

Psidium guajava: A Single Plant for Multiple Health Problems of Rural Indian Population

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ABSTRACT

The rural population in India faces a number of health problems and often has to rely on local remedies. *Psidium guajava* Linn. (guava), a tropical plant which is used as food and medicine can be used by rural communities due to its several medicinal properties. A literature search was undertaken to gauge the rural health scenario in India and compile the available literature on guava so as to reflect its usage in the treatment of multiple health conditions prevalent in rural communities. Towards this, electronic databases such as Pubmed, Science Direct, google scholar were scanned. Information on clinical trials on guava was obtained from Cochrane Central Register of Controlled Trials and Clinicaltrial.gov. The literature survey revealed that guava possesses various medicinal properties which have been reported from across the globe in the form of ethnobotanical/ethnopharmacological surveys, laboratory investigations and clinical trials. Besides documenting the safety of guava, the available literature shows that guava is efficacious against the following conditions which rural communities would encounter. (a) Gastrointestinal infections; (b) Malaria; (c) Respiratory infections; (d) Oral/dental infections; (e) Skin infections; (f) Diabetes; (g) Cardiovascular/hypertension; (h) Cancer; (i) Malnutrition; (j) Women problems; (k) Pain; (l) Fever; (m) Liver problems; (n) Kidney problems. In addition, guava can also be useful for treatment of animals and explored for its commercial applications. In conclusion, popularization of guava, can have multiple applications for rural communities.

Key words: Guava, India, *Psidium guajava*, review, rural communities

INTRODUCTION

Worldwide, the use of traditional medicines (TMs) has a long history and encompasses an easily accessible and affordable source of treatment. In India, one of the earliest uses of TM is cited in Rig Veda, a compilation of Hindu holy verses (1600–3500 BC).^[1] TM has played an important role toward catering health care, especially primary health, of people residing in developing countries; its usage being more widespread in rural areas. Wide availability and accessibility of local plants coupled with a dearth of modern health-related facilities and cultural preferences contribute to dependency of rural populations on local plant remedies.^[2,3] Traditional ethnomedicine is the source of treatment for a number of ailments prevalent in rural populations including those which are contagious, infectious, communicable, and noncommunicable.

Guava, *Psidium guajava* (Linn.), a member of *Myrtaceae* family, is a common tropical plant with a long history of traditional usage. It is used not only as food but also as folk medicine, and various parts of this plant have a number of medicinal properties ranging from antimicrobial activity to anticancer property.^[4] An added advantage is that cultivation of guava is relatively easy as it thrives in a variety of soils and adapts to

different climatic conditions; the fruits are also borne fairly in a short period. Due to the various commercial applications, guava trees are found throughout India. Although they are planted in almost all states, Andhra Pradesh, Assam, Bihar, Maharashtra, Uttar Pradesh, and West Bengal are the important cultivators of this plant.

This review discusses the different medicinal attributes of this versatile plant in the light of its application to the needs related to health care of rural communities to appreciate how this plant can cater to multiple health issues encountered by the rural population in India.

LITERATURE SURVEY

Scientific investigations on the medicinal properties of guava products date back to the 1940s. The present review reports the available literature supporting the efficacy of guava obtained from different electronic databases including PubMed, Scopus, ScienceDirect, and Google Scholar. Information on clinical trials on guava was obtained from the Cochrane Central Register of Controlled Trials and clinicaltrial.gov. The information has been presented under three categories, viz., infectious diseases, noncommunicable diseases, and other properties. In addition, commercial applications with respect to the rural scenario have also been included. As the information available was vast, mainly recent references have been quoted; in case a review was available, the same has been cited. Wherever available, the doses used for the study have been included. Cited databases, as well as health websites, were also searched for gauging data on rural health in India.

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RURAL HEALTH SCENARIO IN INDIA

