Psidium Guajava (Guava): A Plant of Multipurpose Medicinal Applications

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Abstract
Chronic degenerative diseases have reached epidemic proportions in industrialized and developing countries. Many studies have shown that plant can be helpful to prevent or treat diseases. Psidium guajava is a small medicinal tree that is native to South America and Brazil is among the world’s top producers and most of the country’s production is destined for the food industry. It is popularly known as guava and has been used traditionally as a medicinal plant throughout the world for a number of ailments. The aim of this review is to present some chemical compounds in P. guajava and their pharmacological effects. The main constituents of guava leaves are phenolic compounds, isoflavonoids, gallic acid, catechin, epicatechin, rutin, naringenin, kaempferol. The pulp is rich in ascorbic acid, carotenoids (lycopene, β-carotene and β-cryptoxanthin). The seeds, skin and barks possess glycosids, carotenoids and phenolic compounds. All parts of the plant have been used for different purposes: hepatoprotection, antioxidant, anti-inflammatory, anti-spasmodic, anti-cancer, antimicrobial, anti-hyperglycemic, analgesic, endothelial progenitor cells, anti-stomachache and anti-diarrhea. P. guajava has many effects on health and that it should be researched more extensively in clinical trials. Furthermore leaves, seeds and peel are treated as wastes by the food processing industry and are discarded, so their use may reduce the disposal of these parts of guava as pollutants.

Keywords: Psidium guajava; Anti-inflammatory; Antioxidant; Cancer; Diabetes; Dyslipidemia

Introduction
Industrialization has led to many modifications in the lifestyle of the world’s populations, giving rise to increase the indices of several diseases, including chronic degenerative diseases such as insulin resistance, diabetes mellitus, dyslipidemia, metabolic syndrome and cardiovascular diseases, reducing the quality of life and increasing costs on hospitalizations, medications and other public health interventions [1,2].

Studies have demonstrated that the consumption of fruits, vegetables and seeds can be helpful to prevent the risk factors of many diseases due to the bioactive compounds. Many plants have been used for the purpose of reducing risk factors associated with the occurrence of chronic disorders and for many other purposes [3-8].

Psidium guajava L. is a small medicinal tree that is native to South America. It is popularly known as guava (family Myrtaceae) and has been used traditionally as a medicinal plant throughout the world for a number of ailments. There are two most common varieties of guava: the red (P. guajava var. pomifera) and the white (P. guajava var. pyrifera) [9,10].

All parts of this tree, including fruits, leaves, bark, and roots, have been used for treating stomachache and diarrhea in many countries. Leaves, pulp and seeds are used to treat respiratory and gastrointestinal disorders, and as an antispasmodic, anti-inflammatory, as a cough sedative, anti-diarrheic, in the management of hypertension, obesity and in the control of diabetes mellitus. It also possesses anticancer properties [11]. The seeds are used as antimicrobial, gastrointestinal, anti-allergic and anticarcinogenic activity [12-15].

Brazil is among the world’s top producers of guava and most of the country’s production is destined for the food industry to produce candies, juices, jams and frozen pulp. As result of the fruit process there is a discard of the leaves, seeds, part of the peel and pulp fraction not separated in the physical depulping process [9,10,16,17].

The high cost of pharmaceutical medications conduces to the search for alternative medicines to treat many ailments. In view of this, studies are necessary to confirm the effects of medicinal plants. The aim of this review is to show that several studies have demonstrated the presence of many different chemical compounds in P. guajava and their pharmacological effects.

Medical Properties and Composition of Guava Pulp

The main constituents of guava are vitamins, tannins, phenolic compounds, flavonoids, essential oils, sesquiterpene alcohols and triterpenoid acids. These and other compounds are related to many health effects of guava [10].

Some authors have found high concentrations of carotenoids (beta-carotene, lycopen, and beta-cryptoxanthin), vitamin C and polyphenols in guava pulp [18-20]. Lycopene has been correlated with the prevention of cardiovascular damage because of its positive effects on dyslipidemia [21,22]. Ascorbic acid is recognized for its important antioxidant effects [23-25].

