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Psidium guajava: A Review on Its Pharmacological and Phytochemical Constituents

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***Psidium guajava,* belonging to the Myrtaceae family, thrives in tropical and subtropical regions worldwide. This important tropical fruit finds widespread cultivation in countries like India, Indonesia, Syria, Pakistan, Bangladesh, and South America. Throughout its various parts, including fruits, leaves, and barks, guava boasts a rich reservoir of bioactive compounds that have been traditionally utilized as folkloric herbal medicines, offering numerous therapeutic applications. Within guava, an extensive array of Various compounds with antioxidative properties and phytochemical constituents are present, including essential oils, polysaccharides, minerals, vitamins, enzymes, triterpenoids, alkaloids, steroids, glycosides, tannins, flavonoids, and saponins. Notably, different components of the plant, comprising leaves and fruits, contribute to a spectrum of medicinal benefits. These encompass antimicrobial potency and potential anti-cancer properties. This study Investigates the phytochemical constituent and pharmacological activity of Guava by using previous studies and reports to collect more information about the guava plant. versatile properties extend to various therapeutic domains. The fruit has showcased its potential in domains like antidiabetic, antidiarrheal, hepatoprotective, anticancer, antioxidant, anti-inflammatory, antimicrobial, anti-allergy, and anti-plasmodial effects. Both guava leaves and fruits have been historically employed to address an array of conditions, including gastroenteritis, hypertension, diabetes, dental caries, and pain relief. While guava's pharmacological attributes are well-recognized, also all parts of guava have many phytochemical constituents. This review study shows the most important phytochemical constituents and pharmacological properties, it is vital to emphasize the need for further research. Enhanced understanding of the main mechanisms of action and the possible health advantages associated with guava necessitates continued investigation.**

Keywords: Anticancer; Flavonoids; Myrtaceae family; *Psidium guajava.*

Psidium guajava (*P. guajava*), commonly referred to as (guava) is a tropical fruit extensively cultivated across various regions of the globe, encompassing countries like Egypt, India, Indonesia, Syria, Pakistan, Bangladesh, and South America [1]. It belongs to the Myrtaceae family and takes the form of an evergreen shrub or a compact tree [2]. Not only utilized as a dietary staple, guava also holds significance in folk medicine, with distinct components of the plant boasting a spectrum of therapeutic attributes. Renowned for its dual role as sustenance and remedy, guava, originating in the tropics, boasts an extensive historical legacy. Multiple segments of the plant, encompassing leaves and fruits, offer an array of medicinal benefits, spanning from antimicrobial efficacy to potential anti-cancer attributes. Among the noteworthy medicinal characteristics of guava is its efficacy in treating gastrointestinal infections, notably recognized as a traditional solution for conditions such as diarrhea. Additionally, the extract derived from guava leaves has demonstrated antinociceptive properties, effectively mitigating pain. Furthermore, guava leaves find application in diabetes management, and the plant is credited with wound-healing capabilities, regulation of blood glucose levels, and enhancement of cardiovascular well-being [3,4].

Guava harbors an extensive array of various compounds with antioxidative properties and phytochemical constituents are present, comprising polysaccharides, essential oils, minerals, vitamins, enzymes, triterpenoid acid alkaloids, steroids, glycosides, tannins, flavonoids, saponins [4,5]. These constituents play a pivotal role in conferring numerous health advantages to the plant, including its antioxidative, anti-inflammatory, and potentially anticancer attributes. Renowned as a noteworthy repository of nutrients and phytochemical antioxidants, guava encompasses compounds such as ascorbic acid, carotenoids, antioxidant-rich dietary fiber, and polyphenolics [6].

The foliage of the guava plant is notably enriched with bioactive compounds like polyphenolic, among them quercetin and diverse flavonoids, along with ferulic acid, caffeic acid, and gallic acids. These compounds exert potent antioxidant effects and demonstrate stimulant activities [7,8].

