



## **PSIDIUM GUAJAVA – A SCIENTIFIC REVIEW FOR ITS ANTI-OXIDATIVE AND ANTI-INFLAMMATORY POTENTIAL IN THE MANAGEMENT OF PERIODONTAL DISEASES**

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### **ABSTRACT:**

Guava could be used as a potential therapeutic agent for management of periodontal diseases such as gingivitis and periodontitis due to its noteworthy activity against periodontal pathogens.

The bioactive phenolic compounds have a potent anti-inflammatory, anti-microbial and antioxidant activity thus making it a much sought after phytotherapeutic agent in the future clinical evaluations.

### **KEYWORDS:**

PSIDIUM GUAJAVA, GINGIVITIS, ANTI-OXIDANT.

Presence of periodontopathogens in close vicinity of the supporting structures of teeth is a major contributing factor to development of chronic inflammatory diseases. A pathogenic shift in subgingival biofilm seen in Chronic Periodontitis is partly controlled by the constant influx of neutrophils in the gingival crevicular zone. This in turn initiates a cascade of pro-inflammatory cytokines. Periodontitis which if left untreated ultimately results in tooth loss (1,2).

The mainstay of Periodontal therapeutics nonsurgical and surgical intervention. The varied antimicrobials agents employed include chlorhexidine, triclosan and cetylpyridinium chloride in the management of periodontal diseases.

Due to the multifactorial etiology and ensuing complex disease process, the treatment of periodontitis has been hypothesized to benefit from herbal remedies due to their potential to reduce bone loss due to their purported anti-collagenase, antioxidant, antimicrobial, anti-inflammatory and antiseptic effects.

Antioxidant capacity in patients of periodontitis is significantly lower as compared to healthy controls. These findings have paved the way for employing exogenous supplements in the treatment of periodontal diseases. The consumption of vegetables and fruits is considered beneficial to multiple health outcomes. Natural supplements and functional foods are a unique alternative to traditional drug therapies. Investigation into phytochemicals for improvement of periodontal health is necessary as there are still mixed results.

This review aims to give an overview of the botanical *Psidium guajava* used in the management of periodontal disease.

*Psidium guajava* commonly called guava enhances oral hygiene and its bioactive substance content with possible antiresorptive effects, may be used to combat periodontal disease.

### **BIOACTIVES FOUND IN GUAVA**

Vitamins, tannins, flavonoids, essential oils, phenolic compounds, sesquiterpene alcohols and triterpenoid acids.(3) The leaf contain two important flavonoids and quercetin known for its spasmolytic, antioxidant, antimicrobial, anti-inflammatory actions. Guajaverin; has been touted for its antibacterial action.(4)

The polyphenolics in guava convey strong antioxidant properties quercetin has displayed significant antimicrobial and anti-inflammatory actions while guajaverin or its antibacterial action.

The fruit pulp contains ascorbic acid, carotenoids (lycopenes,  $\beta$ -carotene)] The seed contains carotenoids, glycosides and phenolic compounds having antimicrobial actions.

A high content of catechin, epicatechin, gallic acid and rutin is present in guava

Quercetin is a strong antioxidant, as it has been shown to protect osteoblasts from hydrogen peroxide-induced cell death. Rutin is of interest and has been shown to decrease bone loss (5).

### **ETIOPATHOGENESIS OF PERIODONTAL DISEASE**

Periodontal diseases are inflammatory in nature and are regulated partly by oxidative states in the tissues surrounding the teeth. In most cases, chronic periodontitis, the most prevalent form of periodontal disease, is an inflammatory condition initiated by the subgingival

biofilm, resulting in a local immune response and host-mediated tissue destruction. Lipopolysaccharides present in the gram negative bacteria are known to stimulate inflammatory mediators and catabolic cytokines such as arachidonic acid metabolites like prostaglandin E2 (PGE2), interleukins such as interleukin-1: IL-1, interleukin-6: IL-6 and tumour necrosis factor- $\alpha$ :TNF- $\alpha$ . These in turn release tissue-derived enzymes, destructive to the extracellular matrix and bone; namely the matrix metalloproteinases.

