International Journal of Herbal Medicine
Available online at www.florajournal.com

E-ISSN: 2321-2187
P-ISSN: 2394-0514
www.florajournal.com
IJHM 2022; 10(4): 10-16
Received: 06-05-2022
Accepted: 07-06-2022

Bharti Chaudhry
Associate Professor, Department of Botany, Ramjas College, University of Delhi, Delhi, India

Corresponding Author:
Bharti Chaudhry
Associate Professor, Department of Botany, Ramjas College, University of Delhi, Delhi, India

Relevance of traditional herbal interventions for oral health and prevention of periodontitis and dental caries

Bharti Chaudhry

Abstract
Oral health is an integral part of overall health and well-being. The human oral cavity harbors diverse and unique communities of microbes. Oral diseases are chronic and progressive in nature. Periodontitis and dental caries are the two most prevalent oral health diseases that progress with age and despite advancements, continue to be major public health issues. Aging is accompanied by an altered immune function and dysbiosis in the oral microbiome. The increased resistance of pathogenic bacteria to antibiotics as well as the adverse effects of antibacterial agents and chemotherapeutics used in dentistry, are leading to a resurgence of traditional, herbal products. Many recent experimental studies on animal models, clinical trials and *in-vitro* studies, corroborate the therapeutic potential of *Curcuma longa*, *Glycyrrhiza glabra*, *Camellia sinensis*, *Terminalia chebula*, *Phyllanthus emblica* and *Aloe vera*, as alternatives or adjuncts to non-surgical conventional treatments for improvement of periodontal parameters and dental caries prophylaxis. The review article is intended to increase awareness about the impact of oral diseases and the efficiency of natural antibacterial, anti-inflammatory agents in inhibiting the progression of oral diseases.

Keywords: Periodontitis, gingivitis, dental caries, alveolar bone loss, antibiotic resistance, turmeric, liquorice, green tea, chebulic myrobalan, Indian gooseberry, Indian Aloe

1. Introduction
The human oral microbiome is one of the most diverse and unique communities of microbes in the human body. Periodontitis (Gum disease) and dental caries (Tooth decay) are the two most prevalent oral health diseases that increase steadily with age and continue to be major public health issues. Aging is accompanied by an altered immune function and dysbiosis in the oral microbiome with a progressive shift towards pro-inflammatory status [1]. A balanced oral microbiome is important for the maintenance of oral health and symbiosis. The saliva plays an essential role in maintaining the ecological equilibrium of the oral microbiota. The saliva buffers the pH in the bacterial bio-film to near neutral, creating an environment conducive to the growth of oral bacteria that are beneficial to the host [2]. The salivary gland dysfunction disrupts the natural balance of the oral microbiome leading to dysbiosis and associated risks of gingivitis, caries and oral fungal infections [3]. Dental caries and periodontitis are two contrasting infections with supragingival and subgingival medical implications respectively [4]. The process of dental caries involves bacterial adherence to the tooth surface, dental plaque formation and localized demineralization of tooth enamel by acids of bacterial origin, leading to the destruction of enamel and dentine. The main causal organism in cariogenic process is *Streptococcus mutans* (A facultative anaerobic gram-positive bacterium), that readily colonizes the human oral cavity because of its ability to survive in an acidic environment and form bacterial biofilms (Microbial aggregates enmeshed in an extracellular polymer matrix of exopolysaccharides, proteins and nucleic acids). Other species like *Streptococcus sobrinus*, *Lactobacillus acidophilus* and *Actinomyces* are also implicated in the pathogenesis of tooth decay.
Periodontitis, on the other hand, affects the supporting structures of teeth, leading to periodontal pockets, gingival bleeding, receding gums, tooth and alveolar bone loss. Traditional clinical periodontal diagnostic parameters used include probing depth, bleeding on probing, plaque index, clinical attachment levels and radiographs to assess alveolar bone level. The pathogenesis of periodontitis involves complex dynamic interactions between specific bacterial pathogens and destructive host immune responses [5-7]. Other patient-specific risk factors include smoking, stress, diabetes mellitus, socio-economic factors and food habits [8]. Gingivitis is the first plaque induced inflammatory stage that progresses to periodontitis if left untreated.