Botanical description

Morphological features

P. guajava, more commonly referred to as guava, is a compact tree or shrub with a potential height range of 2 to 7 meters. The leaves of the guava plant are characterized by their evergreen nature, leathery texture, and opposite arrangement along the branches as shown in Figure 1. They are distinguished by their short petioles and exhibit a diverse range of irregular shapes, encompassing ovals and other non-uniform forms. The blossoms of the guava are sizable, supported by stems, visually striking, and emit a pleasant fragrance. Notably, guava features branchlets with four distinct angles, and its fruits display a variable assortment of shapes, including pyriform, oblate, rounded, ellipsoidal, oval, and cylindrical. The root system of the guava is relatively shallow, and its fruits possess a limited shelf life of approximately 3 to 5 days when stored at room temperature. This brief duration can be attributed to the fruit's elevated respiration rate and vigorous metabolic processes [9,10].

Phytochemistry

Guava leaves encompass a diverse spectrum of identified compounds, including fatty acids, essential oils, terpenoids, phenolic compounds, carbohydrates, glycosides, alkaloids, saponins, sterols, and other constituents. Within guava leaves, there is a notable abundance of essential oils, featuring compounds like alpha-pinene, beta-myrcene, o-cymene, d-limonene, beta-ocimene, humulene, terpinene, linalool, alpha-terpineol, alloaromadendrene, heptasiloxane, neointermedeol, alpha-calcarine, eicosanoid, 2-Carene, copaene, gamma-muurolene, aromandendrene, beta-bisabolene, cis-calamine, naphthalene, and epicubenol. These constituents were identified through Gas chromatography-mass spectrometry (GC-MS) analysis [11-15].

The analysis conducted using (GC-MS) spectrometry on the hexane fraction of guava seed extract unveiled the existence of a variety of fatty acids, including the search results did not yield specific information regarding the fatty acid profile of guava leaves. However, the studies highlighted in the search results have delved into the fatty acid composition of guava seeds and guava seed oil. The fatty acids that have been identified in guava seeds and guava seed oil incorporate (oleic acid, palmitic acid, stearic acid, linoleic acid, and palmitoleic acid), It's important to recognize that the fatty acid composition of guava leaves might vary from that of guava seeds and guava seed oil. To gain a comprehensive understanding of the fatty acid profile specific to guava leaves, further research is essential [16-19].

Guava leaves encompass a diverse array of chemical constituents, including phenolic acids and flavonoids, which have been analyzed using high-performance liquid chromatography coupled to electrospray ionization quadrupole–time-of-flight mass spectrometry (HPLC–TOF–ESI/MS). These include compounds like Guaijaverin, Quercetin, Avicularin, Myricetin, Hyperin, Kaempferol, Apigenin, Gallic, Rutin, Chlorogenic acid, Pyrogallol, Isoquercitrin, Caffeic acid, Chlorogenic acid, Luteolin, Morin, Prodelphinidin dimer isomer, Pedunculagin, Casuariin, Vanillic acid, Ellagic acid, Myrciaphenone B, Vescalagin, Delphinidin-3-O-glucoside, Gallocatechin, Catechin, Protocatechuic acid, Resveretol and Cyanidin-3-O-glucoside [20-26]. A comprehensive summary of the various phenolic compounds found in guava leaves is presented in Figure 2.

In his publication, *Xinfeng Zou* reported the discovery of over 75 mero terpenoids derived from guava leaves, along with their respective bioactivities. This research spanned from 2007 to May 2022. Notably, it's crucial to acknowledge that the occurrence and makeup of terpenoids within guava leaves can exhibit variations influenced by factors like the particular guava variety and the environmental conditions in which they are cultivated [27]. Further investigations and analyses are warranted to comprehensively understand and describe the complete range of terpenoids present in guava leaves.

