PSIDIUM GUAJAVA: A POTENTIAL ADJUNCT IN THE MANAGEMENT OF PERIODONTAL DISEASES – A REVIEW

Sunaina Shetty[1], Gopinath Vivekanandan[2], Sanketa Patil[3], Sachin B Mangalekar[4]

1) Sunaina Shetty - PhD Scholar, Pacific University, Udaipur

2) Gopinathvivekanandan - PhD guide, Pacific University, Udaipur

3) Sanketa Patil - Senior Lecturer, Department of Periodontics, CDCRI, Sundra, Rajnandgaon

4) Sachin B Mangalekar - Prof and Head, Bharatiya Vidyapeed, Sangli

Abstract: -

Periodontitis is a complex disease which expresses the interactions of the biofilm with the host inflammatory response and subsequent alterations in bone and connective tissue metabolism. With the rise in bacterial resistance to antibiotics, there is a considerable interest in the development of other classes of antimicrobials for the control of infection[2]. Natural phytochemicals which are isolated from plants are considered good alternatives for synthetic chemicals and their application has been carried out in all healthcare specialties including the field of periodontics. The leaves of the plant P. guajava are reported to possess antioxidant, hepatoprotective, antiallergy, antimicrobial, antigenotoxic, antiplasmodial, cytotoxic, antispasmodic, cardioactive, anticough, antidiabetic, antiinflammatory and antinociceptive activities. The leaves of guava are also used to prevent bleeding gums and Halitosis.

INTRODUCTION

Periodontitis is a complex disease which expresses the interactions of the biofilm with the host inflammatory response and subsequent alterations in bone and connective tissue metabolism.The goal of periodontaltreatment is to cure the inflamed tissues, reduce the number of periodontal pathogens and alter the host immunemodulatory response. Mechanical debridement, use of antimicrobial agents is some of the clinical methods employed to treat periodontal disease[1]. Although mechanical treatment significantly decreases the prevalence and levels of subgingival microorganisms, it does not necessarily eliminate all pathogens. Also, as the probing depth increases, the effectiveness of scaling and root planing decreases, leaving subgingival plaque and calculus on root surfaces. In an attempt to over come the limitations of mechanical debridement, surgical procedure, local and systemic antibiotics have been employed to facilitate the elimination of subgingival micro flora.[2]

With the rise in bacterial resistance to antibiotics, there is a considerable interest in the development of other classes of antimicrobials for the control of infection[2]. Natural phytochemicals which are isolated from plants are considered good alternatives for synthetic chemicals and their application has been carried out in all healthcare specialties including the field of periodontics. Phytotherapy is the use of extracts from the natural origin as medicines or health promoting agents. These herbal drugs are the secondary metabolites of plants[3].

Psidium guajava (myrtaceae) is evergreen phytotherapic plant growing up to 10m high , with spreading branches. The leaves are aromatic when crushed, evergreen, opposite, short pedicle, oval or oblong elliptic, somewhat irregular in outline, 7-15m long to 3-5m wide, leathery with conspicuous parallel vein and more or less down on the underside.[4]. The leaves of the plant P. guajava are reported to possess antioxidant, hepatoprotective, antiallergy, antimicrobial, antigenotoxic, antiplasmodial, cytotoxic, antispasmodic, cardioactive, anticough, antidiabetic, antiinflammatory and antinociceptive activities. The leaves of guava are also used to prevent bleeding gums and Halitosis.[5] This review emphasis the methods of antibacterial activity of P.guajava and its therapeutic applications in the management of periodontal diseases.

