

Herbal Antioxidants in Periodontal Therapy: A Review

¹Dr. Vinita Ashutosh Bloor, MDS, Additional Professor, Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be) University, Mangalore – 575018.

²Dr. Justina David Joy, Post Graduate Student, Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be) University, Mangalore – 575018.

³Dr. Rajesh Kashyap Shanker, MDS, Professor & Head, Department of periodontology, Yenepoya dental college, Yenepoya (Deemed to be) university, Mangalore – 575018.

⁴Dr. Shashikanth Hegde, MDS, Professor, Department of Periodontology, Yenepoya dental college, Yenepoya (Deemed to be) university, Mangalore – 575018.

Corresponding Author: Dr. Justina David Joy, Post Graduate Student, Department of Periodontology, Yenepoya Dental College, Yenepoya (Deemed to be) University, Mangalore – 575018.

Citation of this Article: Dr. Vinita Ashutosh bloor, Dr. Justina David Joy, Dr. Rajesh Kashyap, Dr. Shashikanth Hegde, “Herbal Antioxidants in Periodontal Therapy: A Review”, IJDSIR- April - 2022, Vol. – 5, Issue - 2, P. No. 07 – 15.

Copyright: © 2022, Dr. Justina David Joy, et al. This is an open access journal and article distributed under the terms of the creative commons attribution noncommercial License. Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Review Article

Conflicts of Interest: Nil

Introduction

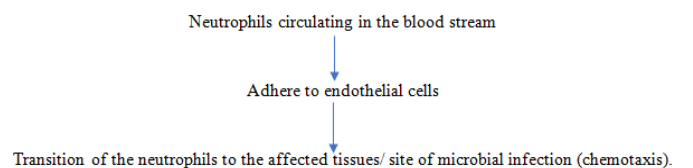
Periodontitis is an oral inflammatory disease presumably caused and perpetuated by predominantly gram-negative, anaerobic or microaerophilic bacteria that are found in the subgingival area. These bacteria bring about visible tissue destruction directly by toxic products and indirectly by initiating inflammation through host defense systems.¹

PMNLs form the first line of defense in the instance of a microbial onslaught and the subsequent inflammation. They constitute 90% of leukocytes entering gingival crevicular fluid (GCF) and 50% infiltrating junctional epithelium in case of clinical inflammation [1]. These neutrophils engage in several intracellular and extracellular oxidative and nonoxidative killing

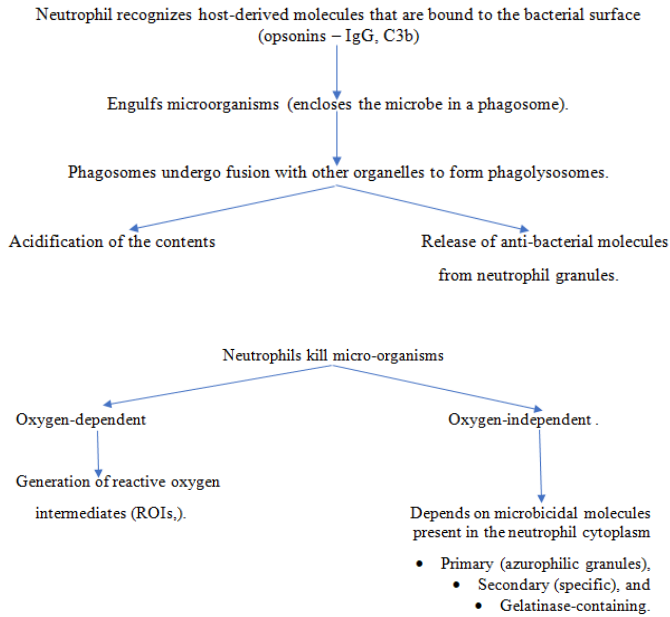
mechanisms to control the microbial invasion. ROS/FRs are formed as a result of this oxidative killing mechanism.²

Role of Neutrophils In Causing The Imbalance In Homeostasis

Neutrophils are highly specialized cells capable for destroying microorganisms. Neutrophil responses to infection can be divided to “3 R’s” – Recruitment, Response, and Resolution. Acquired or genetic defects in one or more of these mechanisms may impair the protective capacity of the neutrophil.