Porphyromonas gingivalis, *Prevotella intermedia*, *Tannerella forsythia*, *Aggregatibacter actinomycetemcomitans* are the main etiological agents in periodontitis (Gram-negative, anaerobic, pathogenic bacteria). Species in the red-complex (*P. gingivalis*, *T. forsythia* and *Treponema denticola*) are associated with deep periodontal pockets and bleeding on probing [7, 9]. Inflammation in gingiva and other periodontal tissues is the major characteristic of chronic periodontitis. The immune and inflammatory response of the host leads to irreversible destruction of periodontium tissue (alveolar bone and periodontal ligament). The lipopolysaccharides of dental plaque bacteria induce production of inflammatory cytokines and matrix metalloproteinases (MMPs) which destroy the extracellular matrix and are critical in developing periodontitis [9]. The risk of breakdown of collagen fibres and bone loss tends to increase in patients with inflammatory conditions.Production of elevated inflammatory cytokines and high mobility group box I (HMGB1) protein are associated with chronic periodontitis [6]. Salivary TNF- α (Tumour necrosis factor-alpha), an inflammatory cytokine is a potential marker of periodontal destruction. Inflammatory cytokines perturb bone homeostasis through increased bone resorption by osteoclasts and inhibiting bone formation by osteoblasts. Dental caries treatment include restorations or fillings, crowns and root canal treatment. The gold standards for conventional non-surgical periodontal therapy include scaling for gingivitis and scaling and root planing for periodontitis. The adjunctive therapies include systemic antibiotics like amoxicillin, azithromycin, metronidazole, doxycycline and locally delivered anti-microbials like chlorhexidine and cetylpyridinium chloride to enhance the efficacy of periodontal therapy.

2. Relevance of herbal interventions

Oral diseases impose serious health and economic burdens, particularly in low-income and middle-income countries, greatly reducing the quality of life for those affected [10]. The study of Global Burden of Disease, 2019 [11] estimated that oral diseases affect close to 3.5 billion people worldwide and untreated dental caries is the most common oral health condition. Also, severe periodontal diseases have been estimated to affect around 14% of the global adult population, representing more than one billion cases world-wide. The high prevalence of dental caries and periodontitis, the increasing resistance of pathogenic bacteria to antibiotics and the adverse effects of antibacterial agents and chemotherapeutics used in dentistry, are leading to a resurgence of traditional, herbal products such as oral medicines, dentifrices, topical gels, gum oils, mouthwashes and intra-root canal medications. Chlorhexidine, commonly used for prevention of dental plaque, has been associated with side-effects like mouth irritation, metallic taste, tooth staining, alteration of oral microbiota and may even be cytotoxic to periodontal ligament cells. In addition, the oral cavity is a passage for the pathogenic bacteria to enter the bloodstream and due to its high vascularity, a direct or indirect association has been found between oral microbiome and cardiovascular diseases/atherosclerosis, diabetes and insulin resistance, gastrointestinal and colorectal cancer, respiratory tract infections, Alzheimer's disease and adverse pregnancy outcomes [12, 13]. Medicinal plants in Indian Traditional systems like Ayurveda have long been associated with oral health and dental hygiene. Herbal products are traditional, safer, efficient and economical, and can prove to be powerful alternatives or adjuncts to synthetic chemicals. The potent antioxidant, anti-inflammatory, antibacterial, antiviral, astringent properties of plants can play a significant role in dental caries prophylaxis and improvement of periodontal parameters. The growth of bacterial biofilms is associated with an increase in antibiotic resistance. Traditional plants can inhibit the growth of oral pathogens, reduce the dental plaque or the development of biofilms. The article is intended to give an update of a few selected plants that have exhibited significant therapeutic potential for prevention and progression of dental caries and periodontitis in the recent years, as evidenced by *in vitro*, animal and clinical studies.

2.1*Curcuma longa* (Zingiberaceae)

Curcuma longa, commonly called as Turmeric is a perennial herb, native to tropical South Asia. Curcumin (Diferuloylmethane) is the most active constituent in the rhizome. The potent antioxidant, anti-inflammatory properties and therapeutic effects of curcumin have been extensively reviewed for metabolic disorders, neurodegenerative, cardiovascular and neoplastic diseases [14, 15]. Many recent studies have demonstrated the therapeutic potential of curcumin in the treatment of Periodontitis and dental caries.

2.1.1 Dental caries

The key to prevent tooth decay are effective eradication of cariogenic biofilms and the pathogenic microbes within it. In an *in-vitro* study, curcumin was found to suppress *Streptococcus mutans* adherence to human tooth surfaces as well as extracellular matrix proteins (Glass surface coated with collagen and fibronectin) [16]. The inhibitory effects of curcumin on metabolism and biofilm function in *Streptococcus mutans* have been evaluated using a *vitro* biofilm model in an artificial oral environment. Curcumin was found to reduce the biofilm metabolism from 5 minutes to 24 hours and inhibited the quantity of live bacteria and total bacteria in both short term and long term, indicating the potential of curcumin to reduce the pathogenic traits of *Streptococcus mutans* [17].