Bioactive constituents and phytochemistry of psidium guajava

The basicbioactive constituents of guava are tan nins,vitamins, phenoliccompounds, flavonoids, essential oils, sesquiterpene alcohols and triterpenoid acids, saponins ,lectin,alkaloids . Moreover,leaves contain phenolic compounds,is oflavonoids, gallic acid, catechin, epicatechin, r

utin, naringenin,kaempferol having hepatoprotective, antioxidant, anti-inflammatory,antispasmodic, anticancer, antimicrobial, anti-hyperglycemic,analgesic actions[6,8,9]The leaf also contain guajaverin known for its anti bacterial action.and contains flavanoids and quercetin known for its anti inflammatory actions [7].Psidium guajava pulp contains ascorbic acid, carotenoids(lycopenes, β-carotene) possessing antioxidant, anti-hyperglycemic, antineoplasticactions. The seeds of guava contain glycosides, carotenoids, phenolic compounds which possess antimicrobial actions. [6]

Basic extraction method of psidium guajava leaves

Super critical fluid extraction (SFE)

The separation of one component from the other component by using extracting solvent is basis for extraction process. Super critical fluid is used as a extracting solvent with some co-solvent to increase its capacity to separate. A sample of guava leaves 1 mg is taken for this type of extraction process in a cell column. In SFE carbon di oxide is mostly taken as supercritical fluid with ethanol and methanol as co-solvents.[10]

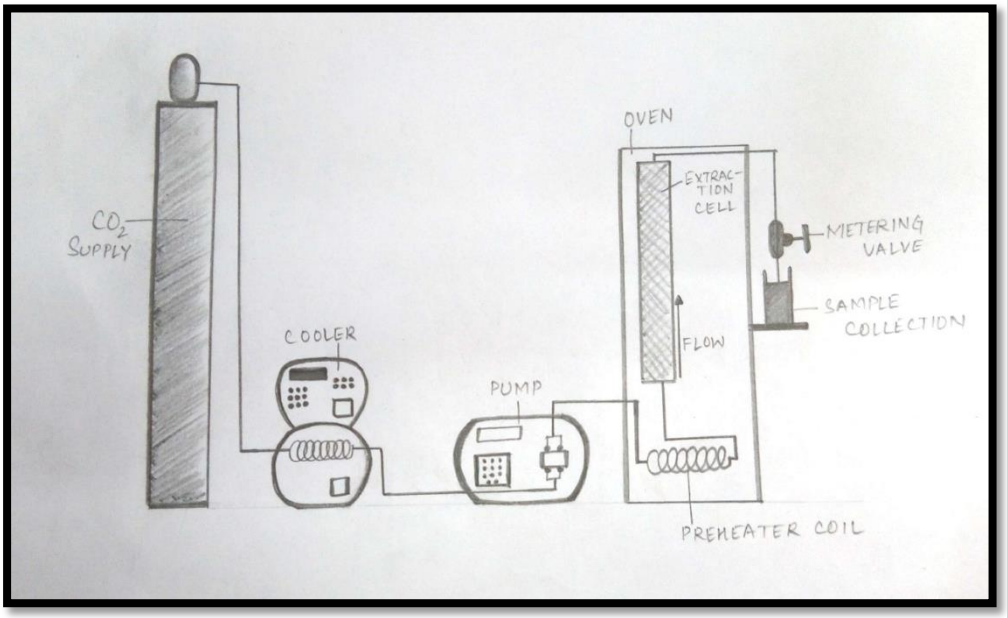

Fig.1. Super critical fluid extraction

The components of SFE are pressure cell, pressure controller, collecting vessel, heating and cooling system and pump. In this process, liquid is converted into supercritical condition and then passs it on to extraction vessel where it is easily diffused into solid matrix of sample and dissolve the material which we have to extract. The dissolved matrix will be swept away from cell column at lower pressure

and extracted material is let out. Carbon di oxide can be recycled, temperature should be 45-55^{0}c and pressure condition should be 200-300 bar[10].

