edema has been most utilized as a perfect model

Table 3: Traditional use of different parts of *Psidium guajava*

Plant parts	Uses	Countries	References
Fruit	Food: Juice, jelly nectar, concentrated, stuffed with candies, gelatins, pastes, tinned products, confectionery, etc.	All the countries	[19]
Wood and leaves	Carpentry and turnery use the leaves to make a black dye for silk	Malaya	[20]
Wood	Engravings	India	[20]
Wood	Spinning tops	Guatemala	[21]
Wood	Hair Combs	El Salvador	[21]
Wood	Construction of houses	Nigeria	[22]
Leaves	Employed to give a black color of cotton	Southeast Asia	[20]
Leaves	Serve to dye matting	Indonesia	[20]
Bark	Dyes, stains, inks, tattoos, and mordants	Africa	[23]
Wood flowers	The tree may be parasitized by the mistletoe, *P. calyculatus* Don, producing the rosette-like malformations called "wood flowers" which are sold as ornamental curiosities. Furthermore, the tree is seeded to give shade to the coffee and its wood is used in the construction	Mexico	[24]

P. calyculatus: *Psittacanthus calyculatus*

for inflammatory changes [45]. Guava leaf removes contain various polyphenolic mixes, and another substance exacerbates that has been appeared to show different pharmacological effects, including prevention [33]. Inflammation is the body's first safeguard against contamination and is an essential standard response for the sign of different ailments related to constant irritation [46]. Irritation, which is started by trauma and pathogens, cell damage, or inflammation, is an ordinary physiological invulnerable reaction intervened by different flagging atoms created by leukocytes, including macrophages, and pole cells [47]. Specifically, macrophages assume an important role in directing irritation and survival reactions to keep up a defensive response. LPS-induced macrophages to discharge inflammatory cytokines, for example, TNF-α, IL-6, and IL-1β, and in addition another inflammatory mediator, for example, NO and PGE2 through the inducible iNOS and cyclooxygenase-2 (COX-2), individually [48]. Polyphenolic mixes are a common substance that is known to have a few mitigating properties [49]. *P. guajava* leaves indicated a critical mitigating effect with an inhibition of 58% [50]. *P. guajava* leaves were found to contain mitigating action, by diminishing serum chemokines, for example, interleukin-8 and eosinophil cationic protein [51].

ANTI-AMEBIC ACTIVITY

Some of the active plant extracts are currently used in the traditional medicine of some African countries for the treatment of intestinal amebiasis. This is the case of Euphorbia hirta, *Mangifera indica*, *Carica papaya*, and *P. guajava* [52].

ANTI-MALARIAL ACTIVITY

So also, an investigation directed on the ethnobotanical overview in Maiduguri, Northeast Nigeria, uncovered that the plants are usually utilized by the three noteworthy ethnic groups in Nigeria (Hausa, Yoruba, and Igbo) for the treatment of intestinal disease. *P. guajava* has been accounted for to be moderately non-poisonous in a saltwater shrimp lethality test [53]. Plants are dominatingly fundamental while poisonous quality *P. guajava* leaf is a phytotherapeutic used to treat antimalarial effect have additionally been reported [10]. In the logical field, numerous pharmacological examinations have exhibited the capacity of *P. guajava* leaves, barks, and phytoconstituents to show antimicrobial, resistance to anti-diarrheal and antimalarial [41]. The parasite lactate dehydrogenase measure technique, as of late created *in vitro* enzymatic strategy for assessing antimalarial, was utilized to look at the antiplasmodial activity of the aqueous leaf, stem bark, and extract of *P. guajava*. An *in vitro* antiplasmodial activity did utilize a chloroquine-sensitive strain of malaria parasite, *Plasmodium falciparum* D10 demonstrated antigiardiasic action with trophozoite mortality (87%±1.0%); guava stem bark separate indicated IC_{50} estimations of 10–20 μg/ml [54], [55]. The aqueous leaf, stem bark, and extract of *P. guajava* L. were utilized to inspect resistance to plasmodial action utilizing *in vitro* parasite lactate dehydrogenase analysis technique [54]. The effect of *P. guajava* leaf extracts was evaluated, as an antimalarial action [56]. The leaves together with the bark and leaves of *P. guajava*, *Cymbopogon citratus*, *and Carica papaya*, citrus foods are grown from the ground gratissimum, are utilized for getting ready blends for the treatment of intestinal sickness and yellow fever by bowel purge or wash. Leaves have been utilized as a purgative and an expectorant [57].