Several factors contribute to health disparities in rural communities. Some of these are geographical isolation, lower socioeconomic status, and limited access to modern healthcare facilities.^[5] Other health concerns arise due to undernutrition, poverty, poor sanitation, and hygiene. Delay in healthcare seeking in rural communities primarily because of difficulties of physical access and dissatisfaction with understaffed and ill-equipped health centers are additional factors.^[6] All these lead to various health problems, and rural India faces a double burden of communicable and noncommunicable diseases. Among the infectious diseases, the burden of malaria is quite high with >90%–95% cases of total malaria being reported from rural India.^[7] Gastrointestinal infections, especially diarrhea and dysentery, are very common and one of the major reasons for infant mortality. Although the prevalence of respiratory infections is high in children below 5 years of age, rural women are also more prone to respiratory disorders such as chronic obstructive pulmonary disease mainly due to the domestic cooking fuel.^[8] Chronic noncommunicable diseases such as diabetes, cardiovascular diseases, cancer, and mental health disorders are highly prevalent in rural regions.^[9] About 13% of the rural Indian population suffers from diabetes,^[10] and the prevalence of hypertension is as high as 20%–50%.^[11] Among the 30 million heart patients in India, 16 million reside in rural areas.^[12] The cancer mortality rates for men and women in rural India have been estimated to be 95.6/100,000 and 96.6/100,000, respectively.^[13] Women health issues and childhood-related ailments are also the alarming causes of concern in rural settings. Malnutrition is common in rural children. Nutritional deficiencies related to iron and vitamins are found in rural women. Anemia in women has been reported from different tribal setups such as 88.85% in Melghat^[14] and 74% in Orissa.^[15] They are also prone to other problems linked to pregnancy and child birth. Osteoporosis and inflammatory diseases such as arthritis and rheumatism also exist. Besides the above, agriculture-related injuries such as mechanical accidents, snake and insect bites, and pesticide poisoning are also common rural health problems.

The following sections cover the reported literature on the efficacy of guava on the multiple health problems stated above. The safety profile of guava has also been included. The various uses of guava have been covered under three categories related to (a) infectious etiology, (b) noncommunicable diseases, and (c) others (which did not fall under a and b). The information has been described under the following headings: (i) ethnomedical which includes ethnobotanical/ethnopharmacological information; (ii) laboratory investigations under which research studies using various *in vitro* and *in vivo* models are included; and (iii) reports of clinical trials, wherever available.

SAFETY PROFILE

The toxicity studies with various parts and extracts of guava which have been comprehensively reviewed by Morais-Braga *et al.*^[16] show that the plant is safe for use. The following two sections cite some additional studies supporting the safety profile.

In vitro studies

The water extract of the leaves was noted to inactivate the mutagenicity induced by 4-nitro-o-phenylenediamine, sodium azide, and the S9-dependent mutagen, 2-aminofluorene, on *Salmonella typhimurium* in the Ames assay.^[17] *In vitro* cytotoxicity and mutagenicity tests of the aqueous extract of the leaves in Wistar rat bone marrow cells and human peripheral blood lymphocytes, respectively, did not show any statistically significant alterations in either the cell cycle or the

number of chromosome alterations.^[18] In studies with antidiabetic and antihyperlipidemic drugs, it has been indicated that the aqueous guava extract and guava leaf tea do not induce mutagenicity, toxicity, or abnormal interaction with these drugs. Instead, they have a lower potential for drug interactions based on either inhibition or induction of cytochrome P450 isoforms.^[19]

In vivo studies

A study carried out by Ojewole *et al.*^[20] has shown an LD₅₀ value of 1534 ± 69 mg/kg (intraperitoneal [IP]) for the aqueous extract of guava leaves in mice, whereas Etuk and Francis^[21] showed that oral administration of 100–500 mg/kg body weight of the aqueous extract was relatively safe in Wistar rats up to 72 h. In addition, an acute toxicity study of ethanolic extract of guava leaves showed no signs of toxicity or cause mortality in albino rats even at doses >2000 mg/kg.^[22]

Infectious etiology

General infections

Ethnomedical information

Guava leaves are widely used traditionally for treating bacterial infections in South Africa^[23] and in Guinea (West Africa) for infectious diseases.^[24]

Laboratory investigations

Morais-Braga *et al.*^[16] in their recent review have stated that guava has efficacy against 34 bacterial species, 19 fungal species, six protozoal species, and four types of viruses.

