

Psidium guajava: A review on its potential as an adjunct in treating periodontal disease

K. Ravi, P. Divyashree

Department of Periodontics, MES Dental College and Hospital, Palachode P.O., Kolathur Via, Malaparamba, Perintalmanna, Malappuram, Kerala, India

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ABSTRACT

Plants for thousands of years have been used to enhance health and for medicinal purposes. *Psidium guajava* is one which has an enormous wealth of medicinal value. It for long has been known for its anti-inflammatory, antimicrobial, antioxidant, antidiarrheal, antimutagenic properties. Despite of its widespread biologic uses there is a dearth of information on its therapeutic effect in the treatment of periodontal disease. Hence, this review is an attempt to highlight the potential of *P. guajava* in the treatment of periodontal disease. Internet databases PubMed, Google Scholar were searched and the most relevant articles were considered for review.

Key words: Antiplaque, gingivitis, guaijaverin, periodontitis, *Psidium guajava*, quercetin

INTRODUCTION

Periodontal disease has been recognized as a major health problem worldwide. Periodontal diseases are infectious diseases caused by bacteria present in dental plaque^[1] and a direct relationship exists between the presence of dental plaque and development of gingivitis.^[2] Gingivitis is a chronic inflammatory process confined to the gingiva.^[3] Periodontitis is a complex disease in which disease expression involves intricate interactions of the biofilm with the host inflammatory response and subsequent alterations in bone and connective tissue metabolism.^[4] The goal of periodontal treatment is to cure the inflamed tissues, reduce the number of periodontal pathogens and alter the host response.^[5] Mechanical debridement, use of chemotherapeutic agents are some of the clinical methods employed to treat periodontal disease. The major disadvantage of these chemotherapeutic agents is the toxicity and development of bacterial resistance.^[5] In an attempt to overcome the limitations of mechanical debridement and adverse effects

of chemotherapeutic agents the search for newer and safer chemotherapeutic agents still continues. Natural phytochemicals isolated from plants are considered good alternatives to synthetic chemicals.

In the recent years, the use of plant extracts as well as other forms of medical treatments have resurfaced and gained popularity.^[6] Various natural products such as *Curcuma zedoaria*, calendula, *Aloe vera* and other herbs have been used effectively to treat oral diseases in Ayurveda^[3] and in the form of mouthwashes and toothpastes to treat periodontal disease.^[7] *A. vera*, star anise oil, myrrh gum, calendula extract, fennel oil, tea tree oil, neem extract are few natural products used to control periodontal disease.^[8] *Psidium guajava* is one such plant that has been used to manage various systemic conditions, enhance oral hygiene and consists of bioactive substances.^[9,10]

Internet database PubMed and Google Scholar were searched for *P. guajava* and periodontitis, gingivitis, periodontal pathogens, antiplaque, oral health. The back references of these articles were hand searched for any suitable articles. Only highly relevant articles were considered for the present review article.

Address for correspondence:

Dr. P. Divyashree, Department of Periodontics, MES Dental College and Hospital, Palachode P.O., Kolathur Via, Malaparamba, Perintalmanna, Malappuram District - 679 338, Kerala, India. E-mail: divya_prasad44@yahoo.com

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Description

Common names of *P. guajava* are guava, guayaba, goiaba, perala, pichi, posh, enand.^[11] It is found in Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, Subclass: Rosidae, Order: Myrtales, Family: Myrtaceae, Subfamily: Myrtoideae, Genus: *Psidium* and species: *guajava*, Binomial name: *P. guajava*.^[9,12,13] It is a small tree which grows up to 20 feet in height. Leaves are opposite, oblong, three to seven inches in length, with prominent veins below. Flowers are of white color and about one inch in

diameter. Fruits of *P. guajava* (hereafter referred to as guava) are round ovoid to pear shape. It is thin shelled with many seeds embedded in a firm pulp or thick shelled with few seeds.^[14]

Phytochemistry and functional components

The important constituents of guava are vitamins, tannins, phenolic compounds, flavonoids, essential oils, sesquiterpene alcohols and triterpenoid acids.^[15] Leaves contain phenolic compounds, isoflavonoids, gallic acid, catechin, epicatechin, rutin, naringenin, kaempferol having hepatoprotective, antioxidant, anti-inflammatory, antispasmodic, anticancer, antimicrobial, anti-hyperglycemic, analgesic actions.^[15] The leaf contain two important flavonoids quercetin known for its spasmolytic, antioxidant, antimicrobial, anti-inflammatory actions^[9,14] and guaijaverin known for its antibacterial action.^[16] Pulp contains ascorbic acid, carotenoids (lycopenes, β -carotene) possessing antioxidant, anti-hyperglycemic, antineoplastic.^[15] The seed contains glycosides, carotenoids, phenolic compounds having antimicrobial actions.^[15]