In the previous study, ten previously unreported mero terpenoids were isolated from a 95% ethanol extract of guava. This isolation was achieved through the utilization of liquid chromatography-tandem mass spectrometry (LC-MS/MS) techniques. These newly identified mero terpenoids possess distinct structural frameworks in comparison to known guava mero terpenoids. The specific compounds discovered include Psidial A, Jejuguajavone B, Jejuguajavone C, Jejuguajavone D, Jejuguajavone E, Jejuguajavone F, Jejuguajavone G, Jejuguajavone H, and Jejuguajavone I, Psiguadial D, Guajamer A, Psigumer C [28-31].

Guava stands as a significant source of essential minerals, vitamins, and electrolytes. The leaves have been found to harbor various minerals, including (Ca), (K), (S), (Na), (Fe), and (Mg), along with vitamins B and C. The notable concentration of these minerals further solidifies their suitability for incorporation into the human diet. Indeed, proteins play a foundational role as crucial macromolecules, vital for a range of biological processes. Guava leaves, contain approximately 10% protein on a dry weight basis [32].

Guava boasts a substantial concentration of antioxidant pigments, including carotenoids and polyphenols. Among these, numerous carotenoids have been identified, such as á-carotene, lycopene, â-carotene, zeaxanthin, diepoxy-â-carotene, 5,8-epoxy-3',4'-trihydroxy-â-carotene. A separate study isolated sixteen carotenoids from the flesh of red guavas, with lycopene emerging as a pivotal pigment. Its content within the fruit can range from 0.04 to 4.04 mg/100 g, and this concentration tends to decrease with variations in pulp coloration, transitioning from dark pink to white [32-38]. A comprehensive summary of the various carotenoids present in guava leaves is presented in Table 2.

The available information indicates the presence of alkaloids in both guava leaves and fruits. Phytochemical screenings of guava leaf extracts have confirmed the existence of alkaloids. Moreover, a review article affirms the presence of alkaloids in guava [38]. However, the precise categories of alkaloids found in guava and their potential health advantages have not been detailed in the search results. Further investigation is necessary to comprehensively ascertain the specific types and quantities of alkaloids in guava, as well as their potential contributions to health benefits [23].

The previous research results highlight the presence of saponins within guava leaves. This is substantiated by phytochemical screenings of guava leaf extracts, which confirm the existence of saponin glycosides [4]. Further qualitative analyses of organic and aqueous extracts of guava leaves have also identified the presence of saponins [1]. Notably, the presence of saponins in guava leaves appears to be linked to their antimicrobial activity. However, the specific classifications of saponins present in guava and the potential health benefits associated with them remain unspecified in the search results. To comprehensively grasp the variations and quantities of saponins in guava, as well as their potential bioactive properties, further research is imperative [4].

Also, the previous research results show that guava contains pseudo-tannins as its type of tannins. Pseudo-tannins are a class of amorphous organic compounds with an acidic pH. They can precipitate alkaloids and glycosides [39]. These compounds are recognized for their antibacterial, neutralizing, absorbent, and astringent properties [40]. Research investigating the tannin content in guava leaves has affirmed the presence of tannins within the extract. Another study delved into the extraction process of tannins from guava leaves, utilizing spectrophotometry to quantify the tannin content. While the specific types of tannins in guava fruits are not explicitly mentioned in the search results, it's plausible that they may also contain pseudo-tannins. To gain a comprehensive understanding of the types, amounts, and potential health benefits of tannins in guava, further investigation is warranted [41].

The search results did not yield specific information regarding the presence of phytosterols in guava leaves. However, findings from a study examining guava seed oil composition revealed the existence of phytosterols in it. The identified phytosterols in guava seed oil include stigmasterol, â-sitosterol, and campesterol, Phytosterols are plant-derived compounds structurally akin to cholesterol, and they have demonstrated cholesterol-lowering effects in humans [42]. Although the search results didn't address the phytosterol content of guava leaves, it's conceivable that they may contain phytosterols as well. To comprehensively understand the presence and potential health advantages of phytosterols in guava leaves, further research is indispensable.

