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Benefits of guava leaves: A comprehensive review

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Abstract
One of the most significant food crops and medicinal plants in tropical and subtropical regions is *Psidium guajava*. The tree, which is a member of the Myrtaceae family, is primarily grown in tropical and subtropical nations. Because of its rich nutritional and botanical compounds profile, pharmacological research has demonstrated that this plant is not only a fruit source but also has beneficial benefits against a range of chronic conditions. The leaves of the guava plant (*Psidium guajava*) are nutrient-rich and a valuable addition to food. It is packed with macro and micronutrients that have a variety of therapeutic benefits, including the ability to treat diabetes, heart disease, cancer, diarrhoea, anaemia, and digestive issues. The pharmacological properties of guava leaves are widely documented; these properties include antibacterial, anti-inflammatory, organo-protective, wound-healing, and anti-diabetic properties. Guava leaves have not been shown to interact in any harmful, mutagenic, or aberrant ways. In order to direct future research toward identifying specific bioactive components, the current review's objective was to gather findings from *in vitro* and *in vivo* investigations conducted using guava leaves over the past ten years and relate the outcomes to their therapeutic uses. Researchers' ongoing efforts are revealing new medical properties linked to *Psidium guajava*, which expands our knowledge of its possible advantages.

Keywords: Antimicrobial, anti-diabetic, antioxidant, myrtaceae family, organo-protective

Introduction
The guava (*Psidium guajava*), a member of the Myrtaceae family, is a tropical and subtropical plant that grows around the world. It can withstand a variety of climates, though it thrives in dry climes (Stone BC *et al*., 1970) [1]. Quercetin is the most powerful antioxidant present in guava leaves (Naseer S. *et al*., 2018; Nantitanon w. *et al*., 2010) [2, 3]. Antibacterial, antifungal, antidiarrheal, antiplasmodial, anti-cough, anti-inflammatory, antipyretic, analgesic, immunomodulatory, spasmolytic, ulcer protective, nephroprotective, hepatoprotective, and hypoglycemic qualities have all been discovered in the organic and aqueous extracts of guava leaves (Daswani PG *et al*., 2017) [4]. Guava leaves are less expensive, have a higher polyphenol content than guava fruit, and are effective at scavenging harmful free radicals (Tran T.T.T. *et al*., 2020) [5]. The tropical fruit and medicinal herb known as guava (*Psidium guajava* L.) is primarily found in tropical and subtropical regions. A natural remedy for gastrointestinal and respiratory disorders is guava leaf extract (GE) (Morais-Braga MFB *et al*., 2016) [6].

Nutritional composition of guava leaves
Benefits of guava leaves
Antidabetic activity of guava leaves
Persistent hyperglycemia resulting from impaired insulin synthesis by pancreatic β-cells and/or peripheral insulin resistance characterizes diabetes mellitus (DM), the most prevalent progressive disease (Oliveira H.C. *et al*., 2008) [9]. Originally from Mexico, the guava tree (*P. guajava* L.) can flourish in both tropical and subtropical climates. In addition to its ability to prevent diabetes, various parts of this crop have demonstrated anti-diabetic properties *in vitro* and *in vivo* against a variety of diseases, including dysentery and diarrhea. These properties have been attributed primarily to the crop's phenolic composition, which is higher in the leaves than in the remainder of the tree (Gutiérrez R.M.P. *et al*., 2008) [10].

The antibacterial, antiviral, anti-inflammatory, and antidiabetic properties of guava leaves are also widely recognized (Shaheena S. *et al*., 2019; Nguyen QV *et al*., 2018) [11, 12].

Table 1: Nutritional profile of guava leaves

Compounds	Content/Composition	References
Elements and ascorbic acid		[Dutta *et al*., 2014] [7]
Potassium	1.11%	
Phosphorus	0.23%	
Nitrogen	1.02%	
Ascorbic acid	142.55 mg/100 g	
Carbohydrates/phenols/sulfates		[Kim *et al*., 2016] [8]
Fucose	1.44%	
Rhamnose	3.88%	
Arabinose	22.6%	
Galactose	29.41%	
Glucose	33.79%	
Mannose	0.59%	
Xylose	7.71%	
Phenol	15.28%	
Sulfate	18.58%	
Carbohydrate	48.13%	
Sulfate polysaccharide	66.71%	
Protein		

Tannins, polyphenolic chemicals, flavonoids, pentacyclic triterpenoids, quercetin, guiajaverin, and other chemical components are present in GL extracts and may be able to control hyperglycemia (Ojewole JAO. *Et al*., 2005) [13]. According to earlier research, guava leaf fruit has anti-oxidative and anti-hyperglycemic effects on diabetic rats produced by streptozotocin (STZ) (H. Chin-Shiu *et al*., 2011) [14]. Additionally, it has been shown that in diabetic rats, both ethanolic and aqueous extracts of leaves of guava reduce blood glucose, boost the production of glycogen, and alter the activities of enzymes that metabolize glucose (S.C. Shen *et al*., 2008) [15].