General uses

Guava is proven for its antidiarrheal, antimicrobial, antiparasitic, antitussive, hepatoprotective, antioxidant, antigenotoxic, antimutagenic, antiallergic, anticancer and anti-hyperglycemic effects.^[13] Acclaimed as the “poor man’s apple of the tropic”^[17] guava has been used for various purposes in different regions of the world. It has been used in the treatment of diarrhea, dysentery, menstrual disorders, vertigo, anorexia, digestive problems, gastric insufficiency, inflamed mucous membrane, laryngitis, skin problems, ulcers, vaginal discharge, cold, cough, cerebral ailments, nephritis, jaundice, diabetes, malaria and rheumatism to mention a few.^[11,18]

THERAPEUTIC APPLICATIONS IN TREATING PERIODONTAL DISEASE

Dental plaque is a prerequisite for periodontal disease. Damage to the periodontium occurs due to direct pathologic effects of bacteria on the periodontal tissues and other indirect means.^[19] Bacterial lipopolysaccharides are known to stimulate the production of both catabolic cytokines and inflammatory mediators including arachidonic acid metabolites such as prostaglandin E₂ (PGE₂), interleukin-1 (IL-1), interleukin-6 (IL-6), TNF- α (tumour necrosis factor- α). These cytokines and inflammatory mediators stimulate the release of tissue-derived enzymes, the matrix metalloproteinases, which are destructive to the extracellular matrix and bone.^[19]

Reactive oxygen species have also been considered as key factor in the pathogenesis of periodontitis. Oxidative stress can lead to direct tissue damage. In addition to direct tissue damage, oxidative stress is a key component of hyperinflammation in periodontitis. It is known to activate key nuclear transcription factors, such as receptor activator of nuclear factor kappa β (NF- κ B) and activated protein-1 (AP-1) which further can

induce gene transcription for key proinflammatory mediators and osteoclastogenesis stimulation.^[19] Thus, periodontitis has a multifactorial etiology.

Guava as an antiplaque agent

Dental plaque is the principal etiologic factor in periodontal disease. Plaque if allowed to accumulate, with no intervention or oral hygiene methods, leads to gingivitis which further progresses to periodontitis.^[20] Effective plaque control strategies to prevent or limit bacterial adhesion and further growth on the tooth surface are essential to prevent and control periodontal disease.^[21] The paste of tender leaves of guava has been traditionally used to maintain oral hygiene.^[22] Guava has shown antibacterial activity against both Gram-positive and Gram-negative bacteria.^[23-25] The antimicrobial activity of guava is mainly attributed to flavonoids, guaijaverin and quercetin.^[22,26-28] The bark has exhibited antibacterial properties due to the presence of tannins.^[29]

Quercetin has shown excellent antibacterial actions against periodontal pathogens *Aggregatibacter actinomycetemcomitans* (*Aa*), *Porphyromonas gingivalis* (*Pg*), *Prevotella intermedia* (*Pi*), *Fusobacterium nucleatum* (*Fn*).^[30,31] It has shown inhibitory actions against *Streptococcus mutans* (*S. mutans*), *Streptococcus sanguinis* (*S. sanguinis*) and *Actinomyces* species.^[30] The antibacterial action of quercetin is probably due to the disruption of membrane and inactivation of extracellular proteins by forming irreversible complexes.^[30] Guaijaverin from leaves of guava has potential as an antiplaque agent due to its bacteriostatic property by inhibiting the growth of *S. mutans* and *Staphylococcus aureus* (*S. aureus*).^[22,32-34] Guaijaverin decreases the hydrophobicity, one of the most important initial factors for the oral pathogenic bacteria to adhere to the tooth surface.^[22] This action is possibly because guava extracts binds to the cell surface proteins reducing the overall cell hydrophobicity and hence guava may have potential for development as a natural antiplaque agent.^[22] Guava and *Piper betle* extracts have shown bacteriostatic effect on the primary colonizers of teeth during plaque formation *S. sanguinis*, *Streptococcus mitis* (*S. mitis*) and *Actinomyces*.^[21,35] *S. mitis* and *S. sanguinis* showed lesser adherence to the experimental pellicle treated with guava extracts when compared with untreated pellicle due to the ability of guava to disrupt the pellicle preventing adherence of bacteria.^[36]

Mouthwash containing aqueous extract of the leaves was highly active against *S. aureus* and *Escherichia coli* (*E. coli*) which could be contributed to the presence of bioactive compounds.^[10] Mouthrinse containing guava leaf extract had a profound effect on gingivitis.^[37] The aqueous extracts of *P. betle* and guava were found to have antiplaque activity by their effect on ultrastructure of plaque bacteria by interfering with normal growth cycle and development,^[38] reducing the adhering capacity of the acquired pellicle which forms on the surface of tooth during early plaque formation, diminishing the cell surface hydrophobicity of bacteria which are required to assist the adherence process.^[39,40] The cytotoxic property of guava would be of added value for the use of guava as adjuncts in the development of oral health care products.^[41] Guava extract has demonstrated *in vitro* antiplaque

actions by inhibiting growth, adherence and co-aggregation of dental plaque bacteria. Guava extracts may inhibit plaque development without disrupting homeostasis of the oral cavity.^[42] Thus, guava an excellent antibacterial and antiplaque agent may be a good adjunct to the mainstream periodontal treatment.