Shu et al. [26] isolated nine triterpenoids from guava fruit: ursoic acid; 1beta, 3beta-dihydroxysters-12-en-28-oic acid; 19alpha-hydroxyurs-12-en-28-oic acid; 1beta, 3beta-dihydroxysters-12-en-28-oic acid; 19a-hydroxyurs-12-en-28-oic acid; 19a-hydroxysters-12-en-28-oic acid; 3-O-alpha-L-arabinopyrano-...
side; 3beta, 23-dihydroxy urs-12-28-oxic acid; 3beta, 19alpha, 23be-ta-tri-hydroxylurs-12-en-28-oxic acid; 2alpha, 3beta,19alpha, 23beta-tetraydroxyurs-12-en-28-oxic acid and 3alpha,19alpha,23,24-tetraydroxyurs -12-en-28-oxic acid. Ursolic acid and other triterpenoids are associated with anti-cancer properties [27].

Shu et al. [28] found three benzophenone glycosides in ripe edible fruits of \textit{P. guajava} L: 2, 6-dihydroxy-3, 5-dimethyl-4-O-beta-D-glucopyranosyl-benzophenone; 2, 6-dihydroxy-3-methyl-4-O-(6''-O-galloyl-beta-D-glucopyranosyl)-benzophenone and 2, 6-dihydroxy-3, 5-dimethyl-4-O-(6''-O-galloyl-beta-D-glucopyranosyl)-benzophenone. Benzophenone glycosides have inhibitory effect on triglycerides accumulation [29].

Thuaytong and Anprung [30] found antioxidant activity in guava and the major constituents identified in white and red guavas were ascorbic acid, gallic acid, catechin equivalents, cinnamyl alcohol, ethyl benzoate, ß-caryophyllene, (E)-3-hexenyl acetate and α-bisabolene. The antioxidant properties of the guava pulp can be related to anticancer effects [15].

Studies with humans have found that the consumption of guava for a period of 12 weeks reduced blood pressure by 8%, total cholesterol levels by 9%, triacylglycerides by almost 8%, and induced an 8% increase in the levels of HDL-c [31,32].

Farinazzi et al. [33] showed that animals treated with guava pulp juice had significantly lower body weight, glycemia, cholesterol and triglycerides levels and significantly augmented the levels of HDL-c when compared to the animals from the control group.

Lyophilized pulp of \textit{P. guajava} in diabetic rats induces to significant hypoglycemic effects probably due to its antioxidant activity of compounds present in the pulp [14].

Medical Properties and Composition of Guava Leaves

Guava leaf extract has analgesic, anti-inflammatory, antimicrobial, hepatoprotective and antioxidant activities. These effects are probably due to the presence of phenolic compounds [11,34-39].

Jiménez-Escrig et al. [40], Wang et al. [41] and Haida et al. [10] reported the presence of higher amounts of phenolic compounds with antioxidant activity in the leaves of white (\textit{Psidium guajava} var. pyrifera L.) and red guava (\textit{Psidium guajava} var. pomifera L.) when compared with other vegetable species. Wu et al [42], Melo et al. [43] and Chen et al. [27] found gallic acid, catechins, epicatechins, rutin, naringenin and kaempferol in the leaves.

Studies have shown that gallic acid, catechin, and epicatechin inhibit pancreatic cholesterol esterase, which decreases cholesterol levels. Catechins are important as a preventive treatment for diabetes type 2 and obesity. Quercetin has been associated to decreased mortality from heart disease and decreased incidence of stroke. Quercetin presents hypcholesterolemic and antioxidant activity. Rutin is effective in the inhibition of triglyceride accumulation in adipocytes. Naringenin and kaempferol can promote moderate cytostatic activity against all cell lines and kaempferol can be useful as anti cancer [44-49].

Fu et al. [50] elucidated the structure of three novel sesquiterpene-bioses of meroterpenoids from psidials A-C found in guava leaves. Matsuzak et al. [51] isolated two new benzophenone galloyl glycosides, guaivinidos A and B, and a quercetin galloyl glycoside, guaivinidine C as well as five known quercetin glycosides from guava leaves. The structures of the novel glycosides were elucidated to be 2,4,6-trihydroxybenzophenone 4-O-(6''-O-galloyl)-beta-D-glucopyranoside (1, guaivinoside A); 2,4,6-trihydroxy-3,5-dimethylbenzophenone 4-O-(6''-O-galloyl)-beta-D-glucopyranoside (2, guaivinoside B), and quercetin 3-O-(5''-O-galloyl)-alpha-L-arabinofuranoside (3, guaivinoside C).