Antibacterial activity of guava leaves

A phytochemical examination of guava leaves revealed that while alkaloids, saponins, and triterpenes are found in relatively less quantities in guava leaf extract, guava leaves are exceptionally high in flavonoids, phenols, and tannins. It is commonly recognized that polyphenolic compounds have strong antibacterial action in addition to their effective anti-inflammatory, free radical-scavenging, antioxidant, and anti-carcinogenic qualities (Xie Y *et al*., 2015) [17]. Significant antibacterial activity of guava has been demonstrated against yeast species like Candida species and microbes like Bacillus, *E. coli*, *Staphylococcus*, *Pseudomonas*, *Clostridium*, *Shigella*, and *Salmonella* (Fugaban HC. *Et al*., 2016) [18].

Alkaloids, flavonoids, tannins, saponins, glycosides, and terpenoids have also been shown to be present in *P. guajava* leaf extracts according to certain studies. Furthermore, it has been demonstrated that these phytochemicals exhibit inhibitory effect *in vitro* against a few clinical bacterial isolates (Cowen JM. *et al*., 1929; Poser CM *et al*., 1999) [19, 20]. Guava leaves and bark have been used to cure edema, toothaches, colds, diarrhea, and other gastrointestinal issues. Guava is used as an astringent for skin conditions like ringworm, rashes, and acne (Eghaeveda *et al*., 2010 [21] Many chemical components of *P. guajava* have been reported to have cytotoxic, antioxidant, antimicrobial, antidiarrheal, antimycobacterial, antihyperglycemic, and antimalarial properties (Roy CK *et al*., 2006) [22]. The *P. guajava* aqueous extract was found to have antibacterial action towards Salmonella typhi and Klebsiella pneumoniae in a recent study, however it had no impact on the spread of Escherichia coli, Staphylococcus aureus, or Streptococcus fecalis pathogens (Geidam YA *et al*., 2010) [23].

Wound Healing Properties of Guava Leaves

The process of healing a wound is intricate and involves numerous physiological processes (Burks RI. *Et al*., 1998) [24]. Wound healing is an essential biological phenomenon and an indication of growth. Wounds, whether new or old, can negatively impact a person's freedom, workability, self-worth, and general well-being (Rahman N *et al*., 2017) [25]. In many regions of the world, guava has been utilized medicinally as an antibacterial and anti-inflammatory. The leaves are used to treat rheumatic discomfort in joints, sores, and ulcers (Cheng L. *et al*., 2011) [26].

Using the excision wound model, the wound healing capabilities of a guava leaf extract in methanol were investigated. After 14 days following surgery, more than 90% of the wounds had healed, compared to 72% in the group that had received distilled water treatment (Chah *et al*., 2004) [27].

Anticancer activity of guava leaves

A number of terpenoid chemicals have recently been identified and analyzed from guava leaf extract. A number of the identified compounds exhibited antifungal and anticancer properties, including meroterpenoids (Qin *et al*., 2017; Liu *et al*., 2021) [28, 29]. Dichloromethane and ethanolic crude extracts of *P. guajava* leaves, as well as their fractions, were employed in an *in vitro* and *in vivo* anticancer study on nine cancer cell lines: NCI-H460 lung cancer, MCF-7 breast cancer, HT-29 colon cancer, PC-3 prostate cancer, K562 leukemia, 786-0 kidney cancer, OVCAR-3 ovarian cancer, NCI/ADR-RES resistant ovarian cancer, and UACC-62 melanoma cell lines (Rizzo *et al*., 2014) [30]. Ascorbic acid (Vitamin C), lycopene, and flavonoids (Apigenin) are the three guava components that have been most commonly linked to *in vitro* anticancer effects (Sato R *et al*., 2010) [31]. Given its exceptionally high polyphenolic and isoflavonoid content, the aqueous extract of *Psidium guajava* leaves (AEG) may have applications in anti-tumor chemoprevention due to its anti-angiogenesis and anti-migration properties (Bontempo *et al*., 2012) [32].

Spermatic protective activity of guava leaves

According to experimental research, rats given *Psidium guajava* leaf extracts had higher concentrations of epididymal sperm, testes and epididymis weight, mobility, and reproductive hormones (FSH, LH, and TSH) (Uboh FE *et al*., 2010a; Uboh FE 2010b; Ekaluo UB *et al*., 2013a; Ekaluo UB *et al*., 2013b) [33, 34, 35, 36]. *Psidium guajava* Linn. leaf extracts have positive effects on sperm production and quality, which may help infertile guys with oligospermia and nonobstructive azoospermia improve their sperm parameters (Akinola OB *et al*., 2007) [37].

Antioxidant activity of guava leaves

The body uses free radicals to suppress germs and viruses and to control the growth of cells (Chen *et al*., 2016) [38]. However, too many free radicals can lead to aging, cancer,

and arteriosclerosis, among other chronic human disorders (Pahlavani *et al*., 1998) [39]. Fresh guava leaves have a total antioxidant capacity of 71.16% RSA (Chan *et al*., 2012) [40]. The antioxidant functions of GLs are caused by the presence of phenolic chemicals, including ferulic acid, gallic acid, pyrocatechol, taxifolin, ellagic acid, and several others (Chen *et al*., 2007; Farag *et al*., 2020) [41, 42]. Antioxidants are generally defined as chemicals that, when compared to oxidizable substrate, are present in low concentrations but considerably slow down or inhibit the substrate's oxidation. Lipoxygenase inhibition and lipid peroxidation have drawn attention to phenolic substances (Stahl *et al*., 1997) [43].

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