Guava as an anti-inflammatory agent

Guava has been known for its anti-inflammatory action.^[25,43] The anti-inflammatory action of guava is in its ability to inhibit prostaglandin, kinin and histamine.^[44] *Aa* is an important periodontal pathogen and is associated with aggressive periodontitis. Guava extract completely neutralized the cytolytic, proinflammatory response of human leukocytes induced by *Aa* leukotoxin and prevented the release and activation of Interleukin-1 β (IL-1 β).^[45] C-reactive protein (CRP) is a positive acute phase protein^[46] whose elevated levels have been demonstrated in periodontitis patients.^[47] Guava leaf and stem extracts possess anti-inflammatory effects by decreasing CRP levels which plays a role as modulator of inflammatory response.^[46] Guava has also been proven for its immunomodulatory activity on NF-k β .^[48] Fermented guava leaf extract is involved in the inhibition of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2). It also inhibited lipopolysaccharide induced NF-k β activation.^[49] Blocking NF-k β is a potential strategy for preventing inflammatory bone resorption in treating periodontal disease.^[50] Guava due to its anti-inflammatory action, ability to inhibit iNOS, COX-2, NF-k β could be a valuable agent in treating periodontal disease.

Guava as an antioxidant agent

Excessive free radical generation by neutrophils can be stimulated by bacteria associated with periodontal disease leading to damage of tissues.^[51] The disequilibrium between oxidative stress and antioxidant activity will lead to periodontal tissue destruction.^[52] Decreased antioxidant activities of crevicular fluid and saliva are associated with development of periodontal disease.^[53-55] Periodontitis patients may be predisposed to oxidative stress by possessing reduced glutathione (GSH) buffering capacity, that may be protected by improving overall antioxidant micronutrient intake like vitamin C.^[56] Antioxidant rich diets are said to inhibit periodontal disease and progression.^[57-60] Antioxidant micronutrients are important not only for limiting oxidative and tissue damage but also in preventing increased cytokine production.^[61] Guava is an excellent antioxidant and a good source of vitamin C. Guava leaf extracts and essential oil from the stem, bark have the ability to scavenge free hydrogen peroxide, superoxide anion radical and inhibit the formation of hydroxyl radical.^[62-65] The antioxidant action can be attributed to quercetin, carotenoids, vitamin C, polyphenols present in guava.^[57,66,67] Thus, guava could satisfy as an antioxidant based approach to periodontal therapy.

Guava as a wound healer

The gingival, periodontal ligament fibers are composed of collagen. Fibroblasts are the principal cell type present in the connective tissue of periodontium. Vitamin C is essential to

maintain the overall integrity of the periodontium. Guava contains high levels of vitamin C (ascorbic acid).^[68] Ascorbic acid can modulate the expression of procollagen gene leading to collagen formation, altering the fibroblast differentiation through its effects on extracellular matrix.^[69] Vitamin C supports immune functions, maintains structural and functional integrity of epithelial tissues and physiological or metabolic parameters relevant to periodontal health.^[70] Vitamin C along with bioflavonoids speed up the healing process.^[5] The decoction of root bark is recommended as a mouthwash for swollen gums and decoction of leaves as an effective gargle for swollen, bleeding gums.^[16] Guava extracts may contribute toward hastening the tissue healing process.^[71]

Safety

Guava has been used for centuries in the folklore medicine without any adverse effects. Toxicity is usually seen when phytochemicals are ingested in excessive amounts. However, treatment of gingival and periodontal disease would not require such toxic levels.^[72] There is limited information available about the quality, safety and efficacy of herbal products used in dentistry. A possibility exists for adverse interactions between phytochemicals and conventional drugs, hence caution should be exercised when using them.^[73]

CONCLUSION

This review attempts to shed light on the therapeutic potential of guava as an adjunct in treating periodontal disease. As an excellent antiplaque, antimicrobial, anti-inflammatory, antioxidant agent guava hopefully will be considered in the future for more clinical evaluations and possible applications as an adjunct to conventional periodontal therapy. Nevertheless, we should emphasize the importance of experimental and clinical studies with emphasis on bioavailability of compounds, effective and safe doses to be used. Our efforts in exploring and valuing newer phytotherapeutics in the treatment of periodontal disease should be maintained.

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