ANTIBACTERIAL ACTIVITY

The essential oils of *P. guajava* L. leaves showed a poor growth preventive action activity yet strong antibacterial and antifungal activity [58]. The leaves of *P. guajava* have antibacterial action [59] because the flavonoids [60] researched the antibacterial action of guava (*P. guajava*). The liquid focus of *P. guajava* leaves indicated an incredible antibacterial effect against various test strains. The report says that flavonoids extract from guava leaves possess antibacterial activity [61]. Leaf extract of guava has been shown to have antibacterial action due to the presence of flavonoid glycosides, Morin-3-O-alpha-L-lyxopyranoside, and morin-3-O-alpha-L-arabinopyranoside [39]. The flavonoids have been displayed to have antibacterial action. The flavonoid compound quercetin-3-O-alpha-l-arabinopyranoside has been shown to counter plaque development [62]. The closeness of the metabolites, for instance, cardiac glycosides, saponins, tannins, alkaloids in *P. guajava* may be accountable for its potential use as a prescription against pathogenic microorganisms [63]. Alkaloids and flavonoids are phenolic structures containing one carbonyl moiety with extracellular and dissolvable protein and bacterial cell wall [64]. It demonstrates antibacterial action through these structures. Leaves of the guava tree are rich in flavonoids, especially quercetin, which is responsible for the antibacterial activity [65]. Three antibacterial substances have been perceived in the leaves, which are congeners of quercetin [38]. *P. guajava* demonstrated strong antibacterial action, especially against Gram-positive bacteria, *B. subtilis*, and *S. aureus* with a mean zone of inhibition of 33.42 mm and 24.83 mm. In addition, antibacterial development connected by guava extract toward this Gram-positive microorganism was more grounded than those resistant to chloramphenicol (ZOI: *B. subtilis* = 26.58 mm and *S. aureus* = 24.75 mm). A similar result was reported by Achudhan [66], Abubakar [67], Anas *et al*. [68] who showed the leaves extract of *P. guajava* to have the broad development against Gram-positive microorganisms, notwithstanding, less for Gram-negative species. It is suggested that the strong bactericidal activity of the leaf extracts against the Gram-positive microorganism due to the presence of growth-inhibiting constituents, which [69,70] also, can combine with bacterial cell wall [66,70,71]. Evaluation of the antibacterial activities of aqueous and ethanolic extract from leaves, roots, and stems bark of *P. guajava* [69] evaluated the antibacterial activity of aqueous and other extracts of *P. guajava* leaves against multidrug safe (MDR) clinical detaches of *Staphylococcus aureus* strains accumulated from recuperating focuses in North (Malabar area) Kerala [72]. Isolate the leaf extract was subjected to phytochemical screening with the ultimate objective to identify the metabolites. The concentrates were studied for the antibacterial action against clinical isolates of *Klebsiella pneumonia*, *Escherichia coli*, *Salmonella sp*., *Pseudomonas aeruginosa*,

Table 4: Structure and pharmacological activity of some chemical constituents of *Psidium guajava*

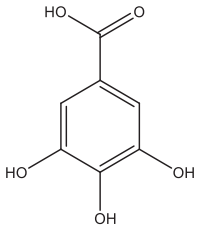
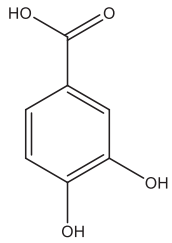
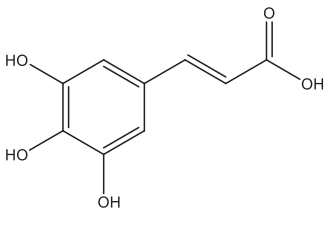
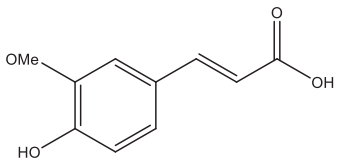
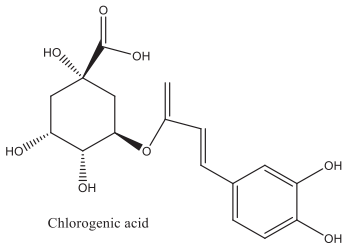
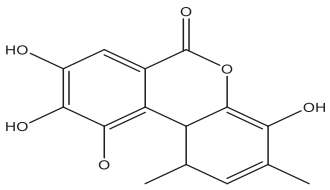
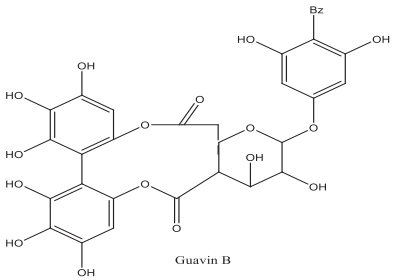
Structure	Biological activity	Reference
 Gallic acid	Cardioprotective effects against ischemia-reperfusion. Antioxidant	[25,26]
 Protocatechuic acid	Antioxidant	[25,27]
 Caffeic acid	Antibacterial activity, antioxidant	[28,29]
 Ferulic acid	Antioxidant	[28-30]
 Chlorogenic acid	Antioxidant, capacity radical scavenging activity, antimutagenic/anticarcinogenic effect, inflammation inhibiting and endothelial protective properties	[28,31,32]
 Ellagic acid	Possesses analgesic and anti-inflammatory properties	[31,33]
 Guavin B	Antioxidant	[25,30]