Kim et al. [52] related that the guava leaves contain ascorbic acid, citric acid, acetic acid, epicatechin, xanthine, protocatechuc acid, glutamic acid, asparagine, malonic acid, trans-aconitic acid, maleic acid and citis-acitic acid.

Ghosh et al. [53] isolated two terpenoids from the leaf extract of \textit{P. guajava} (betulnic acid and lupeol) and reported their potential antimicrobial and phytoxic activities. Betulnic acid and lupeol can be used in the treatment of diabetes, cardiovascular disease, obesity and atherosclerosis [54].

Shao et al. [55] isolated two terpenoids from guava leaves: Psigualdias A and B, two novel sesquiterpenoid-diphenylmethane meroterpenoids with unusual skeletons, along with a pair of known epimers, psidal A and guajadiol.

Shu et al. [56] identified one diphenylmethane, one benzophenone, and eight flavonoids from guava fresh leaves(2,6-dihydroxy-3-formaldehyde-5-methyl-4-O(6''-O-galloyl)-beta-D-glucopyranosyl)-diphenylmethane; 2,6-dihydroxy-3,5-dimethyl-4-O(6''-O-galloyl)-beta-D-glucopyranosyl)-benzophenone; kaempferol; quercetin; quercitrin; isoquercitrin; guaijaverin; avicularin; hyperoside and reynoutrin. Guaijaverin has high potential antiplaque agent by inhibiting the growth of the \textit{Streptococcus mutans}. Avicularin and guaijaverin work as urease inhibitors (against \textit{Helicobacter pylori} urease) [57,58].

Shao et al. [59] isolated four new triterpenoids, psiguanins A-D (1-4), and with 13 known compounds from the leaves of guava.

Guava aqueous leaf extract showed anti-trypanosomal properties in rats experimentally infected with \textit{Trypanosoma brucei brucei} [60].

Rahim et al. [61] evaluated the effects of aqueous mixture and water soluble methanol extract from guava leaves and bark against multi-drug-resistant \textit{Vibrio cholera} and found strong antibacterial activity. They concluded that this plant offers potential for controlling epidemics of cholera.

Birdi et al. [62] and Birdi et al. [63] related that \textit{P. guajava} leaves have a broad spectrum of antimicrobial action (as anti diarrhoidal and antirotaviral activity) that could be effective in controlling diarrhea due to a wide range of pathogens. The antimicrobial activity can be linked to the presence of flavonoids extracted from guava leaves [64,65].

Deguchi and Miyazaki [66] reported that guava leaves infusion not only reduced postprandial glycaemia and improved hyperinsulinemia in murine models but also contributed to reduce hypercholesterolemia, hypertriglycerideridemia and hypoadiponectinemia in the animals of their study.

Rutin and kaempferol found in guava leaves are compounds related to the decrease of HMG-Co-A reductase activity in hepatic tissue and improve lipid profiles [67]. Akinmoladun et al. [68] studied methanol extracts of some fruits, including \textit{P. guajava}, and demonstrated that there is a good correlation between total phenolic contents and reductive potential and a fair correlation between total phenolic contents and lipid peroxidation inhibitory activity.

Several studies have shown that aqueous extract of \textit{Psidium guajava} contains components with LDL-c antiligication activity, suggesting its contribution to the prevention of neurodegenerative and cardiovascular...
diseases [69,70]. Other studies have found cardioprotective effects of aqueous extract of P. guajava in myocardial ischemia-reperfusion injury in isolated rat hearts, primarily through their radical-scavenging actions [71].

Ojewole [72] identified the presence of phenolic compounds in the leaves demonstrating their hypoglycemic and hypotensive effects on diabetic rats treated with aqueous leaf extract. Soman et al. [73] reported a decline in the levels of glycated hemoglobin and fructosamines, as well as a significant reduction in the glycemic levels of diabetic rats treated with guava leaf extract. Singh and Marar [74] studied the effects of Psidium guajava leaves on the inhibition of the activity intestinal glycosidases related with postprandial hyperglycemia, suggesting its use for the treatment of individuals with type 2 diabetes. Other studies have demonstrated that guava leaf and peel extracts also had hypoglycemic effects on experimental models drug-induced to severe conditions of diabetes [17,75,76].