25 mg/ml and 12.5 mg/ml of methanol and acetone extract of guava leaves exhibited antibacterial activity against several Gram-positive and Gram-negative bacteria such as *Staphylococcus* spp., *Bacillus subtilis*, *Micrococcus flavus*, *Pseudomonas* spp., and *Escherichia coli* spp.^[25] Different organic extracts from the leaves of guava, when tested at a concentration of 2 mg/well, were found to have antibacterial activity against pathogens, such as *Staphylococcus aureus* and *Klebsiella pneumoniae*, as well as antifungal activity against *Candida albicans* and *Candida neoformans* with the zones of inhibition ranging between 7 and 25 mm.^[26] Different concentrations (20%–100%) of essential oil extracted from guava leaves were found to inhibit dermatophytes *Microsporium canis*, *Trichophyton rubrum*, *Trichophyton verrucosum*, *Trichophyton tonsurans*.^[27]

Gastrointestinal infections

Ethnomedical information

Although guava has a number of medicinal properties, it is the most common and popular traditional remedy for gastrointestinal infections such as diarrhea, dysentery, stomach aches, and indigestion^[4] and it is used across the world for these ailments.

Guava was listed among the species used for treating gastrointestinal infections during an ethnobotanical study in Mexico.^[28] In India, a study from North Sikkim reported that locals recommend drinking hot water with the bark powder mixed into it as a remedy for blood-associated dysentery.^[29] Guava leaves have been documented to be used for the treatment of diarrhea in Maharashtra^[30] and in South Assam for treating digestive system disorders.^[31] Citing the experiences of some tribal and rural Indians, Melookunnel mentioned that the decoction prepared from a handful of guava leaves is to be taken in a day by diarrheal patients.^[32]

Laboratory investigations

The *in vitro* and *in vivo* studies support the ethnomedicinal antidiarrheal activity of guava leaves especially. These include its ability to inhibit diarrheal pathogens, its effect on intestinal motility, gastric emptying, and decrease in frequency of defecation.

Decoction of guava leaves at 5% and 10% concentrations was cidal against bacterial diarrheal pathogens *Shigella flexneri* and *Vibrio cholerae* and had anti-giardial and antirotaviral activity.^[33,34] A study by Tona *et al.*^[35] documented the *in vitro* activity of decoction of guava leaves and stem bark against *Entamoeba histolytica* with a minimum inhibitory concentration (MIC) of 62.5 µg/ml and <7.81 µg/ml, respectively. Other studies have reported the anti-giardial activity of the bark (0.02 mg/ml)^[36] and antirotaviral activity of leaf extract (8 µg/ml).^[37] The antihelmintic action of butanol extract of the leaf has also been reported.^[38]

In a study undertaken in isolated guinea pig ileum, ethanol and aqueous extracts of guava leaves (80 µg/ml) showed >70% inhibition of acetylcholine and/or KCl solution-induced contractions.^[39] In another study for assessing anti-diarrheal activity of aqueous extract of guava leaves in Sprague–Dawley rats, it was shown that fresh extract at a dose of 0.2 ml/kg (equivalent to 0.2 mg/kg of the standard morphine sulfate) produced 65% inhibition of propulsion in the small intestine of experimental animals treated with Microlax.^[40] Aqueous leaf extract when given orally (50–400 mg/kg) significantly delayed the onset of castor oil-induced diarrhea, decreased the frequency of defecation, and reduced the severity of diarrhea in mice and rats.^[20] Guava leaf extract (400 mg/kg) also inhibits prostaglandin E2 enteropooling and slows down the propulsion of charcoal meal in rats.^[41] In addition, different concentrations (1%, 5%, and 10%) of decoction of guava leaves showed inhibitory effect on bacterial colonization on epithelial cells and on toxin production, binding of bacterial enterotoxins,^[33] and affected the inflammatory response.^[42] Gastric ulcer healing properties of guava leaves (100–200 mg/kg) was demonstrated in animal models by Livingston *et al.*^[43]

Quercetin, a major flavonoid and one of the most reported active constituents found in guava leaf, has been demonstrated to reduce capillary permeability in the abdominal cavity and inhibit intestinal movement in an *in vitro* model using guinea pig ileum.^[44] However, Birdi *et al.*^[33] demonstrated that quercetin alone had limited anti-diarrheal activity and that the crude guava decoction was more effective.

Thus, it can be seen that guava can be used for the treatment of physiological diarrhea as well as infectious diarrhea caused by a wide spectrum of pathogens.