Another key factor in the pathogenesis of periodontitis are the reactive oxygen species and oxidative stress can lead to direct tissue damage. In addition to this, oxidative stress is also a key component in hyperinflammation of periodontitis. It is known to activate key nuclear transcription factors, such as receptor activator of nuclear factor kappa  $\beta$  (RANKF- $\kappa\beta$ ) which further induce gene transcription for proinflammatory mediators and osteoclastogenesis.(6)

### GUAVA'S ROLE AS AN ANTIOXIDANT AGENT

Antioxidant rich diets are said to inhibit periodontal disease and progression.(7,8,9,10) Antioxidant micronutrients are important not only for limiting oxidative and tissue damage but also in preventing increased cytokine production.

Excessive free radical generation by neutrophils may be reduced by improving antioxidant micronutrient intake such as VITAMIN C.(8) Guava is an excellent antioxidant and a good source of VITAMIN C. The antioxidant action is attributable to VITAMIN C, polyphenols quercetin, carotenoids, present in guava.(7) Thus, guava could satisfy as an antioxidant based approach to periodontal therapy.(11,12)

### GUAVA'S ROLE AS AN ANTI-INFLAMMATORY AGENT

The anti-inflammatory action of guava is attributable to its property of inhibition of kinins, histamine and prostaglandin.(13) In an experimental study it was observed that *Aggregatibacter actinomycetemcomitans*, an important periodontal pathogen associated with aggressive periodontitis releases Aa leukotoxin which was completely inhibited by guava extract.(14) Guava stem and leaf extracts possess anti-inflammatory effects by decreasing C-Reactive Protein levels which play a key role as a modulator of inflammatory response.(15) Guava leaf extract has been used for inhibition of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2).(16) Ability to Inhibition iNOS, COX-2, NF- $\kappa\beta$  could be a valuable agent in treating periodontal disease thereby underlining the role of guava extract as a potent anti-inflammatory agent.(17,18)

### GUAVA'S ROLE AS AN ANTIPLAQUE AND ANTIMICROBIAL AGENT

The antimicrobial activity of guava is mainly attributed to quercetin, flavonoids and guaijaverin.(19) The presence of tannins present in bark has exhibited antibacterial

properties.(20,21,22)

Quercetin has shown excellent antibacterial actions against periodontal pathogens such as *Porphyromonas gingivalis*, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Aggregatibacter actinomycetemcomitans* (23,24).

Anti-plaque activity by guava extract has been demonstrated in vitro, as it inhibits growth, co-aggregation and adherence of bacteria present in dental plaque. These extracts inhibit plaque development however homeostasis of the oral cavity is undisrupted.(25,26,27,28)

### CONCLUSION

Unabated dental plaque accumulation is a major contributing factor to development and progression of periodontal disease. The inflammatory cascade leads to destruction of periodontal apparatus and a de-synchronized bone remodeling with formation lagging behind resorption, resulting in net bone loss. Various botanicals such as guava have been employed for their ability to reduce plaque accumulation due to antimicrobial effect and anti-inflammatory role leading to arrest of bone loss.

Future Direction: Further research is mandatory with larger sample size, longer duration of follow up along with biochemical assay and microbiological assay are mandated so as to prove the efficacy of guava as an adjunctive pharmacotherapeutic to mainstay periodontal therapy.

### REFERENCES

1. Raeste AM, Tapanila T, Tupakka R. Leukocyte migration into the healthy dentulous mouth. A study in children, adolescents and adults. *J Periodontol Res* 1977;12:444-449.
2. Listgarten MA. Pathogenesis of periodontitis. *J Clin Periodontol*. 1986;13:418-30
3. Joseph B, Priya RM. Phytochemical and biopharmaceutical aspects of *Psidium guajava* (L.) essential oil: A review. *Res J Med Plant*. 2011;5:432-42.
4. Rishika D, Sharma R. An update of pharmacological activity of *Psidium guajava* in the management of various disorders. *Int J Pharm Sci Res*. 2012;3:3577-84.
5. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007 Natl Health Stat Report. 2008;12:12-23.
6. Chapple IL, Matthews JB. The role of reactive oxygen and antioxidant species in periodontal tissue destruction. *Periodontol* 2000 2007;43:160-232.
7. Battino M, Bullon P, Wilson M, Newman H.

Oxidative injury and inflammatory periodontal diseases: The challenge of anti-oxidants to free radicals and reactive oxygen species. *Crit Rev Oral Biol Med.* 1999;10:458-76.

8. Van der Velden U, Kuzmanova D, Chapple IL. Micronutritional approaches to periodontal therapy. *J Clin Periodontol.* 2011;38(Suppl 11):142-58.