Table 1. Taxonomic classification of *P. guajava* [9]

Kingdom	Plantae
Phylum	magnoliophyta
Class	magnoliopsida
Subclass	rosidae
Order	myrtales
Family	myrtaceae
Genus	psidium
Species	Psidium guajava

Pharmacological actions of *Psidium guajava*

The plant possesses a variety of pharmacological activities, including

Antioxidant activity

Lipid autoxidation is initiated by a sequence of lipophilic radicals. Within the biological context, hydrogen peroxide is enzymatically generated by various oxidase enzymes. hydrogen peroxide, acting via the hydroxyl free radical, assumes the role of a signaling molecule in the synthesis and activation of inflammatory mediators. These signaling molecules have a substantial impact on tissue damage and the development of various diseases, including diabetes, Guava boasts a substantial matter of essential antioxidants and exhibits radio-protective properties [43]. Additionally, it is enriched with a wide array of vitamins and minerals. Notably, guava contains phenolic compounds like flavonoids, as well as vital antioxidants like lycopene and flavonoids. These components contribute to the elimination of cancerous cells and the prevention of premature skin aging. Within guava leaves, quercetin is recognized as the most potent antioxidant and is dependable for its spasmolytic activity. Guava extracts, when subjected to aqueous or organic solvents, display a substantial antioxidant reservoir capable of quenching oxidation reactions [44]. The concentration of these compounds increases proportionally with higher extract concentrations, Furthermore, pink guava exhibits pronounced antioxidant activity,

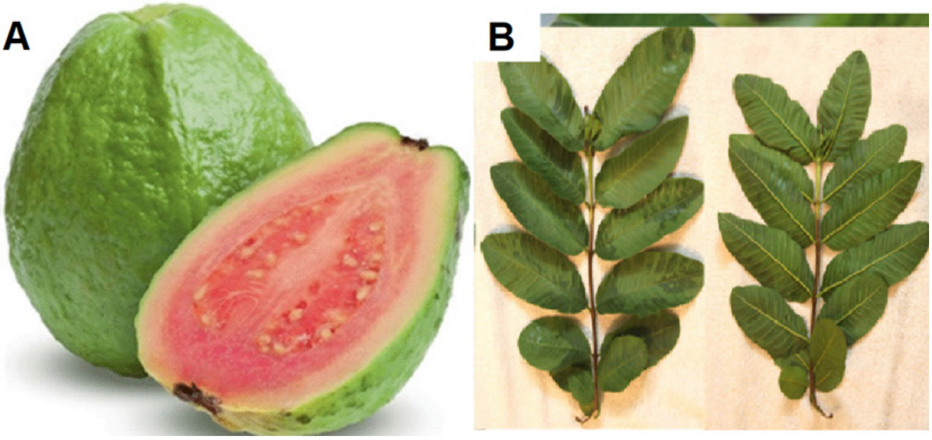


Fig. 1. (A) Guava fruit, (B)Guava leaves [9,10]

Guava stands out for its exceptional richness in antioxidants, which play a pivotal role in reducing the incidence of degenerative ailments such as cognitive dysfunction, cardiovascular diseases, inflammation, cancer, arteriosclerosis, and arthritis. The therapeutic potential of guava extracts, owing to their antioxidative properties, has opened new avenues for combatting diverse complications and diseases. Further investigations are warranted to elucidate the precise mechanisms underpinning guava's antioxidant and other pharmacological activities, Remarkably, the flesh of red guava contains many distinct carotenoids, with thirteen being specifically identified as guava carotenoids responsible for its antioxidant activity [45].

