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Effect of guava leaves on hyperlipidemia patients

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Abstract
Psidium guajava (Guava leaf) is an important medicinal plant. Medicinal plants, also called medicinal herbs, have been discovered and used in traditional medicine practices since prehistoric times. Guava leaf contains phytochemical antioxidants such as lycopene stored in the edible portion of the fruit which is coloured pink. It also contains high levels of copper, vitamin C, iron, vitamin B3 (Niacin), B6 vitamin A, tannin, saponin, flavonoid, alkaloid, cardiac glycosides, flavonolmorin, morin-3-O-lyxoside, morin-3-Oarabinoside, and quercetin-3-O-arabinoside phenol and carbohydrates and dietary fiber. The cardiovascular diseases (CVD) are showing increasing trend particularly in developing countries. Hyperlipidemia, a broad term, also called hyperlipoproteinemia or lipemia is the term used to denote raised serum levels of one or more of total cholesterol (TC), low-density lipoprotein cholesterol (LDLC), triglycerides (TG), or both TC and TG (combined hyperlipidemia). Guava leaves are compounds related to the decrease of HMG-CoA reductase activity in hepatic tissue and improve lipid profiles.

Keywords: *Psidium guajava*, hyperlipidemia, lipid, triglycerides

Introduction
Medicinal plants, also called medicinal herbs, have been discovered and used in traditional medicine practices since prehistoric times. Plants synthesise hundreds of chemical compounds for functions including defence against insects, fungi, diseases, and herbivorous mammals. Numerous phytochemicals with potential or established biological activity have been identified. However, since a single plant contain widely diverse phytochemical, the effects of using a whole plant as medicine are uncertain.

Psidium guajava L. known as Guava is a medicinal plant belonging to the family Myrtaceae. *P. guajava* is a well-known traditional medicinal plant used in various indigenous systems of medicine. Guava leaf (*Psidium guajava*) prevents formation of sugars from complex carbohydrates that could cause excess weight gain. This property could make the intestine more alkaline. Guava leaf also has hypoglycemic property. Guava leaf contains phytochemical antioxidants such as lycopene stored in the edible portion of the fruit which is coloured pink. It also contains high levels of copper, vitamin C, iron, vitamin B3 (niacin), B6 vitamin A, tannin, saponin, flavonoid, alkaloid, cardiac glycosides, flavonolmorin, morin-3-O-lyxoside, morin-3-Oarabinoside, and quercetin-3-O-arabinoside phenol and carbohydrates and dietary fiber (Olaniyan, 2017) [19].

Hyperlipidemia is considered one of the major risk factors causing cardiovascular diseases (CVDs). CVDs accounts for one third of total deaths around the world, it is believed that CVDs will turn out to be the main cause of death and disability worldwide by the year 2020.

Hyperlipidemia, a broad term, also called hyperlipoproteinemia or lipemia is the term used to denote raised serum levels of one or more of total cholesterol (TC), low-density lipoprotein cholesterol (LDLC), triglycerides (TG), or both TC and TG (combined hyperlipidemia). Dyslipidemia is a broader term that also includes low levels of high-density lipoprotein cholesterol (HDL-C). Hyperlipidemia can also be defined as concentration of lipid in the blood of a fasted (>12 h) patient that exceeds the upper range of normal for that species. These fats are important for our bodies to function but when they are high, they can cause heart disease and stroke.

Hyperlipidemia results from abnormalities in lipid metabolism or plasma lipid transport or a disorder in the synthesis and degradation of plasma lipoproteins. Common secondary causes of hypercholesterolemia are hypothyroidism, pregnancy and kidney failure while common secondary causes of hypertriglyceridemia are diabetes, excess alcohol intake, obesity and certain prescription medications. Nevertheless, there is also a genetic predisposition to hyperlipidemia i.e. it can be hereditary. One has a greater chance of developing hyperlipidemia

if age is > 45 years in males and > 55 years in females, which in addition comes with its complications. The consequence of hyperlipidemia is that with time it can cause atherosclerosis, and thus the risk of coronary artery disease (CAD) and stroke is increased. Hyperlipidemia in general has no apparent symptoms but it can be discovered and diagnosed during routine examination or evaluation for atherosclerotic cardiovascular disease (Kingsley *et al.*, 2017) [12].

Chemical components of *Psidium Guajava*

Chemical components of fruit

Psidium guajava is an important medicinal plant. Its fruits show the presence of moisture (77-86%), crude fiber (2.8-5.5%), protein (0.9-1.0%), fat (0.1-0.5%), ash (0.43-0.7%), carbohydrates (9.5-10%), minerals and vitamins. The composition of guava varies significantly with variety, stage of maturity, and season. A water-soluble polysaccharide was isolated from hot aqueous extracts of fruits of *Psidium guajava*. The polysaccharide was found to contain 2-O-methyl-L-arabinose, 2-O-acetyl-D-galactose, and D-methyl galacturonate in a molar ratio of approximately 1:1:1 (Mandal *et al.,* 2009) [15].