Response



Extracellular killing

Extracellularly neutrophils release a web of fibres containing DNA, histones, and granule-derived bactericidal molecules.

Cause considerable collateral damage to the surrounding connective tissue.

Resolution

Acute inflammation depicts a copious number of neutrophils as infiltrates, their elimination, along with the restoration of tissue leucocytes; which is crucial for tissue repair. A defective clearance of normal neutrophils from the Periodontium may lead to nonhealing chronic inflammation that is similar in periodontitis.³

Free Radicals

Free radical may be defined as an atomic or molecular species capable of independent existence with one or more unpaired electrons in its structure. A low concentration of FRs helps to carry out several cell signaling functions; but at higher concentrations, they react with certain cellular components such as DNA, proteins, lipids leading to an oxidative stress in the gingival tissues, PDL, and alveolar bone and mediate

tissue damage. Antioxidants help to maintain the essential balance in their levels.⁴

Oxidative stress is a patho-mechanism associated with various inflammatory conditions leading to destruction of lipids, nucleic acids and proteins; as well as a vital physiological process which helps the immune system to cope with microorganisms and intracellular cell signaling.

Oxidative stress is the disruption in the pro-oxidant – antioxidant balance, leading to potential destruction (Sies). While a wider knowledge regarding the pathological role of oxidative stress is available; the physiological functions of free radicals have been neglected for years. A variety of free radicals is produced and interacts with a variety of substrates; creating a palette of biomarkers that can be used for the assessment of oxidative stress-induced damage.

Recently, studies on reactive oxygen species (ROS) have gained momentum due to its impact in the progression of many inflammatory diseases. They are associated with normal cellular metabolism and the cells in most tissues produce them.^{5,6,7}

An **antioxidant** is a substance that plays a crucial role in hampering or checking the oxidation of a substrate when they are present at concentrations lower than the substrate.

A substantial amount of literature focus on the prevention of ROS formation, enzymatic and non-enzymatic antioxidant mechanisms. Direct neutralisation of ROS is carried out by enzymatic mechanisms which are formed by primary enzymes involved in human organism protection and seek to maintain a normal range of the ROS levels. These enzymes include superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx).

Also, non-enzymatic antioxidants functions as a secondary mechanism to neutralise ROS. Most often, these types of antioxidants are acquired primarily through a balanced diet constituting a wide range of fruits and vegetables. The non-enzymatic antioxidants include fat-soluble vitamins (vitamin A, vitamin E-tocopherol and b-carotene), water-soluble vitamins (vitamin C and vitamin B complex), trace elements (zinc and magnesium), and bioflavonoids (plant derived).

They work by the following three mechanisms :

1. Reduce production of cytokines, chemokines, and proinflammatory proteins by leukocytes, thereby hampering the destruction of cells and other structures.
2. Neutralize ROS and protect the fibroblasts from toxic substances which release ROS. Also, they help reverse the effect of oxidative damage.
3. Promote the process of wound healing

Studies revealed that, oxidative levels are significantly higher in patients with periodontitis than periodontally healthy persons. Nevertheless, the antioxidant levels are found to be significantly lower in chronic periodontitis patients than the periodontally healthy counterparts.⁹

Herbal Antioxidants

Herbal medicines and preparations are made of plant-based elements that apparently have therapeutic benefits. Extensive natural activity, advanced safety margin, and inferior costs make them favoured over conventional drugs which can cause side-effects. Herbal medicines are being used as dietary supplements to prevent and treat common ailments affecting human body and oral cavity.

Periodontal therapy includes both surgical and nonsurgical management of the disease process. Many antimicrobials and chemotherapeutic agents, such as chlorhexidine, triclosan, and cetylpyridinium chloride,

have been used extensively in the management of periodontal diseases.