2.1.2 Periodontitis

A meta-analysis study concluded that curcumin as an adjunct to Non-surgical Periodontal treatment (NPT) demonstrates powerful anti-inflammatory efficiency in terms of reducing GI (Gingival index) and SBI (Sulcus bleeding index) as compared with NPT alone (Zhang *et al.*, 2022) [18]. Curcumin has been reported to show similar efficiency as chlorhexidine in reducing probing pocket depth, clinical attachment loss, GI and Pl (Plaque index) in a meta-analysis study involving four hundred twenty patients [19]. Significant reduction in PI, GI, probing depth (PD) and gain in clinical attachment level was observed with curcumin gel as an adjunct to subgingival scaling and root planing in thirty patients with chronic localized or generalized periodontitis [20]. The efficiency of 2% curcumin with nanocarrier as a local drug delivery in the treatment of periodontal pockets has been reported in forty-five chronic periodontitis patients with 5-7 mm pocket depth, comparable to 1% chlorhexidine gel [21]. Microbiological analysis of sublingual plaque samples have also reported significant reduction in the levels of three periodontal pathogens, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis* and *Tannerella forsythia* [21]. The homeostasis of bone is maintained by a balance between bone resorption by osteoclasts and bone formation by osteoblasts [22]. Local administration of curcumin- loaded nanoparticles resulted in significant inhibition of inflammatory bone

resorption in experimental rat models of periodontal disease, associated with a significant reduction in the number of osteoclast and inflammatory infiltrates [23]. Curcumin has been shown to attenuate the production of IL-β and TNF-α (Pro-inflammatory cytokines in periodontal inflammatory degradation) in rat gingival fibroblasts induced by lipopolysaccharide *in vitro*, indicating the potential of curcumin in modulating immune responses associated with periodontitis [24]. Further, *in vivo* histological and micro-CT (Microcomputed Tomography) studies in rat experimental periodontitis corroborated that curcumin significantly reduced gingival inflammation and modulated collagen fibre and alveolar bone loss [24]. In a clinical study on periodontitis patients, local application of curcumin gel resulted in significant reduction of clinical periodontal parameters, pro-inflammatory mediators (TNF-α and IL-1β) and increased levels of serum micronutrients, Zinc and Magnesium, essential nutrients for periodontal tissue vitality [25].

2.2 *Glycyrrhiza glabra* (Fabaceae)

The roots of *Glycyrrhiza glabra*, commonly called as Licorice or Liquorice, have long been used in the Indian Traditional system of Ayurveda as a demulcent to soothe both respiratory and gastrointestinal symptoms, curative of gastric and duodenal ulcers, chronic hepatitis, liver cirrhosis, and as an expectorant. Glycyrrhizin and glycyrrhizic acid have shown inhibitory action on growth and cytopathology of numerous RNA and DNA viruses including hepatitis A & C, herpes zoster, herpes simplex and HIV [26]. Various forms of liquorice are used as candies, liquid extracts, lollipops, tablets and capsules worldwide in countries like Malaysia, Japan and United States of America [27].

2.2.1 Dental Caries and Endodontitis

Alcoholic licorice root extract has shown inhibitory effects against *Streptococcus mutans* and *Lactobacillus acidophilus* superior to chlorhexidine [28]. Hu *et al.* [29] developed sugar-free licorice lollipops that exhibited significant reduction of cariogenic bacteria in the oral cavity (Salivary *Streptococcus mutans*) of 26 human subjects at different ages after a brief application of these lollipops, twice a day for ten days. The antibacterial effects of licorice are attributed to inhibition of glucosyltransferase activity of *Streptococcus mutans*, which is responsible for the formation of insoluble glucans in biofilms. A systematic review to assess the efficacy of Licorice lollipops in reducing dental caries in children concluded promising results in decreasing *Streptococcus mutans* counts in the saliva [30]. The efficacy of an herbal Licorice mouth wash vs chlorhexidine mouthwash on salivary *Streptococcus mutans* was evaluated in a randomized clinical trial of high caries risk patients. Licorice mouth wash was found to be as effective as chlorhexidine in inhibition of *Streptococcus* bacterial counts. Besides, licorice stimulates salivary flow, raises salivary pH in high risk caries patients, supporting its use as natural, alternative dental caries prophylaxis to synthetic chemoprophylactic agents [31].

The most common irrigants used in endodontitis (Inflammation of dental pulp) are sodium hypochlorite and chlorhexidine which show limited ability to eradicate *Enterococcus faecalis* from infected root canal, resulting in failure of root canal therapy. The inhibitory activity of licorice was studied against *Enterococcus faecalis* cultures and its biofilms, isolated from the root canal of a patient exhibiting repeated root canal treatment failure. The study concluded that *Enterococcus faecalis* biofilms were highly susceptible to licorice at 24 hours and 48 hours at concentrations of 3 and 4 gms [32], indicating its potential as a root canal irrigant and medicament.

2.2.2 Periodontitis

Glycyrrhizin, the major constituent of *Glycyrrhiza glabra*, suppresses inflammatory activities in chronic periodontitis rats, significantly reduces HMGBI and represents a promising molecule for controlling chronic periodontitis [6]. The level of inflammatory cytokines including TNF- α, IL- 1β and IL-6 in gingival crevicular fluid and gingival tissue of chronic periodontitis rats, were found to be significantly reduced, after administration of Glycyrrhizin.