Chemical components of seed

The percentages of the insoluble residue were appropriately 89 g/100g. Glutelin is the major protein fraction from guava seed (Fontanari *et al.,* 2008) [6]. The crude oil extracted from guava seeds showed high levels of unsaturated fatty acids (88.1%), mainly linoleic acid (78.4%). The tocopherol and total phenolic contents in the oil amounted to 29.2 and 92.3 mg/100 g, respectively (Malacrida *et al*., 2013) [14].

Chemical components of leaves

The budding leaves of *Psidium guajava* contained huge amounts of soluble polyphenolics including (in mg/g) gallic acid (348), catechin (102), epicatechin (60), rutin (100), quercetin (102), and rutin (100) (Chen *et al.,* 2009) [3].

Bioactivities of *Psidium Guajava*

Antioxidant and free radical scavenging activities

Antioxidants are substances that can prevent or delay oxidative damage of lipids, proteins and nucleic acids by reactive oxygen species, which include reactive free radicals such as superoxide, hydroxyl, peroxyl, alkoxyl and non-radicals such as hydrogen peroxide and hypochlorous. They scavenge radicals by inhibiting initiation and breaking chain propagation or suppressing formation of free radicals by binding to the metal ions, reducing hydrogen peroxide, and quenching superoxide and singlet oxygen (Lim *et al*., 2007) [13].

Antibacterial activity

Four antibacterial flavonoids (morin-3-O-lyxoside, morin-3-O-arabinoside, quercetin, and quercetin-3-O-arabinoside) were isolated from *Psidium guajava* leaves (Rattana and Phumk, 2010). In addition, the extract from leaves of *Psidium guajava* showed higher antimicrobial activity against Gram-positive bacterial and fungal strains (Nair *et al.,* 2007) [17].

Anti-diarrhoeal activity

The extracts of *Psidium guajava* leaf were tested against diarrhea-causing bacteria: *Staphylococcus aureus*, *Salmonella* spp. and *Echerichia coli*. The methanol extract showed the greatest bacterial inhibition. *Staphylococcus aureus* strains were most inhibited by the extracts. Guava leaf extracts and essential oil are very active against *S. aureus*.

Antihyperglycemic and antidiabetes effects

Hyperglycemia causes increased protein glycation and the formation of early glycation products and advanced glycation end products (AGEs) which are major factors responsible for the complications associated with diabetes.

The tannins, polyphenolic compounds, flavonoids, pentacyclic triterpenoids, guiajaverin, quercetin etc. were speculated to account for the observed hypoglycemic effects of the plant's leaf extract (Ojewole, 2005) [18].

Water-soluble solids showed higher superoxide dismutase-like activity and lipid peroxidation inhibition ability than ethanol-soluble solids *in vitro*, suggesting that anti-peroxidation of lipids is a possible mechanism for guava leaves to retard the progress of type 2 diabetes (Chuang *et al.,* 2008) [5].

Anti-inflammatory activity

Psidium guajava leaf extracts can inhibit the main developer of acne lesions: Propionibacterium acnes (P. acnes). It may be beneficial in treating acne especially when they are known to have anti-inflammatory activities (Qa'dan *et al.,* 2005) [20].

Anticancer activity

The aqueous extract of *Psidium guajava* leaves (PE) bears an extremely high content of polyphenolic and isoflavonoids, it could be used as an anti-tumor chemoprevention in view of anti-angiogenesis and anti-migration. By the means of morphology of cells, cell cycle characteristics and apoptosis and performed immunostaining, differentiation and western blot analyses, the results showed that the *Psidium guajava* extract exerted anti-cancer control on both haematological and solid neoplasias. Guava extract's antitumour properties were found to be tightly bound to induction of apoptosis and differentiation.

Medical attributes 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.

Ojewole 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.* 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 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.

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.

Chen *et al.* 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*. 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.

Effect of guava leaves on health problems

Jiménez-Escrig *et al.,* Wang *et al*. and Haida *et al*., 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.

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.

Ghosh *et al*. 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 disease, obesity and atherosclerosis.

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.

Akinmoladun *et al.* 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.

Conclusion

Many researchers have been demonstrating the presence of a wide variety of bioactive compounds in the leaves of *Psidium guajava* that are capable of showing beneficial effects on human health. Hyperlipidemia is considered one of the major risk factors causing cardiovascular diseases (CVDs). The studies indicate that guava leaves are effective in preventing lower the lipid profile levels and consequently preventing atherosclerosis and its associated coronary heart disease.

The studies using *Psidium 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.

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