Clinical trial

In a clinical trial undertaken by Lozoya *et al.*,^[45] compared to the placebo, patients receiving guava leaf capsules (quercetin-equivalent 1 mg per 500 mg capsule) experienced decreased duration of abdominal pain with no side effects. However, no other significant changes were detected in the consistency and frequency of liquid stools compared with the control group. In contrast, a longitudinal randomized double-blind trial with oral alcohol-based tincture from guava leaves reported that the leaf tincture significantly reduced the time taken for cessation of acute diarrhea with no adverse reactions.^[46] Good curative effect was also reported in a pilot study using guava leaf decoction for treating infantile rotaviral enteritis.^[47]

Malaria

Ethnomedical information

There is widespread knowledge wherein fever “teas” are prepared from a mixture of herbs including guava leaves.^[48] Guava was identified as a remedy for malaria from KwaZulu-Natal Province of South Africa^[49] and North Indian Buchpora and South Indian Eastern Ghats.^[50] In another survey carried out in Northeastern Nigeria, decoction of guava leaves mixed with pineapple and honey was used as a local remedy for malaria.^[51] In a recent ethnobotanical survey, guava leaves were cited by the locals in rural communities of Bagamoyo district, Tanzania, for control of mosquitoes which are the vector for the parasite.^[52]

Laboratory investigations

Antiplasmodial activities of *Nefang*, a polyherbal product, with guava as one of its constituents, have been established using *in vitro* and *in vivo* models.^[53,54] The percent suppression of parasitemia (*Plasmodium berghei/Plasmodium chabaudi*) in mice with 600 mg/kg *Nefang* was reported as 82.9% and 86.3%, respectively.^[53] The EC₅₀ values were noted to be 96.96 and 55 µg/ml against chloroquine-sensitive (3D7) and multidrug-resistant (Dd2) *Plasmodium falciparum* strains, respectively. Using the parasite lactate dehydrogenase assay, the IC₅₀ of aqueous stem bark of guava against a chloroquine-sensitive *P. falciparum* (D10) strain was 10–20 µg/ml.^[49] The IC₅₀ of guava leaves (methanol and ethyl acetate extracts) against a chloroquine-resistant strain of *P. falciparum* has been reported as 12.5–15 µg/ml.^[50]

Respiratory infections

Ethnomedical information

Leaves of guava were mentioned as a remedy for cough during an ethnobotanical survey in Guerrero, México,^[55] in Malaysia,^[56,57] in South Africa,^[58] as well as of the Monpa ethnic group located in Arunachal Pradesh, India.^[59] In North Sikkim, India, use of raw young leaves and tender shoots of guava has been cited to be effective for sore throat and cough.^[29]

As a remedy for tuberculosis, the macerated bark of guava was cited by locals of Ogun State, Nigeria.^[60] Guava leaves are also used in Tanzania for treating tuberculosis in patients with HIV-AIDS.^[61]

Laboratory investigations

The anticough activity of aqueous guava leaf extract following induction with capsaicin aerosol has been evaluated in guinea pigs and rats.^[62] As compared to the control, when given orally, this study reported 35% and 54% decrease in frequency of cough at doses of 2 and 5 g/kg, respectively. The dichloromethane-methanol extract (1 mg/ml) and aqueous leaf extract (4 mg/ml) were found to be effective against different respiratory pathogens such as *Cryptococcus neoformans*, *K. pneumoniae*, *Moraxella catarrhalis*, *Mycobacterium smegmatis*, and *S. aureus*.^[63]

Oral/dental infections

Ethnomedical information

In Andhra Pradesh, India, leaves of guava have been documented for use in mouth ulcers,^[64] while in North Sikkim, raw young leaves and tender shoots of guava have been used for toothache and mouth ulcers.^[29]

Guava leaves were commonly used by traditional healers of Cameroon for treating dental infections.^[65] Guava twigs being effective when used as “chewing sticks” has been reported by Okwu and Ekeke.^[66]

Laboratory investigations

The potential of guava in treatment of periodontal diseases has recently been reviewed by Ravi and Divyashree.^[67] Guava leaf extract has been reported to show antibacterial activity against oral pathogens such as *Streptococcus oralis*, *Streptococcus mitis*, *Streptococcus mutans*, and *Lactobacillus casei*.^[68,69] An *in vitro* study reported aqueous extract of guava leaves (1 mg/ml) to be effective in dental caries and dental plaques.^[70] The aqueous leaf extract of guava was found to have cidal action against oral pathogens associated with earlier stages of plaque formation, viz., *Streptococcus sanguinis*, *S. mitis*, and *Actinomyces* sp., with MIC values ranging between 2.61 and 4.69 mg/ml.