In a randomized clinical control trial on 104 participants with gum paint prepared from *Glycyrrhiza*, pre-intervention and post- intervention scores were analyzed and significant improvement was seen in periodontal parameters such as gingival bleeding, depth of periodontal pockets and sites of loss of attachment [33]. In another *in vivo* experimental study on 39 patients with mild to moderate chronic periodontitis, the effects of adjunctive low dose antibiotic doxycycline and licorice therapy on gingival crevicular fluid matrix metalloproteinase-8 levels were compared and it was found that the decrease in mean of metalloproteinase-8 levels was higher in licorice group than doxycycline group, and that licorice can be as useful as doxycycline for the treatment of periodontitis and other inflammatory diseases [53].

Licorice has shown promising results not only for periodontitis and caries, but also aphthous ulcers and oral cancer [27] and has been labelled as GRAS (Generally Regarded as Safe) by Food and Drug Administration (FDA).

2.3 *Camellia sinensis* (Theaceae)

Camellia sinensis, commonly called as Tea is the most popular beverage used worldwide. While Green tea is unfermented, black tea is fully fermented. Green tea leaves have higher amounts of polyphenols, called as catechins, that are well known to protect against cardiovascular disease, neurodegenerative diseases like Alzheimer's, Parkinson's diseases, and cancer. Epigallocatechin-gallate (EGCG) are the most abundant catechins in green tea responsible for its powerful antioxidant, antimicrobial and anti-inflammatory properties.

2.3.1 Dental caries Protection

Catechins, potent antioxidants in green tea promote oral health, aid in killing and suppressing cavity -causing bacteria, lower the acidity of saliva, and hinder the growth of bacterial enzymes, thus reducing plaque formation responsible for dental caries and tooth decay. An *in vitro* study of green tea extract on clinically isolated cariogenic and periodontopathic bacteria exhibited strong antibacterial activity on *Streptococcus mutans*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *and Prevotella intermedia* and concluded that green tea may be used in mouthwashes and dentifrices for prevention of both dental caries and periodontitis diseases [35].

2.3. 2 Periodontitis and Gum Health

Green tea promotes periodontal health by reducing inflammation, preventing bone resorption and limiting the growth of bacteria associated with periodontitis. In a meta-analysis study, it was concluded that adjunctive topical application of green tea catechins may be beneficial for reduction of probing pocket depth as compared to scaling and

root planning alone [36]. The effect of Green tea extract on bone metabolism of ovariectomized rats with experimental periodontitis was evaluated by histological, morphological and microtomographic parameters in mandible and femur samples. The study concluded that green tea rich in epigallocatechin gallate can have positive and protective effects on bone loss in periodontal disease and osteoporosis by reducing inflammation and inducing apoptotic cell death of osteoclasts [37].

A meta-analysis study of the evaluation of clinical efficiency of green tea containing mouthwash on dental plaque and gingival inflammation, concluded Green tea to be as effective as chlorhexidine without the commonly experienced side-effects of chlorhexidine [38]. In a recent randomized controlled clinical trial on 15 patients with moderate to severe chronic periodontitis, EGCG aqueous solution delivered as an adjunctive modality to scaling and root planing, resulted in a significant improvement of bleeding index, although probing depth and clinical attachment were found to have no additional benefit [39].

2.4 *Terminalia chebula* (Combretaceae)

Terminalia chebula, commonly called as Chebulic Myrobalan is a medium-sized to large deciduous tree widely distributed in India with antibacterial, anthelmintic, antitussive, antiviral, laxative, antioxidant, antidiabetic, retinoprotective, neuroprotective, cardioprotective and hepatoprotective properties. It has been used in Ayurveda for asthma, bleeding piles, gout, ophthalmia, dental caries, bleeding gums, ulcers in oral cavity, chronic diarrhoea, chronic cough, allergies, renal calculi, skin diseases, heart diseases, wound infections, ascites, urinary tract infections, diabetes and as a digestive and liver stimulant. It forms an important ingredient of Ayurvedic formulation, *Triphala* which is a herbal preparation of the dried powder of three fruits from the plants *Phyllanthus emblica*, *Terminalia chebula* and *Terminalia bellirica* [26]. The major phytochemicals include Tannins-Chebulic acid, Chebulinic acid, chebulagic acid, punicalagin, gallic acid, ellagic acid, corilagin; and anthraquinones.

2.4.1 Dental Caries

Many clinical trials of the fruit extracts of *Terminalia chebula*/Triphala as Mouthwash preparation have demonstrated reduced plaque accumulation and gingival inflammation comparable to chlorhexidine [40, 41]. Ethanolic extracts of the fruits of *Terminalia chebula* were found to be effective antibacterial agent against *Streptococcus mutans*, and dental caries through the inhibition of glucan formation and related gene expression of glycosyltransferase B, glycosyltransferase C, glycosyltransferase D and fructosyltransferase [42]. An *in vitro* experimental study on evaluation of anti-adherence and antimicrobial properties of *Terminalia chebula* and *Glycyrrhiza glabra* extracts on *Streptococcus mutans*, revealed inhibitory action of both the plants but a higher anti-adherence effect of *Terminalia chebula* than *Glycyrrhiza glabra* [43].