Owing to its multifactorial etiology and complex disease process; and the side effects of modern chemotherapeutic agents such as tooth discoloration, taste alteration, along with their cost; a surge in the usage of herbal products is seen recently. Herbal remedies have been sought to achieve antimicrobial, antioxidant, antiseptic, anti-inflammatory, and anti-collagenase effects.^{10,11}

The herbal antioxidants that have been tested for treatment of periodontitis are : Aloe vera, Arjuna, Acacia Catechu wild, Neem, Glycyrrhiza glaber, Green tea, Curcumin, Triphala, Sumac, Piperineis, Mastiha, Punica Granatum and Lemon grass.

Aloe Vera: Aloe vera is a cactus plant that belongs to the Liliaceae family that grow in tropical climate and low rainfall areas. Among 300 species of aloe plants only 2 species have been studied, which are Aloe barbadensis Miller and Aloe aborescens. Many cosmetic and medical products are made from the mucilaginous tissue present in the center of the Aloe vera leaf in the form of Aloe vera gel. Reportedly, Aloe vera has anti-inflammatory, antibacterial, antioxidant, antiviral and antifungal actions, as well as hypoglycemic effects. It is extremely helpful in the treatment of diseases like gingivitis, periodontitis. It reduces bleeding, inflammation and swelling of gingiva by destroying bacteria responsible for it and enhance process of healing. Massaging the aloe gel into the gums has also been shown to be beneficial.^{10, 12, 13}

Another study done on type 2 diabetes mellitus patients revealed an intra-pocket placement of aloe vera gel significantly improved clinical factors such as plaque index, probing pocket depth, and gain in clinical attachment.¹⁴

A recent study by Prakash et al proved that aloe vera significantly improved the antioxidant levels at sites where aloe vera gel was used as an adjunct to SRP in chronic periodontitis patients.¹⁵

Azadirachta Indica (Neem): Azadirachta indica, commonly known as neem in India have anti-arrhythmic, anti-arthritis, anti-viral, anti-diabetic and antioxidant properties. Neem leaves have been used in the treatment of gingivitis and periodontitis since a long time. A study found that Neem leaf extract is beneficial in treating dental plaque and gingivitis. Micro-organisms found in inflamed gum are resistant to tetracycline and penicillin but sensitive to the Neem leaf extracts which causes no allergic reaction also. It was found that in Pyorrhoea, when treated with neem-based toothpaste and mouthwash, the bleeding gums healed, the secretion from pockets around the teeth ceased and the blue-tinted gums returned to healthy pale pink colour. The herbal formulation comprising of active fractions from Azadirachta indica, Citrullus colocynthis and Cucumis sativus prevents dental plaque and gingivitis in humans.^{16,17}

Amelia Priscilla Sugiarta, et al. (2018), examined the effect of an herbal toothpaste containing neem leaves extract against gingivitis. Results showed that neem can reduce the counts of plaque-forming bacteria in the oral cavity. A significant reductions in PI and PBI were noted between the test and control groups which affirms that neem leaf extracts are effective in reducing gingivitis.¹⁸

The antioxidant capacity of Neem was studied in vitro, and it was shown to exhibit intense antioxidant activity, that increased in the presence of bacterial adherence.¹⁹

Green Tea: It has been traditionally used in Chinese medicine for headaches, body aches, general pain, digestion, depression, as an energizer, and in general to

prolong life. Green tea also has many oral health benefits.

Widely consumed as liquid refreshment throughout the world, green tea contains flavonoids, carotenoids, tocopherols, ascorbic acid and minerals. Green tea is also effective against Gram-negative anaerobic bacteria. The catechin present in green tea allegedly reduce tissue damage by reducing collagenase activity. Polyphenols in green tea are found to have antioxidant activity.¹¹

Hirasawa et al. demonstrated bactericidal activity of green tea catechins against Prevotella and P. gingivalis at concentration of 1 mg/ml. A significant reduction in markers of gingivitis were seen after the use of slow-release buccal delivery system applied over a period of 8 weeks.²⁰

Tripathi et al, found that green tea along with lycopene as an adjunct to SRP significantly reduced the salivary uric acid levels compared to SRP alone.²¹

Curcumin: Turmeric, known as Curcuma longa, belongs to the zingiberaceae plant family. Curcumin, the natural extract from turmeric, has high safety and low toxicity. It has been widely used as antioxidant, anti-inflammatory, anticancer, neuroprotective, hepatoprotective, antidiabetic, antibacterial, antifungal, and antiviral agent.