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Table 4: ***(Continued)***

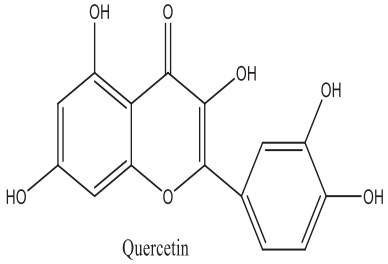
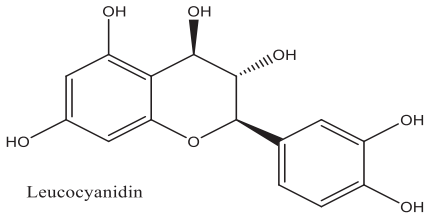
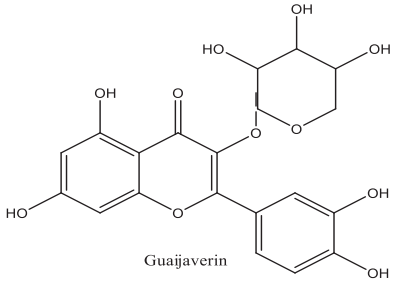
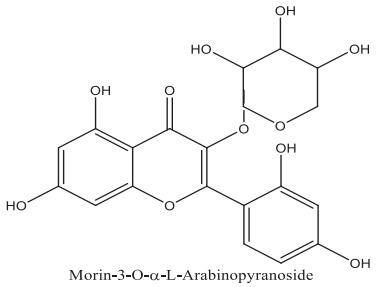
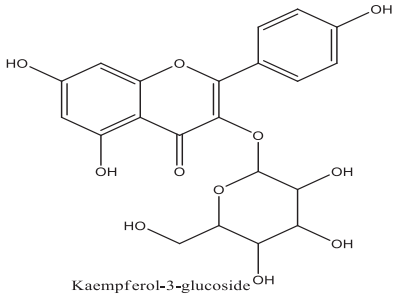
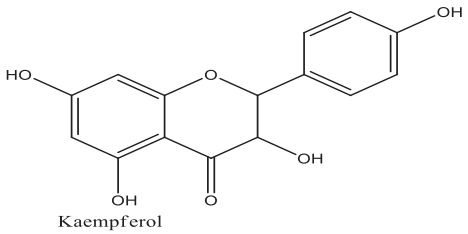
Structure	Biological activity	Reference
 Quercetin	Anti-diarrhea effect, exhibited antioxidant and spasmolytic effects also showed inhibition of skeletal muscles contraction, Induced reduction of presynaptic molecular activity, also showed vasodilator	[26,28,34-36]
 Leucocyanidin	-	[37]
 Guaijaverin	Showed antimicrobial activity against *S. mutans*	[38]
 Morin-3-O-α-L-Arabinopyranoside	Showed antimicrobial activity against *S. enteritidis* and *B. cereus*	[39]
 Kaempferol-3-glucoside	-	[28]
 Kaempferol	-	[28]

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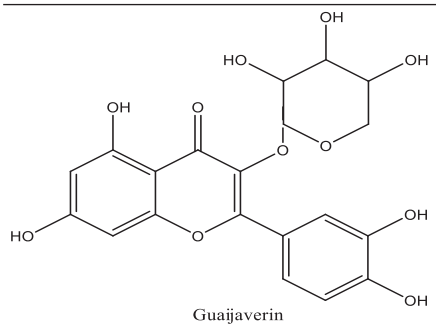
Table 4: ***(Continued)***

Structure	Biological activity	Reference
 Guajaverin	Showed antimicrobial activity against *S. mutans*	-