Antidiabetic activity

Numerous scientists have explored the potential of *P. guajava* in combating diabetes through a series of studies Specifically, investigations have revealed that extracts derived from guava leaves and bark effectively enhance the uptake of glucose in muscular cells and inhibit á-amylase activity Moreover, guava leaves extract has been shown to reduce fasting glucose plasma levels, and fasting insulin levels, with an effect on insulin resistance in diabetic KK and lethal yellow (Ay) mice, and carry a heterozygous mutation of the agouti gene (KK-Ay strain) [46]. Additionally, *P. guajava* leaf extracts have demonstrated the ability to lower fasting blood glucose levels, regulate lipid profiles, and modulate glucose metabolism in diabetic rats induced with streptozotocin (STZ). It is worth noting that even raw fruit peels and aqueous extracts from unripe guava fruit peels exhibit hypoglycemic effects in diabetic rats induced with STZ [47]. Administration of guava fruit at doses of 0.125 and 0.250 g/kg for 1 month resulted in a lessening in blood glucose levels [48]. Furthermore, supplementation with flavonoids extracted from *P. guajava* has shown a marked capacity to lower fasting glucose plasma levels and reduce insulin resistance in diabetic mice [49]. studies have reported on the probable of polyphenols extracted from guava seeds, pulp, and leaves to reduce blood glucose levels in diabetic mice. These anti-diabetic effects may be attributed to *P. guajava's* ability to elevate glycogen synthase levels while reducing the activity of glycogen phosphorylase enzyme [50].

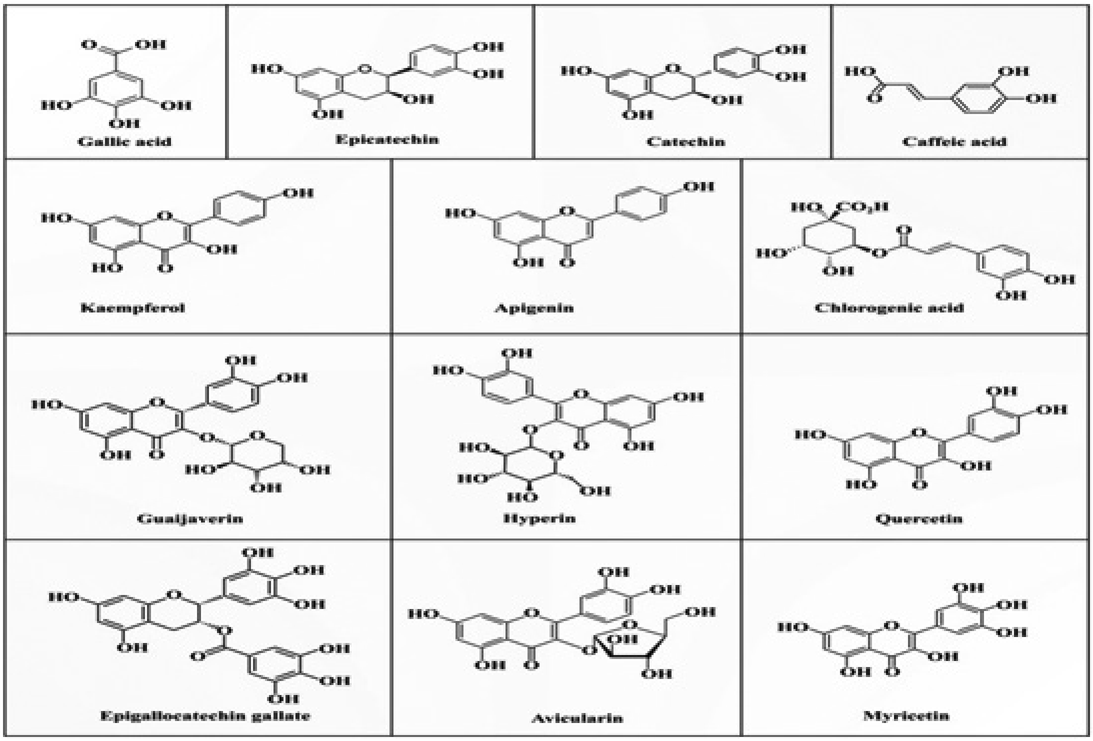
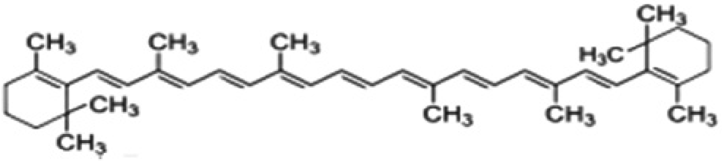
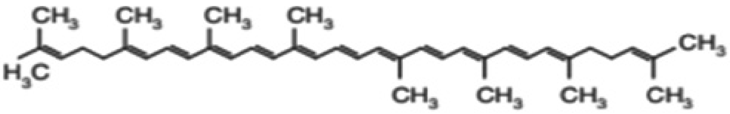
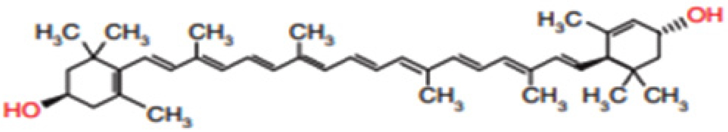
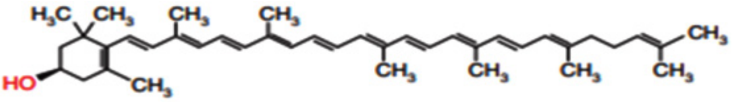
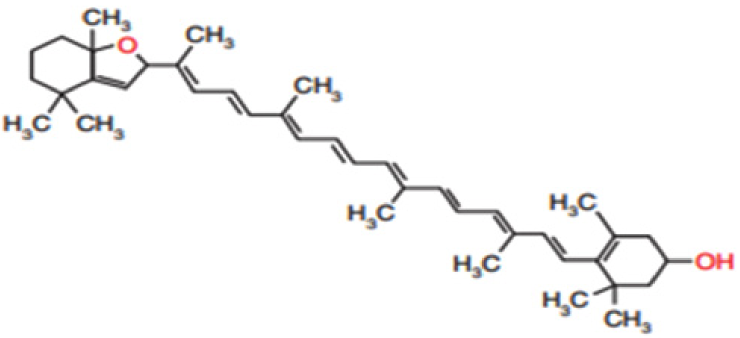