Skin infections

Ethnomedical information

In Tahiti, Samoa, guava shoots have been used as skin tonic,^[71] and in the Philippines, guava leaves are used for treatment of scabies by indigenous groups.^[72] The use of different parts of guava for skin-related ailments in

various regions such as Panama, Bolivia, and Venezuela, Fiji, and Senegal has been documented by Gupta *et al.*^[73]

Laboratory investigations

The antibacterial activity of organic extract of guava leaves against bacterial clinical isolates (*Proteus mirabilis*, *Streptococcus pyogenes*, *E. coli*, *S. aureus*, and *Pseudomonas aeruginosa*) from patients with surgical wound, burns, and skin and soft tissue infections has been reported by Abubakar.^[74] The MIC and minimum bacterial count values ranged between 6.25 and 50 mg/ml. In addition, in a mouse model, cream containing aqueous extract of guava leaves has been demonstrated to be effective on 2,4-dinitrochlorobenzene-induced atopic skin lesions.^[75] Beneficial effect of ethyl acetate extract of guava leaves on atopic dermatitis has also been demonstrated.^[76]

Noncommunicable disease

Diabetes

Ethnomedical information

The use of powder of guava fruit with buttermilk, consumed twice a day for 15 days, was reported as a remedy for diabetes during an ethnobotanical survey in Andhra Pradesh, India.^[77] Similarly, leaves and fruits of guava were cited in a survey undertaken in Tamil Nadu, India.^[78] Guava was also listed among the most common plants used for diabetes in the central region of Togo.^[79]

Laboratory investigations

A number of animal and human studies support the antidiabetic potential of various parts of the guava plant.^[19] Ojewole^[80] reported a dose-dependent hypoglycemia in normal (normoglycemic) and streptozotocin (STZ)-treated, diabetic rats following oral administration of aqueous guava leaf extract (50–800 mg/kg). Besides the leaf extract, guava fruit and stem bark have been evaluated for their ability to reduce blood sugar levels. The significant hypoglycemic activity of the fruit extract (125 and 250 mg/kg) in STZ-induced diabetic animals and the ethanolic stem bark extract (250 mg/kg) in alloxan-induced hyperglycemic rats has been reported.^[81,82] Recently, different extracts of guava leaf were evaluated for their effect on glucose uptake and aldose reductase inhibitory activity at the cellular level.^[83]

Clinical trials

A multicenter randomized controlled trial was conducted in China, to evaluate the efficacy of guava in the management of diabetes. The oral administration of aqueous leaf extract of guava in diabetic patients was less potent than standard chlorpropamide and metformin.^[84] In another clinical study with 40 patients, oral administration of capsules with 500 mg of guava fruit reduced the blood glucose level in weeks 3, 4, and 5 with a decrease of 12.3%, 24.79%, and 7.9%, respectively, as compared with the diabetic control group.^[85] The study also indicated that supplementation of 0.517 g/day of this extract could reduce fasting blood glucose.

A guava leaf tea (Bansoureicha) is now commercially available in Japan which contains aqueous guava leaf extract and is approved as one of the Foods for Specified Health Uses.^[86]

Cardiovascular and hypertensive disorders

Ethnomedical information

Guava leaves have been used in treatment of hypertension in Cuba,^[87] Nigeria,^[88] and Togo.^[79]

Laboratory investigations

Aqueous leaf extract of guava showed cardioprotective effects when studied in models of ischemia.^[89,90] In addition, experiments following intravenous administration of the aqueous leaf extract (50–800 mg/kg) in Dahl salt-sensitive rats showed a dose-dependent, significant reduction in systemic arterial blood pressure and heart rates in hypertensive animals.^[80] In an *in vitro* study, Belemtougri *et al.*^[91] found that aqueous and ethanolic guava leaf extracts inhibited the release of intracellular calcium within the skeletal muscles of rats. Aqueous leaf extract also significantly contracted the aorta rings in a dose-dependent manner (0.25–2 mg/ml).^[92]

Clinical trials

A randomized, single-blind, clinical trial indicated that adding moderate amounts of guava fruit to the diet leads to a decrease in serum total cholesterol, triglycerides, and blood pressure, with a net increase in high-density lipoprotein cholesterol in 50% of the treated patients.^[93] Another single-blind, randomized, controlled trial in 145 hypertensive patients given a potassium and fiber-enriched diet comprising 0.5–1 kg of guava daily for 4 weeks showed improved diastolic and systolic pressures.^[94] A clinical trial was carried out in Malaysia for 9 weeks with 122 people consuming 400 g/day of guava fruit, which reduced oxidative stress and blood cholesterol levels.^[95]

Cancer

Ethnomedical information

Based on an ethnopharmacological survey for treating different types of cancer in West Bank Palestine, a decoction prepared from 100 g guava leaves taken daily was documented to be a remedy for curing lung and stomach cancers.^[96]

Laboratory investigations

Correa *et al.*^[97] recently reviewed literature related to the anticancer properties of guava. In this review, the authors have comprehensively discussed the available literature supporting the theories of its anticancer properties through various mechanisms, such as scavenging-free radicals, regulation of gene expression, modulation of cellular signaling pathways, including those involved in DNA damage repair, cell proliferation, and apoptosis.