S. mutans: *Streptococcus mutans*, *B. cereus*: *Bacillus cereus*, *S. enteritidis*: *Salmonella enteritidis*

and *S. aureus*. *P. guajava* verdant part is used as an antibacterial in the treatment of tropical diseases [73]. Aqueous extract of *P. guajava* was all the more potent in curbing the development of pathogenic *Proteus* mirabilis, Streptococcus pyogenes, *E. coli*, *S. aureus*, and *P. aeruginosa* than used for oral antibacterial prescriptions and had the potential to be [74]. The leaves extract of *P. guajava* can control diseases caused by A. hydrophila [75]. Aqueous and methanol extract from leaf and bark of *P. guajava* exhibited strong antibacterial activity against *V. cholerae O1*, offering the potential for controlling pandemics of cholera *V. cholerae O1* [76]. The ethnobotanical studies on the leaves and bark of the plant *P. guajava* L. show that it is used for wound healing and antibacterial activities. It has a high amount of tannins. *In vitro*, the antibacterial activity of *P. guajava* leaf extract on *S. aureus* was maybe a direct result of protein inhibition by the concentrates [77]. After checking the impact of GLE, *in vitro*, against *Aeromonas hydrophila*, *in vivo* tests were completed in tilapia (*Oreochromis niloticus*), showing the potential effect of *P. guajava* as an antimicrobial agent [75]. Moreover, GLE enhanced the activity of prophenoloxidase and NO synthase in serum, and superoxide dismutase, corrosive phosphatase, soluble phosphatase, and lysozyme in serum and hepatopancreas [78]. Besides, guava leaves have been recommended for trypanocidal action in Wistar albino rats [79]. The concentrate improves the tissue lipid peroxidation related to trypanosomosis and raises the level of the glutathione fixation [80]. Besides, guava leaves are likewise suggested for treating irritable bowels since they counteracted the intestinal colonization of *Citrobacter rodentium* in person [81]. In chicks, guava leaf empowered the control of loose bowels created by *E. coli* and decreased its symptoms [82]. In mice, the reduction of symptoms caused by *V. cholerae*, a human pathogen was additionally affirmed by Yadav and Tangpu [83]. Every one of the outcomes for *in vivo* action and antibacterial properties has been given.

ANTI-CESTODAL ACTIVITY

The leaf concentrate of *P. guajava* has anti-cestodal action. In the investigation [84] in the northeastern part of India, different Naga clans utilize new leaves water decoction of *P. guajava* (privately known as "*Mottram*") as a typical solution for intestinal worm infection. In vivo anti-cestodal activity of *P. guajava* utilizing exploratory *Hymenolepis diminuta* contamination in albino rats [84]. In the present investigation, methanol extract of the leaves of *P. guajava* showed anti-cestodal action against *H. diminuta* infection. The outcomes demonstrate the potential of leaf extract [85].

ANTI-DIARRHEAL ACTIVITY

P. guajava leaves displayed antibacterial and diarrheal effects. The plant has been broadly evaluated for pharmacological development of its extracts, and the results show actions against diarrhea [86]. In the legitimate field, various pharmacological examinations have demonstrated the limit of *P. guajava* leaves, barks, and normal items to appear against diarrhea [41]. The action is attributed to this plant in various countries. Its leaves are used as a cicatrizant. Concentrate extracts with concentrates of the leaves have exhibited anti-diarrheal activity [87]. *P. guajava* L. leaf has a long history of usage as an anti-diarrheal [88]. This development could be understood through understanding the spasmolytic, antibacterial, and anti-amebic activity together with the going with revelations, quercetin was found to reduce the fine permeability in the stomach gap [34], the alcoholic extract of the leaves has a morphine-like action on acetylcholine release in the ileum, this morphine-like action was seen due to quercetin [89]. The extract has shown a dose-related anti-diarrheal effect. Estimations of 0.2 ml/kg of new leaf extract conveyed 65% obstruction (restriction of Microlax response started test detachment of the guts with a sedative like concentrates of *P. guajava* leaf in rats) [90]. The past studies have shown that phenolic extract has other characteristic activities, for instance, against diarrhea [91]. Quercetin is thought to add to another diarrheal effect of guava: It can release up the intestinal smooth muscle and curb gut compressions [92]. It has been represented that quercetin can potentiate the anti-diarrheal action of *P. guajava* extract. These revelations are in confirmation with Mukherjee *et al*. [93] who show that the bark extract of *P. guajava* had anti-diarrheal activity *in vitro*. Past reports have shown the anti-diarrheal action of tannins [94], flavonoids [95], and saponins [96]. The plant has been generally analyzed for the pharmacological development of its genuine parts, and the results exhibit an intense anti-diarrheal action [65]. Quercetin can release up the intestinal smooth muscle [65].