Chatterjee et al. repeated subgingival rinsing of periodontal pockets of patients with chronic periodontitis with a curcumin solution with a concentration of 1%, and the results showed that curcumin effectively inhibited periodontal inflammation.²² Singh et al. injected curcumin sustained release tablets into the periodontal pockets of patients with chronic periodontitis. The plaque index (PLI), gingival index (GI), probing depth (PD), and clinical attachment level of the patients showed significant improvement after 1 month of treatment.²³

In another study, it was shown that followed by the placement of curcumin strip in periodontal pockets, the superoxide dismutase enzyme was significantly increased. Thus proving the antioxidant potential of curcumin.²⁴

Triphala: It has a free radical scavenging property and the antimicrobial activity of Triphala (means three fruits), herbal product, which was made from equal proportions of Terminalia chebula, Terminalia bellirica and Emblica officinalis, have been evaluated. Triphala helps in inhibition of bio-film formation and acts as an antioxidant thereby protecting the gum cells effectively from free radicals than the commercial toothpastes.

Individual Components of Triphala

- Emblica officinalis: It is an immunomodulatory, anti-pyretic, analgesic, cytoprotective, anti-tussive, and gastroprotective agent and as an anti-microbial agent. The drug is not reported to have any side-effects even after prolonged use.
- Terminalia chebula : it has an anti-bacterial activity against a range of Gram-positive and Gram-negative bacterial species. It also exhibits anti-fungal and anti-viral properties along with anti-mutagenic/ anti-carcinogenic activity, antioxidant activity, adaptogenic and anti-anaphylactic activities, immunomodulatory activity, cytoprotective and radioprotective activity.
- Terminalia belerica : The plant is reported to possess antioxidant, anti-spasmodic, bronchodilatory, hypercholesterolemic, anti-bacterial, cardioprotective, hepatoprotective, hypoglycemic, and hypotensive properties.

Triphala in the treatment of gingivitis and periodontitis. Oral rinses made from ayurvedic drugs has been used in periodontal therapy. Triphala is one of these with wide spectrum of activity. According to the Sushruta Samhita,

Triphala can be used as a gargling agent in dental diseases.²⁵

A study by Tandon S et al 0.6% Triphala mouthwash has shown to have significant anti-caries activity, comparable to chlorhexidine but without any disadvantages as staining of teeth and cost much less. However, no evidence of re-mineralization of tooth structure was seen.²⁶

Desai A et al found that Triphala mouth rinse when combined with scaling and root planing showed significant reduction in the plaque, gingival, and oral hygiene indices without any evidence of staining of teeth at seven, 30, and 45 days, which was comparable to reduction obtained by chlorhexidine mouth rinse in combination with scaling and root planing.²⁷

Recently, in an in vitro study, it has been shown that triphala was highly potent in inhibiting DPPH scavenging model even at low doses when compared to Curcumin.²⁸

SUMAC: Sumac (*Rhus coriaria*) is used widely as an herbal medicine for its anti-inflammatory, antimicrobial, and antioxidant properties.¹¹

A study by Mehmet sađlam et al²⁹ assessed the effects of sumac extract on levels of receptor activator of nuclear factor-kappa B ligand (RANKL), osteoprotegerin (OPG) expression, serum oxidative status, and alveolar bone loss in experimental periodontitis. In this study conducted on rats, the systemic administration of sumac extract was found to be possibly decreasing alveolar bone loss by affecting RANKL/OPG balance, TOS and OSI levels in periodontal disease.