Fig. 2. Major phenolic compounds present in guava leaf extracts [1, 27]

Hepatoprotective activity

Multiple scientific investigations have provided evidence that guava leaves extract exhibits antioxidant characteristics, primarily attributable to its elevated phenolic content. This attribute is instrumental in mitigating or preventing liver damage caused by free radicals, particularly in diabetic rats induced with alloxan. Consequently, Guava leaves extract offers dual benefits of antidiabetic and hepatoprotective effects [51,52]. In a previous study, it was observed that the administration of *P. guajava* fruit purée at doses of 200,400 mg/kg to rats led to a weighty drop in serum levels of AST, ALT, and alkaline phosphatase when compared to diabetic control groups. These findings suggest that *P. guajava* fruit purée is safe even at higher doses, effectively conquers hyperglycemia, and provides protection to the liver by reducing lipid peroxidation while enhancing antioxidant status in alloxan-induced diabetic rats. These results offer scientific support for considering *P. guajava* fruit purée as a nutraceutical agent for managing diabetes and hepatotoxicity [53]. Additionally, *P. guajava* root extracts have exhibited potent hepatoprotective properties against damages induced by castor oil in rats, suggesting their potential utility in ethnomedicine, another study has highlighted the hepatoprotective actions of *P. guajava* aqueous leaf extracts and ethanolic extract, administered

Table 2. Several carotenoids were reported in guava [36]

Name	Structure
Beta-carotene	
Lycopene	
Lutein	
Rubixanthin	
Cryptoflavin	

postoperatively at doses of 250, 500 mg/kg, underscoring their effectiveness in safeguarding liver health [54].