ANTI-ROTAVIRUS ACTIVITY

Aqueous extract of guava leaves was shown action against rotavirus [97]. Besides, the aqueous concentrate of guava leaves was viable against various microbial strains [98]. Metwally *et al*. [99] exhibited that a few flavonoids identified in plant concentrates of *P. guajava* could inhibit the rotavirus growth infection. Considering that flavonoids were found in every presenting concentrate, we could guarantee that these mixes could be inhibitors of rotavirus proliferation in MA-104 cells. Nonetheless, our concentrates additionally contain tannins, terpenes, saponins, and nitrogenous mixes. Concentrates of *P. guajava* (*Myrtaceae*) leaves (93.8%) had activity against simian rotavirus [97].

ANTI-HYPERGLYCEMIC ACTIVITY

Guava leaf "*P. guajava* L." of the *Myrtaceae* family has a long history of medicinal uses in Egypt and worldwide as a treatment against hypertension, corpulence, and in the control of diabetes mellitus [100]. During the screening of a few plants, the leaves of *P. guajava* repress the plasma sugar level in alloxan-induced diabetic rats amid glucose tolerance test (GTT) [101]. Different parts of *P. guajava* have been utilized for the treatment of diabetes mellitus. Studies showed the

capacity of the guavanoic acid from *P. guajava* intermediate gold nanoparticles and its antidiabetic activity by PTP 1B inhibition [102]. The aqueous extract had critical anti-hyperglycemic activity. It is, by and large, acknowledged that alloxan treatment causes the lasting destruction of β-cells [103]. Studied the hypoglycemic action of aqueous extract of leaves of *P. guajava* on glycemic control [104]. In spite of this report, many studies have been completed to decide the pharmacological effect associated with hypoglycemic properties. *P. guajava* leaves have been shown to have the hypoglycemic effect, on blood glucose level (BGL) of streptozotocin (STZ)-induced diabetics in GTT and postprandial glucose levels. The aqueous extract shows anti-hyperglycemic action which is associated with its lowering of Mg [105]. Antihyperglycemic action of best plants was due to the capacity of the phytoconstituents to increase glucose transport and metabolism in muscle and additionally to increase insulin secretion [106]. A decoction of *P. guajava* leaves is used for the treatment of different ailments, including diabetes. The various polyphenolic, triterpenoids displayed in the plant may represent the watched antidiabetic action of the leaf extracts. A decoction of *P. guajava* leaves was screened for hypoglycemic activity on alloxan-induced diabetic rats. In both intense and sub-intense tests, aqueous extract, at an oral dosage of 250 mg/kg, demonstrated factually huge hypoglycemic action [107]. The treatment with *P. guajava* leaf extract (0.01–0.625 mg/mL) indicated the signification of LDL in a dosage-dependent in manner. Tannins, flavonoids, pentacyclic triterpenoids, guaijaverin, quercetin, and other concoction mixes exhibited in the plant are hypothesized to represent the hypoglycemic and hypotensive action of the leaf extract [108].

The anti-glycative potential of the guava leaves was assessed, with the conclusion that the concentrate repressed *in vitro* glycation development [109]. Gallic acid, catechin, and quercetin displayed more than 80% inhibitory effect due to ferulic acid [110]. In another investigation, seven unadulterated flavonoids (quercetin, kaempferol, guaijaverin, avicularia, myricetin, hyperin, and apigenin) indicated inhibitory activity against sucrase, maltase, and amylase, and a reasonable synergistic effect against glucosidase [111]. In addition, Deguchi and Miyazaki [112] recommended that the fraction that restrained the *in vitro* activity of – glucosidase catalysts in guava extract was a polymerized polyphenol. Furthermore, polysaccharides from guava leave additionally showed glucosidase inhibitor [113]. Eidenberger [114] showed the inhibitory effect of guava leaf ethanol extract on dipeptidyl-peptidase-IV because of the presence of flavonol-glycosides: Peltatoside, hyperoside, methyl quercetin hexoside, isoquercitrin, quercetin/morin pentosidine, guaijaverin, and quercetin/morin pentoside. Furthermore, the individual flavonol-glycosides found in the guava extract exhibited no huge contrasts and uptake of the entire guava extract into epithelial cells [114]. In a similar cell line, the inhibitor of fructose uptake was likewise tried by Lee [115] who confirmed that catechin and quercetin were added to the inhibitor of glucose transporters. Furthermore, the improvement of aqueous GLE was researched concerning glucose uptake in rodent clone nine hepatocytes. In addition, quercetin was proposed responsible for increasing glucose uptake in liver cells and adding hypoglycemia in diabetes [116]. Furthermore, Basha and Kumari [117] additionally evaluated the glucose take-up of various concentrates. The methanol extract of guava leaves was observed to be the best in bringing down glucose levels. Khaleel Basha *et al*. [102] showed the capacity of guavanoic-acid intervened gold nanoparticles to restrain the protein tyrosine phosphatase 1B movement. Without a doubt, a guava leaf ethanol extract was tried in the pre-adipocyte cell line (3T3-L1), which demonstrated its capacity to inhibit adipocyte separation through down-direction of adipogenic translation elements and markers and subsequently may anticipate corpulence *in vivo* [118]. To assess the capability of the leaves on glucose uptake and glycogen formation, an extract was utilized in insulin-resistant mouse (FL83B) cells. The outcomes confirm the enhanced movement and phosphorylation of insulin-related proteins, advancing glycogen union, and glycolysis pathways. In a similar cell line, vescalagin was hypothesized to reduce insulin resistance in mouse hepatocytes [119]. The most recent investigation in L6 myoblasts and myotubes cells affirmed that the glucose uptake through wortmannin-dependent pathway. Guava also leaves likewise restrained aldose reductase action, up-controlled quality, and protein level articulation of a few insulin receptors and enhanced cell level glucose take-up [120].