Piperines : An alkaloid present in plants such as Piper nigrum and Piper longum, piperine have antioxidant and anti-inflammatory properties.¹¹ In a ligature induced periodontitis study on rats, it was found that piperines was equally effective as curcumin in increasing the

TGF- β level, improving the collagen repair, and in decreasing the cellularity and activation of NF- κ B in the periodontal tissues.³⁰

Punica Granatum: Punica granatum, more commonly known as pomegranate, belongs to family Punicaceae and is “A pharmacy unto itself”. Pomegranate juice contains anthocyanins, glucose, ascorbic acid, ellagic acid, gallic acid, caffeic acid, catechin, epigallocatechin, quercetin, rutin, iron and amino acids possessing anti-atherosclerotic, antihypertensive, antiaging and potent antioxidative properties.

Some potential effects of pomegranate include bactericidal, antifungal, antiviral, immune modulation, vermifuge, stimulant, refrigerant, astringent, stomachic, styptic, laxative, diuretic and anthelmintic properties.³¹

A recent study proved that pomegranate mouthwash had antibacterial efficacy against the most important periodontal pathogens like *Aggregatibacter actinomycetemcomitans* (Aa), *Porphyromonas gingivalis* (Pg), *Prevotella intermedia* (Pi).³²

Deep periodontal pockets are said to be associated with *Helicobacter pylori* (H. pylori) infection. Pomegranate was found to have a significant antibacterial activity against H. pylori, detected from the oral cavities of patients with periodontitis. Hence, pomegranate could be beneficial in treating periodontitis.

Pomegranate has positive effects on growth of enteric probiotic bacteria like *Bifidobacterium* species and *Lactobacillus* species. These probiotic microorganisms affect the growth, adhesion and colonization of periodontal pathogens. It is beneficial in decreasing the IL-1 and TNF- α levels in the gingival crevicular fluid and hinder the activity of tissue destructive enzymes like elastase, myeloperoxidase and metalloproteinase-3.

Pomegranate extracts have the potential to scavenge free radicals and reduce macrophage oxidative stress and

lipid peroxidation, according to a review by Jurenka et al.³³

Lemon Grass

Cymbopogon citratus, Stapf. (lemongrass) is a popular medicinal plant utilized in the treatment of different diseases. It is commonly used in tea, cosmetics, and folk medicine for its antiseptic, antiemetic, anti-rheumatic, analgesic, antispasmodic, and antipyretic properties.

It contains phenol and flavanoid substances which were reported to show many in vitro and in vivo properties such as antioxidant, anti-inflammatory, and antimutagenic activities alongside a wide range of antimicrobial activities such as anti-amebic, antifungal, antimycobacterial, and antibacterial against both gram-positive and gram-negative organisms.

Anand et al. (2011)³⁴ studied the efficacy of lemongrass oil mouthwash and evaluated its antioxidant property by estimating salivary and gingival crevicular fluid GCF superoxide dismutase levels pre and post administration. Lemongrass oil mouthwash was used along with nonsurgical treatment in various concentrations (0.1%, 0.25%, and 0.5%). Superoxide dismutase levels showed an increase post-administration when compared with the pre administration values in all the groups, with reduction in gingivitis. It shows that the lemongrass oil mouthwash may have an additive effect on the treatment outcome, when it is used along with scaling.

Another study by Shivaraj B et al evaluated the efficacy of locally delivered 2% lemongrass essential oil in gel form as an adjunct to scaling and root planing, as compared to scaling and root planing alone for the treatment of chronic periodontitis. Results revealed that 2% lemongrass essential oil gel can be effective and safe local drug delivery used as an adjunct to nonsurgical periodontal therapy.³⁵

Conclusion

Herbs due to their natural source and their ability not to cause any side effects have been recently been studied as anti-inflammatory and antimicrobial agents in various forms such as mouth rinses, local drug delivery etc. Indeed, their potentiality in attacking the free radicals and in reducing the oxidative stress has further encouraged their applicability in the management of periodontal diseases. However, there is no sufficient amount of research in the evaluation of their influence on increasing the antioxidant capacity in periodontitis patients. Further long-term, randomised control trials evaluating and comparing their effect as a potent antioxidant in treating periodontitis should be considered.

