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Review Article

Ethnomedicinal and Mechanism of Phytochemicals Activities of *Psidium Guajava Linn* (Guava) Extracts

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ABSTRACT

Objective: The review focuses on the comprehensive analysis of the medicinal uses of guava (*Psidium guajava Linn*) and relates it with different scientific investigations into phytochemical constituents present in the plant.

Methods: Using search engines such as Wiley, NCBI, Google Scholar, Pubmed, and Intechopen; scientific papers on the plant were searched, by searching for the relevant keywords.

Results: Publications reviewed reported that extracts of the Guava plant (*Psidium guajava L.*) contained phytochemicals that show antioxidant / hepatoprotective, anti-diabetic, antidiarrhea, anti-cancer, anti-microbial, anti-inflammatory activities in pharmacological studies, justifying its ethnomedicinal uses.

Conclusion: *Psidium guajava* possesses essential active organic compounds that are viable in biomedical research for therapeutic studies. There should be increasing interest in discovering new bioactive compounds from the plant through more research to harness its potential for the treatment of diseases and serve as the basis for developing new drugs.

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Introduction

Herbal medicines serve not only as alternatives but complement modern medicines used in treating diseases (Oladunmoye *et al.,* 2009). Many of these herbal plants contain bioactive substances that have important applications in ethnological medicine, and also in the discovery of novel drugs (Newman *et al.,* 2003). Phytopharmaceutical research based on ethnopharmacological knowledge is an effective way to discover new therapeutic agents in plants (Duraipandiyan *et al.,* 2006). Eighty percent (80%) of the world's population directly or indirectly depends on herbs as an alternative treatment; therefore, the World Health Organization (WHO) recommended an improvement in herbal medicines as a viable healthcare mechanism (Peter *et al.,* 2018).

The *Psidium guajava* plant is a small herbaceous tree abundant in South America and African countries, with a common name "Guava" (*Myrtaceae* family). Natives used it as folkloric medicine for curing diseases. It is mostly planted in tropical as well as sub-tropical regions. *Psidium guajava* contains minerals and other bioactive constituents such as ascorbic acid, fibre, carotenes, tannins, flavonoids, phenols and triterpenoid acids (Correa *et al.,* 2011; Usman *et al.,* 2013). These constituents exhibit broad pharmacological activities, which demonstrate a wide range of benefits in ethno-medicine.

Methods of Data Collection

The data were sourced and obtained from relevant online databases such as Wiley, NCBI, Google

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scholar, Pubmed, intechopen, by searching for the following keywords: *Psidium guajava*, guava, ethnomedicine, extracts, pharmacology activities, phytochemicals mechanisms, in-vitro, and in-vivo. We scanned the references of the article obtained for articles we might have missed out. Duplicate articles were removed. Information about the health benefits of the plants was also obtained from Nutritionists and Traditional health Practitioners in Osun State, Nigeria.

Ethnopharmacological Studies

Psidium guajava, has a rich ethnopharmacological history, deeply rooted in traditional medicine across various cultures (Soumya *et al.,* 2009). Its leaves, in particular, are recognized for their antimicrobial, anti-inflammatory, and anti-diarrheal attributes (Kaneria and Chand, 2011). Additionally, guava's antioxidant content, including quercetin and lycopene, has sparked interest in potential applications against oxidative stress-related conditions (Correa *et al.,* 2011). Furthermore, guava's hypoglycemic effects have been explored in the context of diabetes management, showcasing its versatility in addressing multiple health concerns (Soman *et al.,* 2010). Ethnopharmacological studies highlight guava's significance in promoting gastrointestinal health, cardiovascular well-being, and wound healing (Ojewole, 2008).

Antioxidant activity / Hepatoprotective Activity

Psidium guajava is rich in important phytochemicals such as phenols, which ameliorate oxidative stress, and protect vital body organs from oxidative damage. (Usman *et al.,* 2013). An animal experiment of aqueous and ethanolic extracts of *Psidium guajava* showed hydroxyl radical scavenging activity and inhibited lipid peroxides which generate malondialdehyde, with EC_{50} removing hydroxyl radicals ($0H^{-}$) and inhibiting lipid peroxidation (Wang *et al.,* 2007). Phenols structurally can scavenge free radicals and serve as antioxidant supplements (Jayakumari *et al.,* 2012). The antioxidant activity (AOA) of phenols may be a result of their ability to scavenge free radicals that initiate the oxidative stress or the termination of radical chain reactions; this could also be due to their high tendency to chelate metals. An in-vitro study to determine the antioxidant effect of phenolic extracts of guava seeds of 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity (FRSA) shows that guava seed extracts have 93-96% FRSA at 1 mg/ml (Correa *et al*., 2011). Guava leaves showed hepatoprotective effects by reducing serum profile of liver enzyme biomarkers and pathological changes in acute liver injury in rats (Milyani, 2012).