Women's health

Ethnomedical information

Tahitians use the plant for conditions such as painful menstruation, miscarriages, uterine bleeding, and premature labor in women.^[71]

In a review compiled by de Boer and Cottingting,^[98] wherein 1875 plant species from Southeast Asia were documented for various women's health issues, guava was commonly reported mainly for menstrual disorders, amenorrhea, profuse uterine bleeding, blennorrhagia, and postpartum hemorrhage. The guava leaf decoction has also been recorded as a remedy for menstrual disorders in Durgapur, Bangladesh.^[99] Ticzon has reported the use of guava leaf decoction for uterine hemorrhage as a wash for vaginal and uterine problems, especially where an astringent remedy is needed.^[100]

Clinical trial

A total of 197 women suffering with primary dysmenorrhea were included in a double-blinded randomized clinical trial. The trial included four groups, viz., two doses of guava leaf extract (3 mg flavanol/day and 6 mg flavanol/day); ibuprofen (1200 mg/day); placebo (3 mg/day). The outcome was measured in terms of reduction in intensity of abdominal pain by means of a visual analog scale. Group ingesting 6 mg/day of extract showed significant decrease in intensity of pain.^[101]

Anti-inflammatory and antipyretic

Laboratory investigations

Guava leaves has been used for the treatment of various inflammatory ailments including rheumatism.^[4] Methanol extract of guava leaves at 50, 100, and 200 mg/kg levels, given orally, has been reported to exhibit anti-inflammatory activity in carrageenan-induced paw edema in rats.^[102] The aqueous extract of guava leaves on IP administration (50–800 mg/kg) inhibited acute inflammation in fresh egg albumin-induced edema in rats.^[76] Use of the pounded leaves has been recorded in India for rheumatism.^[103] Methanol extract of guava leaves when given orally, at 50, 100, and 200 mg/kg has been reported to exhibit antipyretic activity in yeast-induced hyperpyrexia in experimental mice. The activity of guava was comparable to standard indomethacin (5 mg/kg).^[102]

Others

Nutritional benefits for combating deficiencies/malnutrition

Due to the high nutritional value of guava, this plant is often included among superfruits. Guava fruit is rich in Vitamins A and C, folic acid, dietary fiber, as well as dietary minerals such as iron, manganese, potassium, and copper. It is known that a single guava fruit contains about four times the amount of Vitamin C as an orange. Hence, guava is known as “poor man’s apple of the tropics.”^[104]

A study undertaken in Tamil Nadu, South India, to assess effectiveness of a nutritional intervention of guava and amaranth leaves for anemia in antenatal women showed that it improved maternal hemoglobin.^[105]

In another study, hemoglobin levels of school children were found to increase when they were given guava fruit pulp mixed with sugar and whey.^[106]

Analgesic

Methanol extract of guava leaves at 50, 100, and 200 mg/kg (p.o) has been shown to have beneficial effect on acetic acid-induced writhing response in mice. This effect was comparable to the analgesic effect of 150 mg/kg acetylsalicylic acid.^[107] In another study, organic extracts of guava leaves (20, 100, 500, and 1250 mg/kg) exhibited antinociceptive effects in chemical and thermal tests of analgesia.^[108]

Immunomodulatory activity

Laboratory investigations

Decoction of guava leaves was demonstrated to stimulate macrophages to kill *E. coli* strain (heat stable toxin producers) using murine monocytic cell line, J774.^[109] Ethyl acetate fraction of guava leaves was shown to inhibit COX-2 expression, cytokine secretion, degranulation, and FcεRI-mediated signaling in antigen-stimulated mast cells.^[110] A flavonoid fraction of guava leaf extract was shown to regulate nuclear factor κB activation in an *in vitro* model system using Labeo rohita head kidney macrophages.^[111]