ANTI-STRESS ACTIVITY

Numerous herbs revealed in the classical literature have powerful antistress movement, and their use in the present situation should be evaluated. *P. guajava* acclaimed as a poor man's apple of the tropics has a long history of customary use for extensive types of infections. The natural product, and in addition its juice, is uninhibitedly devoured for its taste and nourishing advantages. A great part of the customary uses has been approved by the research [121]. *P. guajava* has a place with the family *Myrtaceae*. *P. guajava* at the measurements of 200 mg/kg and 400 mg/kg altogether increased the swimming time in the forced swim test. This capacity of the ethanolic extract of *P. guajava* to increase the swimming time in the rodent recommends an antistress property. An ethanolic extract of *P. guajava* L. was examined for anoxia push resilience test and swimming perseverance test in Swiss mice and indicated critical adaptogenic movement against the stress models [122].

CARDIOVASCULAR SYSTEM EFFECTS

The present investigation demonstrated that reduced triglyceride levels in rats after the treatment of ethanolic leaf extract of *P. guajava*. The hypolipidemic impact of *P. guajava* leaf extract can be ascribed to the presence of flavonoids, which can decrease the serum TG level. This may be because of the ideal action of serum lipoprotein lipase and the cancer preventive action of the plant extract. Overall, the investigation shows the impact of *P. guajava* leaves on the diabetic myocardium. One of the possible agents for the cardioprotective impact of PGEt is its high polyphenolic content and its antiglycation action. Chen *et al.* [123] showed an extensive variety of effects of polyphenols, on cancer prevention, antimutagenic, anticarcinogenic, free radical scavenging action, and diminished cardiovascular impact [124]. Being an intense radical scavenger, it prevents the free radical induce formation of AGEs.

INFECTIOUS AND PARASITIC DISEASES

Aqueous extracts of guava leaves have been shown to have antibacterial action because of an inhibitory action against antimicrobials action of *S. aureus* strains [69], [125]. Regardless of utilizing a similar dispersion strategy, contrasts are seen in their restraint zones, as appeared, presumably because of the extraction technique or the measurement examined. A methanol extract applied antibacterial action, keeping the development of various strains from a few microbes, for example, *S. aureus*, *E. coli*, *P. aeruginosa*, *Proteus* spp., and *Shigella* spp. [126]. Besides, extraordinary extracts of the leaves, for example, aqueous, acetone-water, methanolic, shower dried extracts, and the fundamental oil indicated potential inhibitory action against Gram-positive and Gram-negative microorganisms and parasites [127], [128]. In these works, Gram-positive organisms showed more noteworthy restraint zones and least inhibitory fixations (MICs) than Gram negative. Concerning the counter parasitic action, less inhibitory than microorganisms is accounted for Limsong *et al*. [61], Taura *et al*. [71], from Candida krusei and Candida glabrata which gave higher inhibitory action [128], and for *Aspergillus* spp. for which no activity was found [61]. Besides, Betoni *et al*. [129] assessed the action of guava leaves on various bacterial strains, inferring that the synergistic activity between the leaves and different antimicrobials helped its enemy of bacterial action. This action was likewise seen by Mailoa *et al*. [130] with target drugs for the protein combination, cell divider union, and folic acid. Notwithstanding, the last did not discover the synergic impact with gentamicin, maybe because the season of maceration was lower than the time utilized by Betoni *et al*. [129] and the solvent was different