Antibacterial action

Guava leaf extracts have demonstrated strong efficacy in preventing the growth of many strains of bacteria also they exhibit robust antifungal and antibacterial action [55]. The antibacterial properties of *P. guajava* leaves are attributed to their content of flavonoids, Extensive research has emphasized the antibacterial potential of guava, particularly its flavonoid constituents, The concentrated liquid form of *P. guajava* leaves has publicized remarkable antibacterial effects against a variety of test strains. Reports indicate that flavonoid extracts from guava leaves possess antibacterial properties, The antibacterial action of guava leaves extract is attributed to the incidence of flavonoid glycosides, specifically (Morin-3-O-alpha-L-lyxopyranoside) and (morin-3-O-alpha-L-arabinopyranoside) [56]. Studies have shown that these flavonoids have been established to have specific effects. to exhibit antibacterial activity. Moreover, the flavonoid guaijaverin has been shown to combat plaque formation [57].

Analgesic Anti-inflammatory activity

Anti-inflammatory possessions of the leaf extract derived from the *P. guajava* plant are thought to arise from a complex interplay of chemical constituents present within it, which encompass flavonoids, tannins, polyphenols, ellagic acid, triterpenoids, quercetin, guaijaverin, and several other compounds. Experimental studies conducted on animals support these claims by revealing that the aqueous leaf extract of guava possesses anti-inflammatory properties. These findings lend pharmacological support to the traditional and traditional folkloric procedures of the plant in managing and controlling painful, arthritic, and main inflammatory disorders in certain rural African communities. The anti-inflammatory activities of *P.guajava* ethanolic leaf extract have been observed both in *vitro* and in *vivo*. Results indicate that guava leaves significantly reduce the creation of inflammatory mediators (nitric oxide and prostaglandin E2), which are induced by lipopolysaccharides [58].

Anticancer activity

P. guajava plant contains bioactive phytochemicals in various parts, and these compounds have demonstrated anticancer properties. Multiple studies have highlighted the ability of *P. guajava* and its bioactive molecules, particularly those derived from its leaves, to selectively inhibit the growth of cancerous cells without harming normal cells. Researchers researched the potential anti-cancer properties of guava seed polysaccharides against Michigan Cancer Foundation-7 cells (MCF-7). Their findings indicated a significant dose-dependent inhibition of MCF-7 cell viability [59]. Other researchers explored the anticancer potential of red *P. guajava* extract and reported the anticancer activity of a lycopene extract of *P. guajava*, with an IC_{50} value of 29850 at 5964 ng/mL. A recent study recognized compounds with anticancer activity versus a human colorectal carcinoma cell line initiated from an adult male (HCT116) and a human colorectal adenocarcinoma cell line with epithelial morphology cells (HT29). another study demonstrated the maximum inhibitory activity of *P. guajava* versus cancerous cells, with an IC_{50} value of less than 0.03 µg/mL [60]. The anticancer effects of *P. guajava* are thought to be attributed to the presence of chemical components such as vitamin E, â-sitosterol, and tetracosane. Guava extracts have demonstrated their effectiveness in combating various types of cancer, including (lung cancer, colorectal carcinoma, breast cancer, cervical cancer, and prostate cancer). The bioactive phytochemicals found in different parts of the guava plant have exhibited medicinal properties encompassing antimicrobial, antioxidant, anti-inflammatory, and antidiabetic activities, these results suggest that guava extracts and their bioactive constituents have the potential to serve as viable alternatives or supplementary treatments for human cancers[59, 60].