Wu et al. [42] found that the phenolic compounds, gallic acid, catechins and quercetins in guava leaves inhibited the glycation of proteins suggesting its use for the prevention of diabetes complications. The Psiquiddals A, B and guajadial isolated by Shao et al. [55] exhibited potent inhibitory effects on the growth of human hepatoma cells. Kim et al. [52] related that the guava leaves contain compounds that promote free radical scavenging activity showing promising antioxidant properties.

Dutta and Das [77] identified significant anti-inflammatory activity of the ethanol extract of guava leaves in experimental models, while Kawakami et al. [78] observed the antiproliferative activity of the leaves through inhibition of the catalytic activity of prostatlandin endoperoxide H synthases involved in the inflammatory process. Guava budding leaves aqueous extract possesses an extremely high content of polyphenolic and isolavonoids and suppresses the cell migration and the angiogenesis. In view of this, clinically it has the potential to be used as an adjuvant anti-cancer chemopreventive [79,80]. Matsuzak et al. [51] isolated phenolic glycosides from guava leaves and showed significant inhibitory activity against histamine release from rat peritoneal mast cells, and nitric oxide production from a murine macrophage-like cell line.

Roy and Das [81] studied the hepatoprotective activity of different extracts of P. guajava (petroleum ether, chloroform, ethyl acetate, methanol and aqueous) in acute experimental liver injury induced by carbon tetrachloride and paracetamol. The effects were compared with a known hepatoprotective agent and observed that the best effects were treated with guava leaf extract. Singh and Marar [74] studied the effects of Psidium guajava leaves on the inhibition of the activity intestinal glycosidases related with postprandial hyperglycemia, suggesting its use for the treatment of individuals with type 2 diabetes. Other studies have demonstrated that guava leaf and peel extracts also had hypoglycemic effects on experimental models drug-induced to severe conditions of diabetes [17,75,76].

Psidium Guajava (Guava)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaves</td>
<td>Phenolic compounds, isoflavonoids, gallic acid, catechin, epicatechin, rutin, naringenin, kaempferol</td>
<td>Hepatoprotection, antioxidant, anti-inflammatory, anti-spasmodic, anti-cancer, antimicrobial, anti-hyperglycemic, analgesic</td>
</tr>
<tr>
<td>Pulp</td>
<td>Ascorbic acid, carotecoids (lycopene, β-carotene, β-cryptoxanthin)</td>
<td>Antioxidant, anti-hyperglycemic, Anti-neoplastic</td>
</tr>
<tr>
<td>Seed</td>
<td>Glycosids, Carotenoids, phenolic compounds</td>
<td>Antimicobial</td>
</tr>
<tr>
<td>Skin</td>
<td>Phenolic compounds</td>
<td>Endothelial progenitor cells and improvement of their intestinal absorption</td>
</tr>
<tr>
<td>Bark</td>
<td>Phenolic compounds</td>
<td>Strong antibacterial activity (against multi-drug-resistant Vibrio cholera); stomachachae and diarrhea</td>
</tr>
</tbody>
</table>

Table 1: Some compounds in guava leaves, pulp, seed, skin and bark and their pharmacological effects.
Rai et al. [94] reported hypolipidemic and hepatoprotective effects in diabetic rats treated with aqueous extract of lyophilized guava peel.

Psidium guajava stem-bark extract can be used to treat malaria because it presents antiplasmodial activities possibly due to the presence of anthraquinones, flavonoids, secoirridoids and terpenoids. [95]

Table 1 presents some compounds in guava leaves, pulp, seed, skin and bark and their pharmacological effects.

**Conclusion**

Many researchers have been demonstrating the presence of a wide variety of bioactive compounds in the leaf, seed and bark of *Psidium guajava* that are capable of showing beneficial effects on human health. If we consider that chronic degenerative diseases have reached epidemic proportions in many countries and increase the socio-economic burden for the public health system, it is necessary to find non-allopathic alternatives that minimize risk factors of these diseases and help in the treatment. Furthermore, population consumes medicinal plants also to treat other kind or diseases because of high costs of allopathic medications.

The studies using *P. guajava* bring information that may provide validation for its medicinal uses but it should be researched more extensively in clinical trials so it could be used for prevention and as an adjuvant in the treatment of numerous disorders.

Nevertheless we should emphasize the importance of experimental and clinical studies involving more specific factors related to the bioavailability of the compounds, as well as the effective and safe doses to be used by individuals for the prevention and treatment of various disorders.

**Author Disclosure Statement**

All the authors report no conflicts of interest.

**References**