[100], related the antimicrobial action against a few microorganisms and parasites with five flavonoids separated from the clears out. This action was likewise identified with the convergence of tannins in the takes off [131] and to the content of gallic acid and catechin [128]. Furthermore, the action against bacterial and parasitic pathogens was followed by betulinic acid and lupeol [132]. Truth be told, these works are centered on the action of these mixes, instead of the action of the entire extract of the takes off. Likewise, leaf acetone extract of *P. guajava* has additionally displayed direct acaricidal and insecticidal action causing the death of *Hippobosca maculata* grown-up fly [133]. Besides, Kaushik *et al*. [134] proposed that an ethanol extract from the leaves work as a trypanocide operator since its restraint of Trypanosoma brucei development demonstrated like that of the reference drugs. Lee *et al*. [135] proposed the leaves as an enemy of jungle fever specialists, because of their inhibitory action and the obstruction records. Moreover, the action of guava leaf basic oil against toxoplasmosis caused by the development of *Toxoplasma gondii* was accounted for Thiyagarajan and Jamal [136]. Furthermore, guava leaves were proposed for the treatment of looseness of the bowels caused by enteric pathogens since it demonstrated huge inhibitory action against Vibrio cholera and *V. parahaemolyticus*, *Aeromonas hydrophila*, *E. coli*, *Shigella* spp. what's more, *Salmonella* spp. [137]. It is assumed that a similar plant beginning and comparable extraction strategy makes that these works demonstrate tantamount hindrance zones for the microorganisms tried [137]. Instead of the leaves of India and Bangladesh, where MIC esteems did now not exhibit any concordance [77], [138]. What's more, a decrease was portrayed for S. flexneri and V. cholera attack and their adherence to the human laryngeal epithelial cells, and for the creation of *E. coli* warm labile poison and cholera poison, and their office to ganglioside monosialic acid catalyst [139]. In addition, different examinations likewise showed the antimicrobial action of a few microbes that reason gastrointestinal disarranges through various techniques [140], [141]. Rather than past outcomes [138], [142], no restraint of the hydrodistillation and n-hexane separate was found against *E. coli and Salmonella* spp. [138]. Besides, guava leaf tea helped control the development of flu infections, including oseltamivir – safe strains, using the counteractive action of viral passage into having cells, presumably because of the nearness of flavonols [143].

PHARMACOLOGICAL EFFECT OF *PSIDIUM GUAJAVA* [TABLE 5]

CONCLUSION

The broad utilization of allopathic medications in the treatment and avoidance of sicknesses has prompted the quick advancement of medication opposition. Drug resistance is one of the main sources of disappointment in drug treatment. Among all, drug obstruction is much of the time experienced during antimicrobial treatment. In any case, the advancement of obstruction on account of regular treatment or Ayurvedic treatment is extremely uncommon which urged individuals to change from allopathic to Ayurvedic treatment. Nonetheless, the dynamic fixing is extremely challenging to extract from the crude natural compound which turns into a huge challenge for the specialists for which a worked-on strategy must be created. The utilization of natural therapy in the treatment and avoidance of infection is not just protected, effectively accessible yet is efficient too. As of now, even doctors or experts are searching for elective treatment of medication for restoring different infections, so significance should be given to the improvement of traditional herbal medicine from natural resources.

AUTHORS' CONTRIBUTIONS

Adil Ahmad made a substantial contribution to the conception, acquisition of data, and took part in drafting the review article. Prof. S. H. Ansari gives the direction for writing the review paper. Adil Ahmad is the corresponding author with the responsibility to review the content and English grammar.

Pharmacological effect	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 a dose-dependent manner, had EC50 on scavenging hydroxyl radicals of 0.63, 0.47, and 0.58 g/L had EC50 on inhibiting lipid peroxidation of 0.20, 0.035, and 0.18 g/L	[144]
Treatment of a cough	The water extract of the plant at doses of 2 and 5 g/kg, post-operative decreased the frequency of a cough induced by capsaicin aerosol by 35 and 54%, respectively, as compared to the control, within 10 min after injection of the extract ($p<0.01$)	[145]
Antidiabetic activity	The ethanolic stem bark extract exhibited statistically significant hypoglycemic activity in alloxan-induced hyperglycemic rats but was devoid of significant hypoglycemic effect in normal and normal glucose-loaded rats (OGTT). In both acute and subacute tests, the water extract, at an oral dose of 250 mg/kg, showed statistically significant hypoglycemic activity	[146]
Antimicrobial activity	*P. guajava* aqueous bark and methanolic extracts were found to possess antibacterial 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-larabopyranoside were 200 μg/ml for each against *S. enteritidis*, and 250 μg/ml and 300 μg/ml against *B. cereus*, respectively. The hot water extract and the methanol extract of *P. guajava* showed high activity against *Arthrinium sacchari* and *Chaetomium funicola* strains	[12,39,147]
Hepatoprotective activity	*P. guajava* aqueous leaf extracts (250 and 500 mg/kg, post-operative) possess good hepatoprotective activity	[148]
Antidiarrheal activity	*P. guajava* leaf aqueous extract (PGE) (50–400 mg/kg post-operative) produced dose dependent and significant protection of rats and mice against castor oil-induced diarrhea, inhibited intestinal transit and delayed gastric emptying. Like atropine (1 mg/kg, post-operative), PGE produced a dose dependent and significant anti-motility effect and caused dose-related inhibition of castor oil induced to enter polling in the animals. Like loperamide (10 mg/kg, post-operative), PGE is dose dependently and significantly delayed the onset of castor oil-induced diarrhea, decreased the frequency of defecation, and reduced the severity of diarrhea in the rodents	[149]
Treatment of plaque	The active flavonoid compound, quercetin-3-O-alpha l-arabinopyranoside (guaijaverin) isolated from *P. guajava* demonstrated a high potential antiplaque agent by inhibiting the growth of *S. mutans*	[38]