B. Soxhlet extraction

The components used in soxhlet extraction are thimble, water cooling system, and reservoir, by pass tube, siphon tube and condenser. 10 mg of solid material of leaves taken and kept in thimble which is loaded into soxhlet vessel having flask containing extractor solvent Solvent vapor flows up to the column and floods into the chamber having the thimble of solid. A part of non volatile compounds dissolves in solvent. Process is repeated many times until we get desired concentrated compounds in flask. Process is done at boiling temperature of solvent and extraction is done in 100 ml ethanol for 3-5 hrs[10].

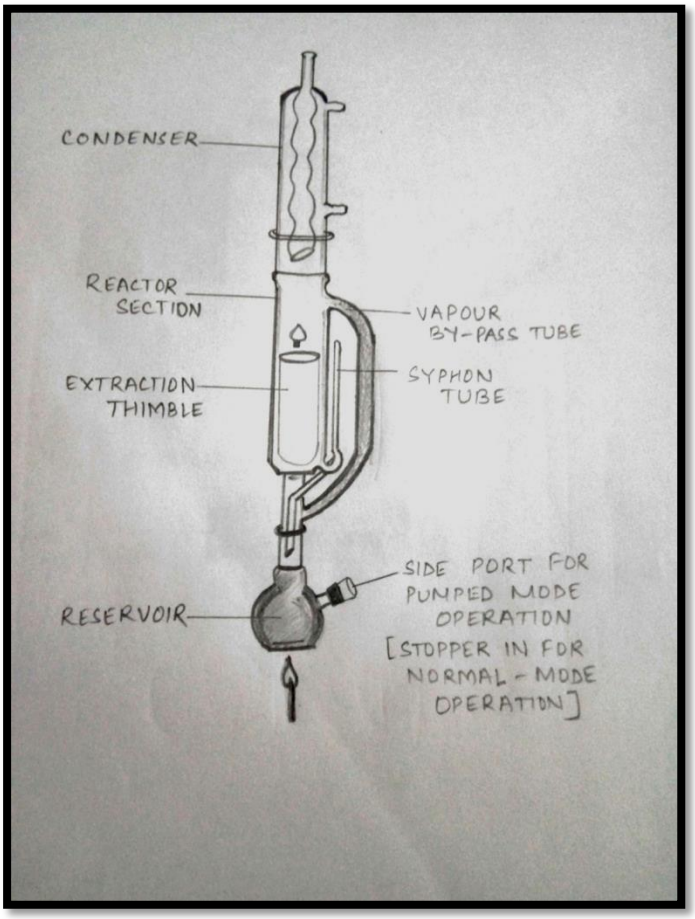

Fig-2 Soxhlet extractor

Toxicity and safety

Guava has been used for centuries in ancient medicine without adverse effects. Toxicity is seen usually when phytochemicals are ingested in excessive amounts. However, treatment of gingival and periodontal disease does not

require such toxic levels.[11]There is limited information available regarding the quality, safety and efficacy of herbal products used in dentistry.

There are acute toxicological studies done for determining acute toxicity of guava. Mean lethal dose LD50test in swiss mice and alternate toxicology in wister rats.[12]

Acute toxicity tests in rats and mice have proven the LD50 of guava leaf extract to be more than 5g/kg [12].In vitro genotoxicity and mutagenicity tests on Psidium guajava in human peripheral blood lymphocytes found no disturbances in cell division.[12]

Therapeutic applications

Guava as an antiplaque agent

Dental plaque is the principal etiologic factor in periodontal disease.[13] The adhesion of early colonisers of dental plaque to the tooth surface has a role in the initiation of the development of dental plaque.. The treatment of the early colonisers with 1 mg/ml aqueous extract leaf of *Psidiumguajava* reduced the cell-surface hydrophobicity of *Staphylococcussanguinis*, *Staphylococcus mitis* and *Actinomyces* sp. by54.1%, 49.9% and 40.6%, respectively .[14]Plaque if allowed to accumulate, with no intervention or oral hygiene methods, leads to gingivitis which further progresses to periodontitis.[13] The paste of tender leaves of guava has been traditionally used to maintain oral hygiene. Guava has shown antibacterial activity against both Gram positive and Gram negative bacteria.[15]