2.4.2 Periodontitis

In vitro experimental studies of treatment with ethanolic extract of fruits of *Terminalia chebula* have demonstrated suppression of the growth of dental plaque bacteria, modulation of the dental plaque bacteria-induced inflammatory cytokines and proteases involved in gingivitis and periodontitis disease, as well as inhibition of osteoclast formation and bone resorption [9]. The anti-inflammatory effect was determined by molecular biological analysis of the dental plaque bacteria-mediated culture cells and prevention of osteoclastic bone resorption by osteoclast formation and pit formation assays. The study concluded that *Terminalia chebula* extract can effectively abolish dental plaque bacteria-lipopolysaccharides-induced osteoclastic bone resorption *in vitro* and can be a promising antibacterial and anti-oral inflammatory agent capable of preventing the development of gingivitis and periodontitis.

2.5 *Phyllanthus emblica* (Phyllanthaceae)

Phyllanthus emblica, commonly called as Indian Gooseberry or Amla is much revered in Ayurveda for its antioxidant, anti-inflammatory, antipyretic, analgesic, antitussive, adaptogen, anti-carcinogenic, cardioprotective, gastroprotective, hepatoprotective, nephroprotective and neuroprotective properties. The fruits are an excellent source of vitamin C and hydrolysable tannins like emblicanin A and B, punigluconin, pendunculagin; Gallic acid, ellagic acid, Chebulinic acid; and flavonoids, quercitin and kaempferol. Amla nourishes the brain and mental functioning, supports the heart and blood circulation, strengthens the lungs and vision, reduces macular degeneration, increases skin health, promotes healthier bones, teeth, nails, hair, enhances vitality, immunity and fertility[15].

2.5.1 Dental caries

The effect of crude extract and ethanolic fractions of *Phyllanthus emblica* fruits were analyzed against *Streptococcus mutans* for its cariogenic properties, including acid production, biofilm formation, cell surface hydrophobicity, glucan production, biofilm architecture and revealed promising results by inhibiting virulence factors of *Streptococcus mutans* [44]. In a short term study involving twenty healthy young adults, the use of sugar-free chewing gum containing the fruit extract of amla, was found to be effective in altering the oral microbiome and decreasing the salivary levels of both *Streptococcus mutans* and *Porphyromonas gingivalis* [45].

2.5.2 Periodontitis

In an experimental study, subgingival application of indigenously developed 10% *Phyllanthus emblica* sustained-release gel used as an adjunct to scaling and root planing, was found to be more effective in reduction of inflammation and periodontal destruction in patients with chronic Periodontitis when compared to scaling and root planing alone [46]. In a randomized controlled clinical trial, the effect of 10% *Phyllanthus emblica* irrigation as an adjunct to scaling and root planing was evaluated in a study population of sixty six patients with chronic periodontitis and compared with that of chlorhexidine. The study reported significantly greater reduction in inflammation and improved periodontal healing in deep pockets with *Phyllanthus emblica* than chlorhexidine [47].

2.6 *Aloe vera* (Asphodelaceae)

Aloe vera commonly called as Indian Aloe, is a perennial succulent with fleshy green leaves and exhibits several therapeutic properties including antibacterial, anti-inflammatory, antiviral, catharitic, anthelmintic, refrigerant, digestive, rejuvenative, aperient, adaptogen, anticancer, hepatoprotective and skin healer.

2.6.1 Dental caries and Periodontitis

The efficacy of *Aloe vera* mouth wash has been reported in

improving plaque, gingival and gingival bleeding indices, similar to Chlorhexidine mouthwash in triple-blind trials in children of age 8 to 12 years [48]. *Aloe vera* tooth gel was found to be equally effective as two other commercial toothpastes in inhibiting the growth of *Streptococcus mutans*, *Lactobacillus acidophilus*, *Prevotella intermedia*, *Enterococcus faecalis*, and *Peptostreptococcus anaerobius* [49]. In a clinical study involving 96 participants, using 4 day plaque regrowth methodology, the antiplaque and antibacterial efficacy of commercially available *Aloe vera* mouthwash was found to be similar to that of cetylpyridinium chloride and significantly better than that of hydrogen peroxide mouthwash, supporting use of *Aloe vera* as an alternative to chemically formulated mouthwashes [50], although lower than chlorhexidine. The potent antibacterial effects of *Aloe vera* have been attributed to anthraquinones and aloin derivatives that facilitate cellular invasion.

In a clinical study of 15 patients, subgingival application of *Aloe vera* gel as a medicament in periodontal pocket, resulted in improvement of periodontal condition in terms of significant reduction in pocket depth when compared to controls and reduction in gingival index, which has been attributed to its potent antioxidant, anti-inflammatory and wound-healing properties [51].

