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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, epicathechin, 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, tanins, 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, lycopene, 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: ursolic acid; 1beta, 3beta-dihydroxyurs-12-en-28-oic acid; 2alpha,3beta-dihydroxyurs-12-en-28-oic acid; 3beta,19alpha-dihydroxyurs-12en-28-oic acid; 19a-hydroxylurs-12-en-28-oic acid-3-O-alpha-L-arabinopyrano-

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side; 3beta, 23-dihydroxy urs-12-en-28-oic acid; 3beta, 19alpha, 23beta-tri-hydroxylurs-12-en-28-oic acid; 2alpha, 3beta,19alpha, 23beta-tetrahydroxyurs-12-en-28-oic acid and 3alpha,19alpha,23,24-tetrahydroxyurs -12-en-28-oic 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 *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 anti-cancer 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 *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 (*Psidium guajava* var. pyrifera L.) and red guava (*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 hypocholesterolemic 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 sesquiterpenoid-based meroterpenoids of psidials A-C found in guava leaves. Matsuzak et al. [51] isolated two new benzophenone galloyl glycosides, guavinosides A and B, and a quercetin galloyl glycoside, guavinoside 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, guavinoside A); 2,4,6-trihydroxy-3,5-dimethylbenzophenone 4-O-(6”-O-galloyl)-beta-D: -glucopyranoside (2, guavinoside B), and quercetin 3-O-(5”-O-galloyl)-alpha-L: -arabinofuranoside (3, guavinoside C).

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

Ghosh et al. [53] isolated two terpenoids from the leaf extract of *P. guajava* (betulinic acid and lupeol) and reported their potential antimicrobial and phytotoxic activities. Betulinic acid and lupeol can be used in the treatment of diabetes, cardiovascular desease, obesity and atherosclerosis [54].

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

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-β-D-glucopyranosyl)-diphenylmethane; 2,6-dihydroxy-3,5-dimethyl-4-O-(6″-O-galloyl-β-D-glucopyranosyl)-benzophenone; kaempferol; quercetin; quercitrin; isoquercitrin; guaijaverin; avicularin; hyperoside and reynoutrin. Guaijaverin has high potential antiplaque agent by inhibiting the growth of the *Streptococcus mutans*. Avicularin and guaijaverin work as urease inhibitors (against *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 *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 *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 *P. guajava* leaves have a broad spectrum of antimicrobial action (as antigiardial 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 glycemia and improved hyperinsulinemia in murine models but also contributed to reduce hypercholesterolemia, hypertriglyceridemia and hypoadiponectinemia in the animals of their study.

Rutin and kaempferol found in guava leaves are compounds related to the decrease of HMG-CoA reductase activity in hepatic tissue and improve lipid profiles [67]. Akinmoladun et al. [68] studied methanol extracts of some fruits, including *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 *Psidium guajava* contains components with LDL-c antiglycation 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 Psiguadials 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 prostaglandin endoperoxide H synthases involved in the inflammatory process. Guava budding leaves aqueous extract possesses an extremely high content of polyphenolic and isoflavonoids 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 came from guava methanolic leaf extract that significantly reduced the elevated serum levels of enzymes (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase) and bilirubin.

P. guajava leaves exhibit high capacity to reduced polymerization and aggregation of sickle cell hemoglobin molecule. This molecule is a product of a defective genetic code of hemoglobin molecule and is prone to deoxygenation-induced polymerization and has low insolubility. The development of chemical modification agents that reduce the tendency of sickle cell hemoglobin molecule to aggregate represents an important chemotherapeutic goal [82].

Guava extract leaves can be responsible for membrane stabilizing effect on sickle erythrocytes that are susceptible to endogenous free radical-mediated oxidative damage. This effect can be attributed to the flavonoids, triterpenoids and host of other secondary plant metabolites [83].

Chen et al. [80] found that aqueous extract of guava budding leaves possess anti-prostate cancer activity in a cell line model and concluded they are promising anti-androgen-sensitive prostate cancer agent.

Han et al. [84] studied the effects of *P. guajava* ethyl acetate extract on atopic dermatitis and found that it inhibits chemokine expression in keratinocytes what suggests this extract can have possible therapeutic application in atopic dermatitis and other inflammatory skin diseases.

Methanol extracts of the leaves can also be useful in the treatment of gastric ulcer disorders possibly due to the presence of volatile oil, flavonoids and saponins [85].

Methanolic extract of guava leaves can exhibit wound healing effects and this property can be explained by the presence of tannins and flavonoids [86,87].

Guava leaves extract also can show anti cough effects as shown by Jaiarj et al [88].

Medical Properties and Composition of Guava Discarded Products

As told before, the fruit process results in the discard of the leaves, seeds, part of the peel and pulp. Some studies showed the presence of total phenolic compounds in the agroindustrial wastes (seeds, skin and pulp) of guava, confirming its antioxidant activity [16,32,72].

Leaves, seeds and peels of fruits have significant proportions of bioactive compounds with beneficial physiological and metabolic properties. Its antioxidants can control body weight and biochemical variables like glycemia, dyslipidemia, hypertension and other risks of cardiovascular diseases. The antioxidant properties of the guava seeds extracts can be associated to anti-cancer effects on both hematological and solid neoplasms and the antioxidant properties of the guava peel can be related to anti-cancer effects. [5,15,89-91]

Castro-Vargas et al. [92] and Ojewole [72] extracted and identified significant levels of carotenoids and total phenolic compounds from guava seeds. Seeds exhibit antimicrobial, gastrointestinal and

	Compound	Effects	Reference
Leaves	Phenolic compounds, isoflavonoids, gallic acid, catechin, epicathechin, rutin, naringenin, kaempferol	Hepatoprotection, antioxidant, anti-inflammatory, anti-spasmodic, anti-cancer, antimicrobial, anti-hyperglycemic, analgesic	Ryu et al.[11]; Metwally et al.[13]; Roy et al.[34]; Ojewole [35]; Nair and Chanda [36]; Hui-Yin and Gowdhin [37]; Peng et al. [79]; Chen et al. [80]
Pulp	Ascorbic acid, carotecoids (lycopene, β-carotene, β-cryptoxanthin	Antioxidant, anti-hyperglycemic, Anti-neoplasic	Huang et al [14]; Bomtempo et al. [15]; Oliveira et al. [18]; Thuaitong and Anprung [30]
Seed	Glycosids; Carotenoids, phenolic compounds	Antimicrobial	Pelegrini et al. [12]; Castro-Vargas et al. [92]
Skin	Phenolic compounds	Endothelial progenitor cells and improvement of their intestinal absorption	Nascimento et al.[16]; Felice et al. [90]
Bark	Phenolic compounds	Strong antibacterial activity (against multi-drug-resistant *Vibrio cholera*); stomachache and diarrhea	Ryu et al. [11]; Rahin et al. [61]

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

anticarcinogenic activities probably due to the presence of phenolic glycosides in the composition [12,93].

Farinazzi et al. [33] showed that Wistar rats treated with guava seed had significantly lower glycemia, cholesterol and triglycerides levels and body weight. These animals significantly increased HDL-c levels.

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, seccoirridoids 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.

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