Quercetin has shown excellent antibacterial actions against periodontal pathogens *Aggregatibacter actinomycetemcomitans*(*Aa*), *Porphyromonas gingivalis* (*Pg*), *Prevotella intermedia* (*Pi*),*Fusobacterium nucleatum* (*Fn*). Theantibacterial action of quercetin is due to the disruption ofmembrane and inactivation of extracellular proteins by the formation of irreversible complexes.[16,17]

Mouthrinse containing guava leaf extract had a profound effect on gingivitis[18] .Guava extract has demonstrated *in vitro* antiplaque actions by inhibiting growth, adherence and coaggregation of dental plaque bacteria. Guava extracts may inhibit plaque development without disrupting homeostasis of the oral cavity.[19] Thus, guava extract is an anti plaque agent that can be used as an adjunct for treatment of the periodontal disease.

Guava as an anti-inflammatory/ analgesic agent

Periodontal surgical procedures commonly require the support of the analgesics as part of home care management. There are a wide range of analgesics which are available for management of the postoperative pain following a periodontal surgery[20]. A extract of *guava* leaves is used

worldwide for the treatment of various inflammatory diseases including rheumatism. The anti-inflammatory property of the aqueous leaf extract was investigated in rats, using fresh egg albumin induced pedal (paw) oedema. While the analgesic effect of the guava plant extract was evaluated by the hot-plate and acetic acid test models of pain in mice. *Guava aqueous* extract (50–800 mg/kg, i.p.) produced dose-dependent and significant inhibition of fresh egg albumin-induced acute inflammation (edema) in rats. The leaf extracts (50–800 mg/kg, i.p.)Also produced dose-dependent and significant analgesic effects.

The anti-inflammatory action of guava is in its ability to inhibit prostaglandin, kinin and histamine.[21, 22] Aggregatibacter actinomycetum comitans[*Aa]* is an important periodontal pathogen which associated with aggressive periodontitis. Guava extract completely neutralized the cytolytic,proinflammatory response of human leukocytes induced by *Aa* leukotoxin. C reactive protein (CRP) is a positive acute phase protein which is elevated in periodontitis patients. Guava leaf and stem extracts decreases CRP levels which plays a role as modulator of inflammatory response.[23,24]

Fermented guava leaf extract inhibits inducible nitric oxide synthase (iNOS) and cyclooxygenase2 (COX2).It also inhibits lipopolysaccharide induced NFkβ activation.[25]. Blocking NFkβ is a potential strategy for preventing inflammatory bone resorption.Guava due to its anti-inflammatory action, ability to inhibit iNOS, COX2,NFkβ could be used as an therapeutic agent in treating inflammatory component of periodontal disease.[25]

Guava as a wound healer

Vitamin C is one of the essential component which helps in maintaining the overall integrity of periodontium. Vitamin c (ascorbic acid) is present abundantly in guava. Ascorbic acid can help in collagen formation, fibroblast differentiation through its effects on extracellular matrix.[26,27] Vitamin c supports the functioning of immune system and maintains structural and functional integrity of epithelial tissue in periodontium. Vitamin C enhances the healing process with the help of bioflavonoid present in guava. Thus guava extract contributes towards hastening the healing process in the periodontal tissues[28,29.]