References

1. Waddington RJ, Moseley R, Embery G. Reactive oxygen species: a potential role in the pathogenesis of periodontal diseases. *Oral Dis* 2000;6(3):138-51.
2. Kaur G, Kathariya R, Bansal S, Singh A, Shahakar D. Dietary antioxidants and their indispensable role in periodontal health. *Journal of food and drug analysis*. 2016 Apr 1;24(2):239-46.
3. Nussbaum G, Shapira L. How has neutrophil research improved our understanding of periodontal pathogenesis?. *Journal of clinical periodontology*. 2011 Mar;38:49-59.
4. Halliwell B. Tell me about free radicals, doctor: a review. *J R Soc Med* 1989;82:747e52.
5. Celec P. Oxidative stress and antioxidants in the diagnosis and therapy of periodontitis. *Frontiers in physiology*. 2017 Dec 14;8:1055-68.
6. Sies H. Oxidative stress: oxidants and antioxidants. *Exp Physiol*. 1997. 82 :291-95
7. Khan SN, Kumar S, Iqbal S, Joy MT, Ramaprabha G. Oxidative stress, antioxidants, and periodontitis: How are they linked. *Int J Oral Care Res*. 2018;6(2):107-12.
8. 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. *Critical Reviews in Oral Biology & Medicine*. 1999 Jul;10(4):458-76.
9. Muniz FW, Nogueira SB, Mendes FL, Rösing CK, Moreira MM, de Andrade GM, de Sousa Carvalho R. The impact of antioxidant agents complimentary to periodontal therapy on oxidative stress and periodontal outcomes: A systematic review. *Archives of oral biology*. 2015 Sep 1;60(9):1203-14.
10. Abdelmagyd HA, Shetty SR, Al-Ahmari MM. Herbal medicine as adjunct in periodontal therapies- A review of clinical trials in past decade. *Journal of Oral Biology and Craniofacial Research*. 2019 Jul 1;9(3):212-7.
11. Anand B. Herbal therapy in periodontics: a review. *J. Res. Pharm. Sci*. 2017;3(5):1-7.
12. Bhat G, Kudva P, Dodwad V. Aloe vera: Nature's soothing healer to periodontal disease. *Journal of Indian society of periodontology*. 2011 Jul;15(3):205-209.
13. Chhina S, Singh A, Menon I, Singh R, Sharma A, Aggarwal V. A randomized clinical study for comparative evaluation of Aloe Vera and 0.2% chlorhexidine gluconate mouthwash efficacy on de-novo plaque formation. *J Int Soc Prev Community Dent*. 2016 May-Jun;6(3):251-255
14. Pradeep AR, Garg V, Raju A, Singh P. Adjunctive local delivery of Aloe vera gel in type 2 diabetics with chronic periodontitis: A randomized controlled clinical trial. *J Periodontol* 2015:1-1