3. Conclusions

Oral health can no longer be ignored as strong interrelationships exist between oral health, inflammation and systemic diseases. The emergence of new genomic technologies and bioinformatics tools have unravelled the complexities of oral microbiome and their role in health and disease. Periodontal pathogens can have direct or indirect impact on non-oral systemic diseases. Several oral pathogens have been implicated in cardiovascular diseases and lung infections. Awareness and communication of knowledge regarding prevention and treatment of oral diseases is extremely significant in a country like India with a large ageing population, low levels of awareness, poor access to dental care, and high cost of oral diseases treatment. Traditional plants including Turmeric, Licorice, Green Tea, Indian Gooseberry, Chebulic Myrobalan and Indian Aloe are a source of natural, antibacterial agents, easily accessible, cost-effective, safer and can provide promising alternative therapy in the form of oral medicines/ capsules, mouthwash, dentifrices, gels, gum paints for long term use without the ill effects of antibiotics and synthetic chemicals used in dentistry. As an adjunct to non-surgical treatments, they can be effective in inhibition of progression of dental caries and periodontitis. The synergistic interactions of several secondary metabolites present in medicinal plants result in pleiotropic effects and may also be effective in management of non-oral systemic diseases. However, the interactions between the oral microbiome and host immune response are very complex and many more experimental studies and clinical trials are required to determine the efficacy, safety and the optimum dosage of natural agents. Besides, vitamin supplements, particularly vitamin D that helps in calcium absorption and bone remodeling may help in protection of periodontal tissues [52]. Good oral hygiene, regular dental visits, a nutritive balanced diet, limiting sugary food and drinks, abstinence from smoking and tobacco are lifestyle interventions that must be adopted.

4. References

1. Preshaw PM, Henne K, Taylor JJ, Valentine RA, Conrads G. Age-related changes in immune function (Immune senescence) in caries and periodontal diseases: a systematic review. J Clin Periodontol. 2017 Mar;44 Suppl 18:S153-S177.
2. Marsh PD, Do T, Beighton D, Devine DA. Influence of saliva on the oral microbiota. Periodontol 2000. 2016 Feb;70(1):80-92.
3. Lynge Pedersen AM, Belstrøm D. The role of natural salivary defences in maintaining a healthy oral microbiota. J Dent. 2019 Jan;80(Suppl1):S3-S12.
4. Loesche W. Dental caries and periodontitis: contrasting two infections that have medical implications. Infect Dis Clin North Am. 2007 Jun;21(2):471-502.
5. Cekici A, Kantarci A, Hasturk H, Van Dyke TE. Inflammatory and immune pathways in the pathogenesis of periodontal disease. Periodontol 2000. 2014 Feb;64(1):57-80.
6. Sun Y, Zhao B, Li Z, Wei J. Beneficial Effects of Glycyrrhizin in Chronic Periodontitis Through the Inhibition of Inflammatory Response. Dose Response. 2020 Sep 10;18(3):1559325820952660.
7. Kwon T, Lamster IB, Levin L. Current Concepts in the management of periodontitis. International Dental Journal. 2021;71(6):462-476.
8. Clarke NG, Hirsch RS. Personal risk factors for generalized periodontitis. J Clin Periodontol. 1995 Feb;22(2):136-45.
9. Lee J, Nho YH, Yun SK, Hwang YS. Use of ethanol extracts of *Terminalia chebula* to prevent periodontal disease induced by dental plaque bacteria. BMC Complement Altern Med. 2017;17(1):113.
10. Peres MA, Macpherson LMD, Weyant RJ, Daly B, Venturelli R, Mathur MR, *et al*. Oral diseases: A global public health challenge. Lancet. 2019 Jul 20;394(10194):249-260.
    DOI: 10.1016/S0140-6736(19)31146-8. Erratum in: Lancet. 2019 Sep 21;394(10203):1010. PMID: 31327369.
11. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019). Seattle: Institute of Health Metrics and Evaluation (IHME); 2020. Available from http://ghdx.healthdata.org/gbd-results-tool.
12. Bui FQ, Almeida-da-Silva CLC, Huynh B, Trinh A, Liu J, Woodward J, Asadi H, *et al*. Association between periodontal pathogens and systemic disease, Biomedical Journal. 2019;42(1):27-35.
13. Willis, Jesse R, Toni Gabaldón. The Human Oral Microbiome in Health and Disease: From Sequences to Ecosystems. Microorganisms. 2020;8(2):308.
14. Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. Foods. 2017 Oct 22;6(10):92.
15. Chaudhry B. Key Rasayana Plants of Ayurveda. Env. & We, Int. J Sci. Tech. 2021;16:53-73.
16. Song J, Choi B, Jin EJ, Yoon Y, Choi KH. Curcumin suppresses Streptococcus mutans adherence to human tooth surfaces and extracellular matrix proteins. Eur J Clin Microbiol Infect Dis. 2012 Jul;31(7):1347-52.
17. Li B, Li X, Lin H, Zhou Y. Curcumin as a Promising Antibacterial Agent: Effects on Metabolism and Biofilm Formation in *S. mutans*. Biomed Res Int. 2018 Feb 28;2018:4508709.
18. Zhang Y, Huang L, Zhang J, De Souza Rastelli AN, Yang J, Deng D. Anti-inflammatory efficacy of curcumin as an adjunct to Non-surgical Periodontal treatment: A