Antidiabetic activity

Diabetes mellitus is a metabolic disorder, associated with body hormonal deficiency and blood glucose uptake (Soman *et al.,* 2010). The inability of insulin to regulate blood sugar results in high blood sugar, and this could lead to many health complications. Research into folk use of guava plants as an alternative therapy in the treatment of high blood sugar validates its antidiabetic use (Mukhtar *et al.,* 2006). Scientific investigation of different extracts of *Psidium guajava* leaf showed that the extracts have activity against diabetes mellitus and body system changes caused as a result of the disease. The leaves inhibited aldose reductase activity, regulated the gene and protein expression of several insulin receptors, and also improved cellular glucose uptake (Mansoori *et al.,* 2012). Ethanolic extract of guava stem bark has a significant effect in reducing sugar levels in alloxan-induced hyperglycemic rats (Mukhtar *et al.,* 2006). However, long-term administration of guava leaf extracts increased plasma insulin levels, glucose utilization, and liver enzyme activity in low-dose streptozotocin- and nicotinamide-induced diabetic Sprague-Dawley rats (Soman *et al.,* 2010).

Antimicrobial activity

Microbial infections caused by microorganisms are prominent among locals, and indigenous approaches to control and cure these infections prompted the use of guava and other plants as anti-infectious agents (Duraipandiyan *et al.,* 2006). To scientifically justify its ethnomedicinal potency for this purpose, experiments were carried out on extracts of different parts of the Guava plant. *Psidium guajava* stem bark extracts are reported to have a bactericidal effect against *Arthrinium sacchari* and *Chaetomium funicola* strains (Ojewole *et al.,* 2008). Aqueous and organic extracts of guava leaves showed antibacterial activity against antibiotic-resistant clinical isolates of *Staphylococcus aureus* strains (Wang *et al.,* 2007), methanol extract showed bacteriostatic activity, inhibiting the growth of various bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus spp*. and *Shigella spp*. (Milyani, 2012). Leaf extracts of *Psidium guajava* showed probable inhibitory activity against Gram-positive and Gram-negative bacteria and fungi. *Guajaverine* isolated from guava leaves had strong inhibitory activity against *Streptococcus mutans* (Anand *et al.,* 2016).

Antidiarrheal activity

Psidium guajava, commonly known as guava, is believed to possess anti-diarrheal properties. High fiber content may contribute to reducing diarrhea

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symptoms by promoting firmer stools and soothing the digestive tract (Chulasiri *et al.,* 1986). Experimental evaluation of antidiarrheal property of guava extract in rodents showed that the effect is similar to control drug, it inhibited intestinal motility and delayed gastric emptying (Ojewole *et al.,* 2008). *Psidium guajava* leaf extract administered orally protect against ricin-induced diarrhea in a dose dependent manner, similar to standard drug (atropine 1 mg/kg, p.o.), provides antimotor effect and inhibit castor oil-induced diarrhea in rodents dose dependently, it also produces effects similar to that of loperamide (10 mg/kg, p.o.), delayed onset of ricin-induced diarrhea, reduced stool frequency, and diarrhea severity in rodents (Chah *et al.,* 2006).

Anticancer activity

Research suggests that *Psidium guajava* may exhibit anti-cancer effects due to its rich phytochemical composition. Compounds like quercetin and lycopene found in guava possess antioxidant properties that may help combat oxidative stress, linked to cancer development (Levy and Carley, 2012). Additionally, guava's potential role in inhibiting the growth of cancer cells, inducing apoptosis, and reducing inflammation could contribute to its anti-cancer effects (Bontempo *et al.,* 2012). The ability of the Guava plant to regulate and control abnormal cell growth and development in the body was tested in in vitro and in-vivo experiments. Experimental treatment with germinated leaves of *Psidium guajava L.* (1.5 mg/day) significantly reduced serum prostate-specific antigen (PSA) and tumor size in a xenografted mouse tumor model (Ryu *et al.,* 2012). Anti-proliferative effect of guava leaf extract on the human colon adenocarcinoma cell line (COLO320DMA) indicated reduced proliferation due to the presence of triterpenoids (Ryu *et al.,* 2012). An organic extract of guava leaves showed cytotoxic or antitumor effects in human benign breast cancer cells (MCF-7) and fibrosarcoma mouse cells (L929sA) (Levy and Carley, 2012). Ethanol extract from guava leaves was tested for anti-cancer effects in an in vivo study, which showed the extract produced a vaccine-like effect but not curative effect against tumors by preventing the growth of T-regulatory cells in B6 mice inoculated with melanoma cells (Sen *et al.,* 2015).