Guava as an Antioxidant, free radical scavenger

Excessive free radical generation by neutrophils can be stimulated by periodontal pathogens leading to damage of tissues.[30] The imbalance between oxidative stress and antioxidant activity will lead to periodontal tissue destruction. Decreased antioxidant activities of Crevicular fluid and saliva are associated with development of periodontal disease.[31,32]

Guava is an excellent antioxidant and a good antioxidant rich diets are said to inhibit periodontal disease and progression.[33]The antioxidant activity of lyophilized leaf extracts was determined using free radical DPPH (2,2-diphenyl-1-picrylhydryzyl) scavenging showed that ascorbic acid present in guava leaf was a substantially more powerful antioxidant These antioxidant properties are also associated with its other phenolic compounds such as protocatechuic acid, ferulic acid, quercetin and guavinB and gallic acid.Guava leaf extracts and essential oil from the stem, bark have the ability to scavenge free hydrogen peroxide, superoxide an ion radical and inhibit the formation of hydroxyl radical.[34] Thus, guava could be used even for antioxidant based approach to periodontal therapy source of vitamin C.

Conclusion

Herbal products can be used as an adjunct to mechanical periodontal therapy. Guava extract is an antiplaque, antimicrobial, anti-inflammatory, antioxidant agent. This review sheds light upon the phytochemistry,basic extraction method, and therapeutic applications including wound healing capacity of Psidium guajava. The guava extract could be used in the future for more clinical research to compare it with conventional antibiotics to evaluate their *in vivo* and *in vitro* efficacy. Hence, future studies should be conducted to analyse the preventive and therapeutic aspects of Psidium guajava as herbal medicine in periodontal therapy.

References

1. Ravi K and Divyasree P. Psidium guajava : A review on its potential as an adjunct in treating periodontal disease.Pharmacogn Rev.2014 Jul-Dec;8(16):96-100.

2. Priyavadhana, P. "Prabhu Manickam Natarajan The role of antibiotics in treatment of chronic Periodontitis." *International Journal of Dental Sciences and Research* 2.1 (2014): 16-18.

3. Shah R,Gayatri GV, Mehta DS. Application of herbal products in management of periodontal diseases: A mini review.International Journal of Oral Health Sciences. 2015;5(1):.

4. Motan J. Guava.In:Fruits of warm climates,Florida Flair Book,1987;p 356-363.

5.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.

6. Barbalho SM, FarinazziMachado FM, de Alvares Goulart R,Brunnati AC, Ottoboni AM. Psidiu m guajava (Guava): A plant ofmultipurpose medicinal plants. Med Aromat Plants. 2012;1:104.

7. Mittal P, Gupta V, Kaur G, Garg AK, Singh A. Phytochemistryand pharmacological activities of Psidium guajava: A review. Int J Pharm Sci Res. 2010;1:9–19.

8. Veerakumar, R., M. Arul Pari, and M. N. Prabhu. "Caution! We are erupting as twins." Journal of Clinical and Diagnostic Research 5.5 (2011): 1123-1124.

9. Groppo FC, Bergamaschi Cde C, Cogo K, FranzMontan M, Motta RH, de Andrade ED. Use of phytotherapy in dentistry. Phytother Res. 2008;22:993–8.

10. Devi BP, Ramasubramaniaraja R. Dental caries and medicinal plants. An overview. J Pharm Res. 2009;2:1669–75.

11. Rao NJ, Subash KR, Kumar KS. Role of phytotherapy in gingivitis: A review. Int J Pharmacol. 2012;1:1–5.

12. Rosa Martha perezgutierrez et al; Psidium guajava : A review of traditional uses ,phytochemistry and pharmacology; J of ethnopharmacology117;2008;1-27

13. Bansal S, Rastogi S, Bajpai M. Mechanical, chemical and herbal aspects of periodontitis: A review. Int J Pharm Sci Res. 2012;3:1260–7.

14. Razak FA, Othman RY, Rahim ZH. The effect of *Piper betle* and *Psidium guajava* extracts on the cellsurface hydrophobicity of selected early settlers of dental plaque. J Oral Sci. 2006;48:71–5.

15. Joseph B, Priya RM, Helen PA, Sujatha S. Bioactive compounds in essential oil and its effects of antimicrobial, cytotoxicactivity from the *Psidium Guajava* (L.) leaf. J Adv Biotechnol. 2010;9:10–4.