systematic review and meta-analysis Front. Pharmacol. 2022;13:808460.
19. Zhang Y, Huang L, Mazurel D, Zheng H, Yang J, Deng D. Clinical efficacy of curcumin versus chlorhexidine as an adjunct to scaling and root planing for the treatment of periodontitis: A systematic review and meta-analysis. Phytother Res. 2021 Nov;35(11):5980-5991.
20. Anuradha BR, Bai YD, Sailaja S, Sudhakar J, Priyanka M, Deepika V. Evaluation of Anti-Inflammatory Effects of Curcumin Gel as an Adjunct to Scaling and Root Planing: A Clinical Study. J Int. Oral Health. 2015 Jul;7(7):90-3.
21. Guru SR, Reddy KA, Rao RJ, Padmanabhan S, Guru R, Srinivasa TS. Comparative evaluation of 2% turmeric extract with nanocarrier and 1% chlorhexidine gel as an adjunct to scaling and root planing in patients with chronic periodontitis: A pilot randomized controlled clinical trial. J Indian Soc Periodontol. 2020 May-Jun;24(3):244-252.
22. Tanaka Y, Nakayamada S, Okada Y. Osteoblasts and osteoclasts in bone remodeling and inflammation. Curr Drug Targets Inflamm Allergy. 2005 Jun;4(3):325-8.
23. Zambrano LMG, Brandao DA, Rocha FRG, Marsiglio RP, Longo IB, Primo FL, *et al*. Local administration of curcumin-loaded nanoparticles effectively inhibits inflammation and bone resorption associated with experimental periodontal disease. Sci Rep. 2018;8(1):6652.
24. Xiao CJ, Yu XJ, Xie JL, Liu S, Li S. Protective effect and related mechanisms of curcumin in rat experimental periodontitis. Head Face Med. 2018;14(1):12.
25. Mohammad CA, Ali KM, Sha AM, Gul SS. Antioxidant Effects of Curcumin Gel in Experimental Induced Diabetes and Periodontitis in Rats. Biomed Res Int. 2022;2022:7278064.
26. Chaudhry B. A Handbook of Common Medicinal Plants Used in Ayurveda, Kojo Press, India, 2019.
27. Sidhu P, Shankargouda S, Rath A, Hesarghatta Ramamurthy P, Fernandes B, Kumar Singh A. Therapeutic benefits of liquorice in dentistry. J Ayurveda Integr Med. 2020 Jan-Mar;11(1):82-88.
28. Ajagannanavar SL, Battur H, Shamarao S, Sivakumar V, Patil PU, Shanavas P. Effect of aqueous and alcoholic licorice (*Glycyrrhiza glabra)* root extract against *Streptococcus mutans* and *Lactobacillus acidophilus* in comparison to chlorhexidine: an *in vitro* study. J Int. Oral Health. 2014 Jul;6(4):29-34.
29. Hu CH, He J, Eckert R, Wu XY, Li LN, Tian Y, *et al*. Development and evaluation of a safe and effective sugar-free herbal lollipop that kills cavity-causing bacteria. Int J Oral Sci. 2011 Jan;3(1):13-20.
30. Nuvvula S, Nunna M, Almaz ME, Mallineni SK. Efficacy of Licorice Lollipops in Reducing Dental Caries in a Paediatric Population: A Systematic Review. Oral Health Prev Dent. 2020;18(1):97-102.
31. Helmy N, Hafez S, Farid A. Efficacy of Licorice on Salivary *Streptococcus mutans* Levels vs Chlorhexidine Mouthwash in High Caries Risk Patients: A Randomized Clinical Trial. J Contemp Dent Pract. 2021 Aug 1;22(8):914-921.
32. Chittrarasu M, Sathyanarayana SS, Ahamed S, Aberna A, Bhavani S, Rajaraman G. Antimicrobial efficacy of liquorice against *Enterococcus faecalis* biofilms in various concentrations at time-dependent variables: An *in vitro* study. J Conserv Dent. 2019 Jan-Feb;22(1):7-11.
33. Madan S, Kashyap S, Mathur G. *Glycyrrhiza glabra*: An efficient medicinal plant for control of periodontitis - A randomized clinical trial. J IntClin Dent Res Organ. 2019;11(1):32.
34. Turaeva FA. Comprehensive treatment of generalized periodontitis using autotrombocytic mass. Pharma Innovation. 2020;9(6):599-600.
35. Araghizadeh A, Kohanteb J, Fani MM. Inhibitory activity of green tea (*Camellia sinensis*) extract on some clinically isolated cariogenic and periodontopathic bacteria. Med Princ Pract. 2013;22(4):368-72.
36. Gartenmann SJ, Weydlich YV, Steppacher SL, Heumann C, Attin T, Schmidlin PR. The effect of green tea as an adjunct to scaling and root planing in non-surgical periodontitis therapy: A systematic review. Clin Oral Investig. 2019 Jan;23(1):1-20.
37. Vargas-Sanchez PK, Pitol DL, de Sousa LG, Beloti MM, Rosa AL, Rossi AC, Siéssere S, Bombonato-Prado KF. Green tea extract rich in epigallocatechingallate impairs alveolar bone loss in ovariectomized rats with experimental periodontal disease. Int. J Exp. Pathol. 2020 Dec;101(6):277-288.
38. Gartenmann SJ, Severine L, Steppacher SL, Weydlich YV, Heumann C, Thomas Attin T, *et al*. The Effect of Green Tea on plaque and gingival inflammation: A systematic review, J Herb Med. 2020;21:100337.
39. Zeng J, Wang Y, Yuan Q, Luan Q. The effect of (-)-epigallocatechin gallate as an adjunct to non-surgical periodontal treatment: A randomized clinical trial. Trials. 2022 May 3;23(1):368. Doi:10.1186/s13063-022-06298-6.
40. Gupta D, Gupta RK, Bhaskar DJ, Gupta V. Comparative evaluation of *Terminalia chebula* extract mouthwash and chlorhexidine mouthwash on plaque and gingival inflammation-4-week randomised control trial. Oral Health Prev Dent. 2015;13(1):5-12. Erratum in: Oral Health Prev Dent. 2016;14(3):274.
41. Naiktari RS, Gaonkar P, Gurav AN, Khiste SV. A randomized clinical trial to evaluate and compare the efficacy of triphala mouthwash with 0.2% chlorhexidine in hospitalized patients with periodontal diseases. J Periodontal Implant Sci. 2014 Jun;44(3):134-40.
42. Nam YJ, Hwang YS. Antibacterial and antioxidant effect of ethanol extracts of *Terminalia chebula* on *Streptococcus mutans*. ClinExp Dent Res. 2021 Dec;7(6):987-994.
43. Bhadoria N, Gunwal MK, Suryawanshi H, Sonarkar SS. Antiadherence and antimicrobial property of herbal extracts (*Glycyrrhiza glabra* and *Terminalia chebula*) on *Streptococcus mutans*: An *in vitro* experimental study. J Oral Maxillofac Pathol. 2019 Jan-Apr;23(1):73-77.
44. Hasan S, Danishuddin M, Adil M, Singh K, Verma PK, Khan AU. Efficacy of *E. officinalis* on the cariogenic properties of *Streptococcus mutans*: A novel and alternative approach to suppress quorum-sensing mechanism. PLoS One. 2012;7(7):e40319.
45. Gao Q, Li X, Huang H, Guan Y, Mi Q, Yao J. The efficacy of a chewing gum containing *Phyllanthus emblica* fruit extract in improving oral health. Current Microbiol. 2018;75(5):604-610.
46. Grover S, Tewari S, Sharma RK, Singh G, Yadav A, Naula SC. Effect of Subgingivally Delivered 10% *Emblica officinalis* Gel as an Adjunct to Scaling and Root Planing in the Treatment of Chronic Periodontitis: A Randomized Placebo-controlled Clinical Trial. Phytother