Anti-inflammatory and Immuno-modulatory activity

Psidium guajava exhibits notable anti-inflammatory and immunomodulatory effects. Its rich content of bioactive compounds, including flavonoids and polyphenols contribute to these properties (Jang *et al.,* 2014). Studies suggest that guava extracts can inhibits inflammatory cytokines. Additionally, guava's immune-modulatory effects may involve enhancing the activity of immune cells, such as macrophages and lymphocytes, contributing to a balanced immune response (Madduluri and Sitaram, 2014). A fermented guava leaf extract was examined in mouse macrophage (RAW264.7) cells, and the effects established its doable to limit the expression of lipopolysaccharide-inducible nitric oxide synthase and cyclooxygenase-2 proteins level, two pro-inflammatory mediators, through the down-regulation of nuclear factor-_B transcriptional activity (NF-_B) (Laily *et al.,* 2015). Furthermore, methanol and ethanol leaf extracts also showed the inhibition of hypotonicity-induced lysis of the erythrocyte membrane (Levy and Carley, 2012). The anti-inflammatory response of the leaves used to be dose-dependent on hyperalgesia in Sprague-Dawley rats, lowering in paw-withdrawal latency, and significantly enhancing the survival of mice with deadly endotoxemia (Anyachukwu *et al.,* 2016). Meanwhile, studies suggested the use of guava leaves as an immune-stimulant agent because they modulated the lymphocyte proliferation response (Laily *et al.,* 2015). The outcomes of this activity, confirm the attainability of guava leaves as an anti-inflammatory treatment and as an immune-system stimulatory agent.

Antihypertensive activity

Psidium guajava exhibits potential anti-hypertensive effects attributed to its unique nutritional composition (Mansoori *et al.,* 2012). Rich in potassium, guava may contribute to blood pressure regulation by promoting vasodilation and counteracting the hypertensive effects of excessive sodium intake (Anyachukwu *et al.,* 2016). Distilled water extract of *Psidium guajava* leaf (50-800 mg/kg i.v.) in a dose-dependent manner reduced systemic arterial blood pressure and heart rate in hypertension (Wang *et al*., 2007). Moreover, the presence of antioxidants like vitamin C may help improve endothelial function and reduce oxidative stress, both linked to hypertension (Duraipandiyan *et al.,* 2006). In addition, flavonoids and phenolic acids in the leaves ought to contribute to the prevention and amelioration of hypertension, since, in rat tissues homogenates, they inhibit the activity of angiotensin 1-converting enzymes which is related to the development of the disorder. (Mukhtar *et al.,* 2004).

Anti-malaria activity

Malaria is a parasitic disease caused by plasmodium and it poses a significant threat public health, especially in tropical and sub-tropical regions (Ojewole, 2008). The increasing drug resistance of plasmodium parasites to convectional anti-malarial

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drugs has prompted the search for alternative treatment options. One such option is *Psidium guajava*, a plant with a long history of medicinal use in traditional systems. The stem bark extract contained anthraquinones, flavonoids, and terpenoids discovered to be potent for the cure and/or prophylaxis of malaria (Nundkumar and Ojewole, 2002). The leaves also confirmed anti-malarial impact in BALB/c mice inoculated with *Plasmodium berghei* by way of parasitemia suppression. The anti-malarial activity of *Psidium guajava* may be attributed to various mechanisms, including the disruption of plasmodium's life cycle, inhibition of enzymes crucial for parasite survival and modulation of the host immune response (Nundkumar and Ojewole, 2002).

Anti-allergic activity

Allergic disorders, such as allergic rhinitis, asthma, and atopic dermatitis, affects a significant portion of the population. Traditional medicine systems have long recognized the therapeutic properties of guava and recent research has delved into its anti-allergic potential. Guava leaves have been proven to possess anti-allergic outcomes in rat mast (RBL-2H3) cell lines by inhibiting degranulation and cytokine production, as well as blocking high-affinity immunoglobulin E-receptor signaling (Sumanmanee *et al.*,2014). Studies have demonstrated that guava leaf extracts can inhibit histamine release and reduce allergic reactions. (Kawakami *et al.,* 2009).

Cough treatment

Guava leaf infusions have been traditionally used in various cultures to soothe cough symptoms. Studies by PJaiarj *et al.,* 1999, have shown that the compounds in guava leaves possess anti-tussive (cough-suppressing) properties, possibly by affecting neural pathways involved in the cough reflex. Animal experiments on cough suppressing potential of *Psidium guajava* extract showed the aqueous extract of *Psidium guajava* plant in doses of 5mg/kg, p.o. reduced the incidence of capsaicin aerosol-induced cough, within 10 minutes of extract injection. However, the anti-tussive effect is less effective than 3 mg/kg p.o. dextromethorphan, which reduced the incidence of cough by 78% (Pjairaj *et al*. 1999).

Conclusion

The focus of ethno-pharmaceutical industry has been to explore the lines of traditional medicine to design and develop new innovative/indigenous herbal medicines (Chen, 2011). Traditional use of organic compounds (herbs) in recent years has gained momentum because their efficacy has been well tested and they are generally believed to be safe for humans. It is the best classical approach to finding new lead molecules to treat various diseases. A comprehensive review of the available literature on *Psidium guajava* revealed that it is a popular remedy among various ethnic groups, and traditional health practitioners for the treatment of diseases. This plant needs to be studied in depth and further investigate the medicinal potential of this plant.

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Conflict of Interests

The authors declare no conflict of interest.

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