16. Shu Y, Liu Y, Li L, Feng J, Lou B, Zhou X, et al. Antibacterial activity of quercetin on oral infectious pathogens. Afr J Microbiol Res. 2011;5:5358–61.

17. Geoghegan F, Wong RW, Rabie AB. Inhibitory effect of quercetin on periodontal pathogens *in vitro*. Phytother Res. 2010;24:817–20.

18. Kraivaphan V, Boonyamanound L, Amornchat C, Trirantana T, Kraivaphan P. The effect of a mouthrinse containing *Psidium guajava* leaf extract on gingivitis. J Dent Assoc Thai. 1991;41:323– 8.

19. John NR, Gala VC, Sawant CS. Inhibitory effects of plant extracts on multispecies dental biofilm formation *invitro*. Int J Pharm Bio Sci. 2013;4:487–95.

20. MN Prabhu. ANALGESICS USED IN PERIODONTAL SURGERY. INTERNATIONAL JOURNAL OF INNOVATIONS IN DENTAL SCIENCES.2016,1(1),pg:2-9.

21. Gashe F, Belete A, GebreMariam 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.

22. Kavimani S, Ilango R, Vertichelvan T. Antiinflammatory activity of volatile oil of *Psidium guajava*. Anc Sci Life. 1998;17:300–4.

23. 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.

24. Archana, Sasireka, M.N Prabhu, Bobby and Venkata Srikanth. Correlation between Circulatory and Salivary IL 10 Levels in Periodontal Health and Disease – A Report, International Journal of Dental Sciences and Research. 2014, 2(4B), 7-10 doi:10.12691/ijdsr-2-4B-325.

25. Choi SY, Hwang JH, Park SY, Jin YJ, Ko HC, Moon SW, et al. Fermented guava leaf extract inhibits LPS induced COX2 and iNOS expression in mouse macrophage cells by inhibition of transcription factor NFkB. Phytother Res. 2008;22:1030–4.

26. Priyavadhana Prabhu, A.Julius, M.N. Prabhu et al. Wound Healing in Periodontics. BIOSCIENCES BIOTECHNOLOGY RESEARCH ASIA, August 2014;11(2),pg:791-796.

27.Brown LA, Jones DP. The biology of ascorbic acid. In: Cadenas E, Packer L, editors. Handbook of Antioxidants. New York: Marcel Dekker, Inc; 1996. pp. 117–54.

28.Chapple IL. Role of free radicals and antioxidants in the pathogenesis of the inflammatory periodontal diseases. Clin Mol Pathol. 1996;49:M247–55.

29. Fernandes KP, Bussadori SK, Marques MM, Wadt NS, Bach E, Martins MD. Healing and cytotoxic effects of *Psidium guajava* (Myrtaceae) leaf extracts. Braz J Oral Sci. 2010;9:449–54.

30.Asman B, Bergström K. Expression of Fc gamma RIII and fibronectin in peripheral polymorphonuclear neutrophils with increased response to Fc stimulation in patients with juvenile periodontitis. Arch Oral Biol. 1992;37:991–5.

31. DiabLadki R, Pellat B, Chahine R. Decrease in the total antioxidant activity of saliva in patients with periodontal diseases. Clin Oral Investig. 2003;7:103–7.

32.Pavlica Z, Petelin M, Nemec A, Erzen D, Skaleric U. Measurement of total antioxidant capacity in gingival Crevicular fluid and serum in dogs with periodontal disease. Am J Vet Res. 2004;65:1584–8.

33. Battino M, Bullon P, Wilson M, Newman H. Oxidative injury and inflammatory periodontal diseases: The challenge of antioxidants to free radicals and reactive oxygen species. Crit Rev Oral Biol Med. 1999;10:458–76.

34. Qian H, Nihorimbere V. Antioxidant power of phytochemicals from *Psidium guajava* leaf. J Zhejiang Univ Sci. 2004;5:676–83.