9. Sculley DV, Langley-Evans SC. Salivary antioxidants and periodontal disease status. *Proc Nutr Soc.* 2002;61:137-43. [PubMed] [Google Scholar]

10. Ritchie CS, Kinane DF. Nutrition, inflammation, and periodontal disease. *Nutrition.* 2003;19:475-6. [PubMed] [Google Scholar]

11. Figuero E, Soory M, Cerero R, Bascones A. Oxidant/antioxidant interactions of nicotine, coenzyme Q10, pycnogenol and phytoestrogens in oral periosteal fibroblasts and MG63 osteoblasts. *Steroids.* 2006;71:1062-72. [PubMed] [Google Scholar]

12. Carnelio S, Khan SA, Rodrigues G. Definite, probable or dubious: Antioxidants trilogy in clinical dentistry. *Br Dent J.* 2008;204:29-32.

13. Kavimani S, Ilango R, Vertichelvan T. Anti-inflammatory activity of volatile oil of *Psidium guajava*. *Anc Sci Life.* 1998;17:300-4.

14. Kwamin F, Gref R, Haubek D, Johansson A. Interactions of extracts from selected chewing stick sources with *Aggregatibacter actinomycetemcomitans*. *BMC Res Notes.* 2012;5:203.

15. Joyce OO, Chinwe ND, Kwaku JP, Tabot PD. *Psidium guajava*'s effect on acute phase protein levels during acute inflammation. *Am J PharmTech Res.* 2012;2:424-33.

16. Yamazaki K, Honda T, Oda T, Ueki-Maruyama K, Nakajima T, Yoshie H, et al. Effect of periodontal treatment on the C-reactive protein and proinflammatory cytokine levels in Japanese periodontitis patients. *J Periodontal Res.* 2005;40:53-8.

17. Koide M, Kinugawa S, Takahashi N, Udagawa N. Osteoclastic bone resorption induced by innate immune responses. *Periodontol 2000.* 2010;54:235-46. [PubMed]

18. Kaileh M, Vanden Berghe W, Boone E, Essawi T, Haegeman G. Screening of indigenous Palestinian medicinal plants for potential anti-inflammatory and cytotoxic activity. *J Ethnopharmacol.* 2007 ; 113 : 510-6.

19. Fathilah AR, Sujata R, Norhanom AW, Adenan MI.

Antiproliferative activity of aqueous extract of *Piper betle* L. and *Psidium guajava* L. on KB and HeLa cell lines. *J Med Plant Res.* 2010;4:987-90. [Google Scholar]

20. John NR, Gala VC, Sawant CS. Inhibitory effects of plant extracts on multi-species dental biofilm formation in-vitro. *Int J Pharm Bio Sci.* 2013;4:487-95.

21. Ushimaru PI, Silva MT, Di Stasi LC, Barbosa L, Fernandes A., Jr Antibacterial activity of medicinal plant extracts. *Braz J Microbiol.* 2007;38:717-9.

22. Joseph B, Priya RM, Helen PA, Sujatha S. Bio-active compounds in essential oil and its effects of antimicrobial, cytotoxic activity from the *Psidium Guajava* (L.) leaf. *J Adv Biotechnol.* 2010;9:10-4.

23. Prabu GR, Gnanamani A, Sadulla S. Guaijaverin: A plant flavonoid as potential antiplaque agent against *Streptococcus mutans*. *J Appl Microbiol.* 2006; 101: 487-95.

24. Gashe F, Belete A, Gebre-Mariam T. Evaluation of antimicrobial and anti-inflammatory activities and formulation studies on the leaf extracts of *Psidium guajava* L. *Ethiop Pharm J.* 2010;28:131-42.

25. Arima H, Danno G. Isolation of antimicrobial compounds from guava (*Psidium guajava* L.) and their structural elucidation. *Biosci Biotechnol Biochem.* 2002;66:1727-30.

26. Adeyemi OS, Akanji MA, Oguntoye SA. Ethanolic leaf extract of *Psidium guajava*: Phyto-chemical and trypanocidal activity in rats infected with *Trypanosoma brucei*. *J Med Plants Res.* 2009;3:420-3.

27. Metwally AM, Omar AA, Harraz FM, El Sohafy SM. Phytochemical investigation and antimicrobial activity of *Psidium guajava* L. leaves. *Pharmacogn Mag.* 2010;6:212-8.

28. Tona L, Kambu K, Ntondele D, Cimanga K, Luki N. Antimicrobial activity of tannins. *Fitoterapia.* 1994;65:276-8.