Hepatoprotective

Laboratory investigations

Aqueous leaf extracts (250 and 500 mg/kg) on oral administration have shown to significantly reduce the elevated serum levels of alanine aminotransferase, alkaline phosphatase, bilirubin, and aspartate aminotransferase in acute liver damage induced by hepatotoxins in rats.^[112]

Nephroprotective

Laboratory investigations

In an animal model for nephrotoxicity, ethanolic extracts of guava leaf were reported to prevent renal damage induced by paracetamol. The extracts, given orally, at 200 and 400 mg/kg normalized blood urea, blood creatinine, urinary sodium, urinary creatinine, in a dose-dependent

manner. The observations were also supported by histopathology.^[9] A similar observation was also made in cisplatin-induced nephrotoxicity in rats.^[113] In addition, guava fruit extract has been shown to protect against kidney damage in diabetic rats.^[114]

Veterinary uses

Use of by farmers in Plateau State, Nigeria, and in Central Kenya, for the management of veterinary diarrhea has been documented.^[115,116] The antidiarrheal activity of guava buds and leaves has been reported in pet dogs.^[117] In Java, farmers use guava leaves for treating diarrhea in ruminants, and the root and stem of the plant are used in treating diarrhea in sheep and goats.^[118] Guava leaves, young fruits, and/or buds are boiled and mixed with mash or bran or a combination of both and given to horses suffering from diarrhea in Trinidad.^[119] Another study by Rahman *et al.* recommended supplementation of guava leaf meal (leaves boiled in water and then in an alkaline and acidic solutions, up to 4.5% levels) in broiler’s diet to significantly improve the fat content of broiler as this meal serves as a good source of nutrients.^[120] This study also demonstrated guava leaf to improve broiler’s mortality rate due to its antimicrobial effect. Guava has been shown to possess antibacterial activity against pathogenic bacteria in pigs.^[121] In the Philippines, 5% and 10% guava leaf meal (dried and ground) added to pig diets was found to reduce diarrhea in piglets.^[122] In Thailand, ground guava leaves when given as a supplement to weaned piglets prevented postweaning diarrhea.^[123]

Commercial applications

Guava fruits are utilized in food industry for different preparations such as juices, jellies, nectars, concentrates, candies, and gelatins and in confectioneries;^[124] the wood has applications in areas such as construction^[125] and engravings.^[126] The bark has been used for stains, dyes, inks, and tattoos and as mordant.^[127] Apart from the medicinal value, guava could also be explored for its commercial applications and thus help the community generate extra income.

DISCUSSION AND CONCLUSION

P. guajava, guava, documented to possess several medicinal properties, has been extensively researched for various pharmacological properties. The laboratory studies and clinical trials provide a strong scientific base supporting the various ethnobotanical/ethnopharmacological reports from across the world. In addition, as guava propagates easily and thrives in almost all the climatic conditions, it is widely available for medicinal use as well as commercial applications. A single plant with multiple benefits has the advantage especially where back yard plots are small and/or water limited. In addition, it is preferable to limit the variety of plants suggested for cultivation so as not to overwhelm the individuals maintaining the backyard nurseries.

Although the review discusses the extensive use of guava for multiple health problems faced by the Indian rural communities, its usage can be applicable to rural population elsewhere since the health scenario across rural communities is likely to be similar. The available literature on safety and the clinical studies on guava add to its advantage. In addition, since plant-derived antimicrobials have been explored as alternatives to control antibiotic resistance in microbial infections,^[128] the guava extract with its multiple modes of action may minimize the emergence of drug resistance to common infectious diseases such as diarrhea that are prevalent amongst the communities.

This review besides discussing the promising potential of guava brings to light some lacunae. Most ethnobotanical surveys published do not include the dose used by the communities. In addition, some of the ethnobotanical surveys reported give limited or incomplete information

on type of extract, and information from traditional healers should also record seasonal variation in efficacy if present. Direct extrapolation of laboratory investigations to community settings can sometimes be difficult, especially if organic extracts have been used. Acceptability of herbal remedies by rural communities is influenced by other socioeconomic factors as stated by Daswani *et al.*^[129]

Thus, guava extract with its multiple medicinal properties needs to be further developed for wider use for the treatment of communicable diseases and noncommunicable diseases. Identification and isolation of promising compounds for the development of products are also needed.^[130]

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Conflicts of interest

There are no conflicts of interest.

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