(Contd...)

Pharmacological effect	Details	Reference
Spermatoprotective activity	The extracts of the leaves of *P. guajava* Linn. possess beneficial effects on sperm production and quality and may thus improve the sperm parameters of infertile males with oligospermia and non-obstructive azoospermia	[150]
Antimutagenic activity	The water extract of *P. guajava* was effective in inactivating the mutagenicity of direct-acting mutagens	[151]
Inotropic effect	The extract from *P. guajava* leaves depresses myocardial inotropism	[145]
Spasmolytic effect	The spasmolytic activity of *P. guajava* leaf remedy is mainly due to the aglycone quercetin, present in the leaf and the extract mainly in the form of five flavonols, and whose effect is produced when these products are hydrolyzed by the gastrointestinal fluid	[152]
Treatment of infantile rotaviral enteritis	*P. guajava* showed a good curative effect on infantile rotaviral enteritis	[99]
Anticancer activity	Aqueous extract of *P. guajava* L. budding leaves has been shown to possess anti-prostate cancer activity in a cell line model. Treatment with *P. guajava* L. budding leaves (1.5 mg/mouse/day) significantly diminished both the PSA serum levels and tumor size in a xenograft mouse tumor model. Guava leaf essential oil has been shown to possess a cytotoxic effect on Human cervical cancer cell lines	[153,154]
Analgesic and anti-inflammatory activity	The aqueous extract of *P. guajava* leaves possesses analgesic and anti-inflammatory properties. The hexane, ethyl acetate, and methanol extracts of *P. guajava* leaves (20, 100, 500, and 1250 mg/kg) exhibited mostly dose-dependent antinociceptive effects in chemical and thermal tests of analgesia	[33,155]
Immunomodulatory activity	Extracts derived from *P. guajava* revealed immunomodulatory activities	[156]
Treatment of acne	*P. guajava* leaf extracts are used in the treatment of acne	[157]
Antiproliferative activity	Guava leaf extract has antiproliferative activity caused by inhibition of the catalytic activity of PGHS isoforms	[158]
Antipyretic	The methanol extract of the leaves of *P. guajava* exhibited an antipyretic effect	[159]
Contractile effect	Aqueous leaves extract of *P. 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 through calcium ion channel	[160]
Hypotensive	*P. guajava* leaf aqueous extract (PGE, 50–800 mg/kg IV) 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 through cholinergic mechanisms	[5]
Malaria	The leaves are used as an ingredient in the preparation of fever "teas." They are also used as a part of the potherb used in steam treatment for malaria. The stem bark extract contained anthraquinones, flavonoids, secoiridoids, and terpenoids and was found to be effective for the treatment and/or prophylaxis of malaria	[55]
Oral care	In South Nigeria, the twigs are used as chew sticks and the presence of bioactive compounds comprised saponins, tannins, flavonoids, and alkaloids is responsible for their effectiveness. Chewing sticks, when used without toothpaste, is very efficient, effective, and reliable for cleaning teeth. The teeth of chewing sticks users are usually strong, clean, fresh, and devoid of dental plaque carries	[161]

EC50: 50% effective concentration, *B. cereus*: *Bacillus cereus*, *S. enteritidis*: *Salmonella enteritidis*, OGTT: Oral glucose tolerance test, PGE: Prostaglandin E, *S. mutans*: *Streptococcus mutans*, PSA: Prostate-specific antigen, PGHS: Prostaglandin endoperoxide H synthase, IV: Intravenous

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CONFLICTS OF INTEREST

The authors declared that there are no conflicts of interest related to this study.

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