15. Singh P, Jain M, Saxena V, Sharva V, Boddun M, Jain N. Evaluation of local-delivery system containing 80% aloe vera gel used as an adjunct to scaling and root planning in chronic periodontitis: A clinical study. *Dent Oral Maxillofac Res.* 2019;5(4):1-5.
16. Pandita V, Patthi B, Singla A, Singh S, Malhi R, Vashishtha V. Dentistry meets nature-role of herbs in periodontal care: A systematic review. *Journal of Indian Association of Public Health Dentistry.* 2014 Jul 1;12(3):148-156.
17. Kulshrestha N, Panwar D, Singh RR. Effect of Ayurvedic herbs Neem (*Azadirachta indica*), Khadir (*Acacia catechu*), Madhuk (*Madhuka indica*) on Periodontal Disease. *Journal of Ayurveda and Integrated Medical Sciences.* 2021 Apr 30;6(02):143-7
18. Sugiarta ap, lessang r. effect of herbal toothpaste containing neem leaves extract (*azadirachta indica*) against gingivitis: a clinical study. *International Journal of Applied Pharmaceutics.* 2019 Apr 5:117-9
19. Heyman L, Hourri-Haddad Y, Heyman SN, Ginsburg I, Gleitman Y, Feuerstein O. Combined antioxidant effects of Neem extract, bacteria, red blood cells and Lysozyme: possible relation to periodontal disease. *BMC complementary and alternative medicine.* 2017 Dec;17(1):1-8
20. Hirasawa M, Takada K, Makimura M, Otake S. Improvement of periodontal status by green tea catechin using a local delivery system: a clinical pilot study. *J Periodontal Res.* 2002;37:433-8.
21. Tripathi P, Blaggana V, Upadhyay P, Jindal M, Gupta S, Nishat S. Antioxidant therapy (lycopene and green tea extract) in periodontal disease: A promising paradigm. *Journal of Indian Society of Periodontology.* 2019 Jan;23(1):25-30.
22. Li Y, Jiao J, Qi Y, Yu W, Yang S, Zhang J, Zhao J. Curcumin: A review of experimental studies and mechanisms related to periodontitis treatment. *Journal of Periodontal Research.* 2021 Oct;56(5):837-47.
23. Singh A, Sridhar R, Shrihatti R, et al. Evaluation of turmeric chip compared with chlorhexidine chip as a local drug delivery agent in the treatment of chronic periodontitis: a split mouth randomized controlled clinical trial. *J Altern Complement Med.* 2018;24(1):76-84.
24. Elavarasu, S., Suthanthiran, T., Thangavelu, A., Alex, S., Palanisamy, V.K. and Kumar, T.S., 2016. Evaluation of superoxide dismutase levels in local drug delivery system containing 0.2% curcumin strip as an adjunct to scaling and root planing in chronic periodontitis: A clinical and biochemical study. *Journal of Pharmacy & Bioallied Sciences*, 8(Suppl 1), p.S48- S52.
25. Prakash S, Shelke AU. Role of Triphala in dentistry. *Journal of Indian Society of Periodontology.* 2014 Mar;18(2):132-135
26. Bajaj N, Tandon S. The effect of Triphala and Chlorhexidine mouthwash on dental plaque, gingival inflammation, and microbial growth. *International journal of Ayurveda research.* 2011 Jan;2(1):29.
27. Desai A, Anil M, Debnath S. A clinical trial to evaluate the effects of triphala as a mouthwash in comparison with chlorhexidine in chronic generalised periodontitis patient. *Indian Journal of Dental Advancements.* 2010 Jul 1;2(3):243-8.
28. Padmawar A, Bhadoriya U. Phytochemical investigation and comparative evaluation of in vitro free radical scavenging activity of Triphala & Curcumin. *Asian Journal of Pharmacy and Medical Science.* Vol. 2011;1-4.

29. Sağlam M, Köseoğlu S, Hatipoğlu M, Esen HH, Köksal E. Effect of sumac extract on serum oxidative status, RANKL/OPG system and alveolar bone loss in experimental periodontitis in rats. *Journal of Applied Oral Science*. 2015 Jan;23:33-41.
30. Guimaraes-Stabili MR, de Aquino SG, de Almeida Curylofo F, Tasso CO, Rocha FR, de Medeiros MC, de Pizzol JP, Cerri PS, Romito GA, Rossa C. Systemic administration of curcumin or piperine enhances the periodontal repair: a preliminary study in rats. *Clinical Oral Investigations*. 2019 Aug;23(8):3297-306.
31. Prasad D, Kunnaiah R. *Punica granatum*: A review on its potential role in treating periodontal disease. *Journal of Indian Society of Periodontology*. 2014 Jul;18(4):428-432.
32. Bhadbhade SJ, Acharya AB, Rodrigues SV, Thakur SL. The antiplaque efficacy of pomegranate mouthrinse. *Quintessence Int*. 2011;42:29–36.
33. Jurenka J. Therapeutic applications of pomegranate (*Punica granatum* L.): a review. *Alternative medicine review*. 2008 Jun 1;13(2) 128-144.
34. Anand KM, Goyal R, Bhat SGGS, Kamath S, Anand KM, Aggarwal M, et al. A novel anti-oxidant lemon grass oil mouthwash- a clinical trial. *Asian J Exp Biol Sci*. 2011;2:482–486
35. Warad SB, Kolar SS, Kalburgi V, Kalburgi NB. Lemongrass essential oil gel as a local drug delivery agent for the treatment of periodontitis. *Ancient Science of life*. 2013 Apr;32(4):205-211.