Anthelmintic Activity

The leaf extract has demonstrated anthelmintic activity, with the ethanolic extract (100 mg/ml) exhibiting higher anthelmintic activity compared to the aqueous extract. In recent study reported that *P. guajava* leaves methanolic extract displayed significant anthelmintic activity when compared to other extracts. The methanolic extract induced the highest rates of paralysis 1.820±0.242 min and death 5.573±0.315 min in earthworms, surpassing the effects of the Piperazine citrate. This suggests that Guava leaf extract could be effective in treating parasitic infections in beings, validating its traditional use as a natural therapy for anthelmintic infections [61]. Furthermore, the antiparasitic mechanism of action appears to involve pro-oxidative activity, as evidenced by an increase in total proteins, intracellular H_2O_2, lipid peroxidation products, and the action of enzymes such as glutathione S-transferase and superoxide dismutase. Consequently, the hydro-alcoholic extract of the guava tree's stem bark demonstrated antiparasitic activity in *vitro* [62]. Numerous studies have investigated the anthelmintic properties of guava extracts, particularly focusing on the hydroalcoholic extracts derived from the stem bark and leaves of the guava tree, these extracts have been found to contain various bioactive compounds, including flavonoids, tannins, saponins, alkaloids, and steroids. These chemical constituents are believed to be the primary contributors to the anthelmintic activity observed in guava extracts, The anthelmintic activity of guava extracts has been assessed in experiments involving gastrointestinal sheep nematodes and Levamisole-resistant strains of Caenorhabditis elegans. The outcomes of these investigations indicate that guava extracts have the potential to serve as natural anthelmintics and may be considered for inclusion in drug formulations aimed at treating diseases caused by parasitic worms. However, it is essential to do further research to establish the efficacy and safety of guava extracts as anthelmintic agents for use in humans.

Antidiarrhoeal activity

Guava leaves have a traditional history of practice in African folk medicine for the management and treatment of diarrhea [63]. Numerous reports have provided evidence of the antidiarrheal effects of guava extracts, particularly the aqueous extract of guava leaves, in various research papers, these studies have typically employed rodent and mouse models to assess the antidiarrheal effects [64,65]. primarily focusing on infectious diarrhea. The collective findings from these investigations suggest that guava extracts have the potential to serve as a natural remedy for treating, managing, and controlling diarrhea, particularly in certain rural communities of southern Africa. The antidiarrheal activity of guava extracts is linked with the presence of chemical constituents such as flavonoids, tannins, and saponins, which are believed to contribute to their effectiveness in alleviating diarrhea [66]. Nevertheless, further research is essential to ascertain the efficacy and safety of guava extracts as antidiarrheal agents for human use.

The aqueous extract of guava leaves demonstrated significant dose-dependent activity in rats and mice with antidiarrhea induced by castor oil. This extract inhibited intestinal transit and late gastric emptying, which resembled the effects of atropine. Guava leaves also exhibited dose-dependent and significant antimotility activity and reduced (castor oil) made (enteropooling) in both rats and mice. Similar to loperamide 10 mg/kg, guava leaves dose-dependently and significantly delayed the onset of diarrhea induced by castor oil, reduced the frequent defecation, and mitigated the severity of diarrhea in these animals. It's worth noting that ripe guava fruit is known for its laxative properties, making it useful for relieving constipation. In contrast, unripe guava fruit is primarily employed as an astringent and antidiarrheal agent. However, excessive consumption of unripe guava fruit can lead to indigestion, vomiting, and feverishness, Guava leaves are rich in various compounds that exhibit fungistatic and bacteriostatic properties. They are known for their ability to impede the growth of numerous bacteria and possess antifungal properties, against *Geotrichum candidum* RIBB-SCM43 and *Geotrichum candidum* RIBB-SCM44. These properties make guava leaves valuable in traditional medicine and as potential sources of natural antimicrobial agents [67].

CONCLUSION

Guava is a tropical fruit-bearing plant that has gained attention for its potential health benefits due to its rich phytochemical constituents and associated pharmacological activities, it's important to note that while guava has demonstrated these potential pharmacological activities in various studies, more study is needed to fully understand the mechanisms and establish concrete therapeutic uses. Moreover, the specific phytochemical composition and pharmacological effects may vary depending on factors such as the guava variety, ripeness, and preparation method. Therefore, for therapeutic purposes, it is advisable to consult with a healthcare professional and consider guava as part of a balanced diet rather than a standalone remedy.

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Conflict of Interest

There is no conflict of interest.

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