Res. 2016 Jun;30(6):956-62.
47. Tewari S, Grover S, Sharma RK, Singh G, Sharma A. *Emblica officinalis* Irrigation as an Adjunct to Scaling and Root Planing: A Randomized Controlled Clinical Trial. J Dent Indones. 2018;25(1):15-23.
48. Alnouri DMA, Kouchaji C, Nattouf AH, Hasan MMA. Effect of *Aloe vera* mouthwash on dental plaque and gingivitis indices in children: A randomized controlled clinical trial. Pediatr Dent J. 2020;30(1):1-8.
49. George D, Bhat SS, Antony B. Comparative evaluation of the antimicrobial efficacy of *Aloe vera* tooth gel and two popular commercial toothpastes: An *in vitro* study. Gen Dent. 2009 May-Jun;57(3):238-41. PMID: 19819812.
50. Pattnaik N, Mohanty R, Satpathy A, Nayak R, Shamim R, Praharaj AK. *Aloe vera* mouthwashes can be a natural alternative to chemically formulated ones: A randomized-controlled trial, Journal of Taibah University Medical Sciences. 2022;17(3):424-432.
51. Bhat G, Kudva P, Dodwad V. *Aloe vera*: Nature's soothing healer to periodontal disease. J Indian Soc. Periodontol. 2011 Jul;15(3):205-9.
52. Varela-López A, Navarro-Hortal MD, Giampieri F, Bullón P, Battino M, Quiles JL. Nutraceuticals in Periodontal Health: A Systematic Review on the Role of Vitamins in Periodontal Health Maintenance. Molecules. 2018 May 20;23(5):1226.
53. Farhad SZ, Aminzadeh A, Mafi M, Barekatain M, Naghney M, Ghafari MR. The effect of adjunctive low-dose doxycycline and licorice therapy on gingival crevicular fluid matrix metalloproteinase-8 levels in chronic periodontitis. Dent Res J (Isfahan). 2013 Sep;10(5):624-9.