

## **PHYTOMEDICINE AND ITS INDISPENSABLE ROLE IN PLAQUE INDUCED DISEASES**

**Running Title: Phytochemicals: Emerging natural cure for periodontal diseases**

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### **ABSTRACT**

Medicinal plants have been used since centuries to prevent and treat various diseases in folk medicine due to their therapeutic effects. Herbs and their extracts have been found to possess potent anti-inflammatory, antioxidant and antimicrobial actions that reduce the periodontal inflammation. With progressing science we always want the positive results in less time, therefore allopathic medications has gained its popularity but their prolonged use could result in side effects and increased antimicrobial resistance. These limitations

encouraged the search of an alternative natural plant product for the treatment of plaque induced diseases. Literature search revealed few clinical trials on evaluation of clinical effectiveness of phytochemicals or herbs in the treatment of periodontal diseases. By this review attempt has been made to enlighten the future researchers about mechanism of action and therapeutic potential of various herbs such as neem , tulsi, curcumin, aloe vera etc in the reduction of dental plaque , plaque induced gingivitis and periodontitis.

Key words: ayurveda, herbs, phytomedicine, phytochemicals, plant extracts, plaque, periodontitis

## INTRODUCTION

Plaque related diseases particularly periodontitis is the most common infectious microbial disease encountered in the oral cavity. Periodontitis is a complex disease characterized by interactions of the biofilm with host inflammatory response thus resulting in loss of connective tissue attachment to teeth, a clinical feature that differentiates periodontitis from gingivitis.<sup>[1]</sup> *Aggregatibacter actinomycetemcomitans* has been implicated to cause aggressive periodontal disease. Other bacteria found in deep periodontal pockets include *T.denticola*, *T. socranskii* and *P. gingivalis* which are difficult to eradicate by conventional plaque control measures.<sup>[2]</sup> Now a days the clichés “Mouth is the mirror to the body” and “you cannot have good general health without good oral health” are gaining popularity. In context of this various epidemiological studies have found close association between poor oral health and cardiovascular diseases, diabetes mellitus, osteoporosis, preterm delivery, low birth weight babies and other systemic diseases and conditions.<sup>[3]</sup> Recent evidence suggests that oral infections and inflammatory mediators’ interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis

factor- $\alpha$  (TNF- $\alpha$ ) play an important role in initiation and progression of periodontal and associated systemic diseases.<sup>[4]</sup>

Mechanical plaque control is the primary recommended measure to prevent the onset of gingivitis and its progression to periodontitis but factors such as individual host response and presence of plaque retentive areas could affect the disease progression.<sup>[5]</sup> To overcome these limitations, chemotherapeutic agents such as oral antibiotics, antiseptic mouth washes, local drug delivery and host modulating agents have been used as adjuncts to the mechanical measures. Literature revealed that most of these chemotherapeutic agents have significant adverse effects and cause antimicrobial resistance on prolonged use.<sup>[6]</sup> Chlorhexidine (CHX) gluconate mouthwash is widely regarded as gold standard in plaque removal but its chronic usage has been reported to cause staining of teeth, tongue, taste alterations and plaque accumulation.<sup>7</sup> These drawbacks of allopathic medicine has encouraged the search of an alternative natural therapies for treatment of plaque related diseases.

Plant kingdom is full of bioactive compounds which have marvellous curing capacity. Herbal products of folk medicine have been used since centuries for the treatment of various ailments. Although dentists believes in allopathic medicine and proper dental procedures but with increasing curiosity in ayurveda and naturopathy with minimal side effects to maximum benefits researchers are moving towards botanical based medicines or phytomedicine .<sup>[1,7]</sup> In view of potential of phytochemicals as an effective antimicrobial agents, the present review discusses mechanism, advantages, clinical applications and beneficial effects of recent diverse herbs or phytomedicines on the development of biofilm and dental plaque and how these phytochemicals strike a balance between health and disease.

## **PHYTOCHEMICALS, OXIDATIVE STRESS AND PERIODONTAL DISEASES**

There have been advancements in chemotherapeutic agents but still there is need to overcome drug resistance and adverse effects of these agents. To the above consideration, several trials have focussed on the naturally

occurring plant products with wide range of biological activity that includes their antibacterial, anti-inflammatory, anti oxidant and anti proliferative properties.<sup>[8]</sup> Figure 1 classifies the phytochemicals based on their chemical structure.<sup>[9]</sup>

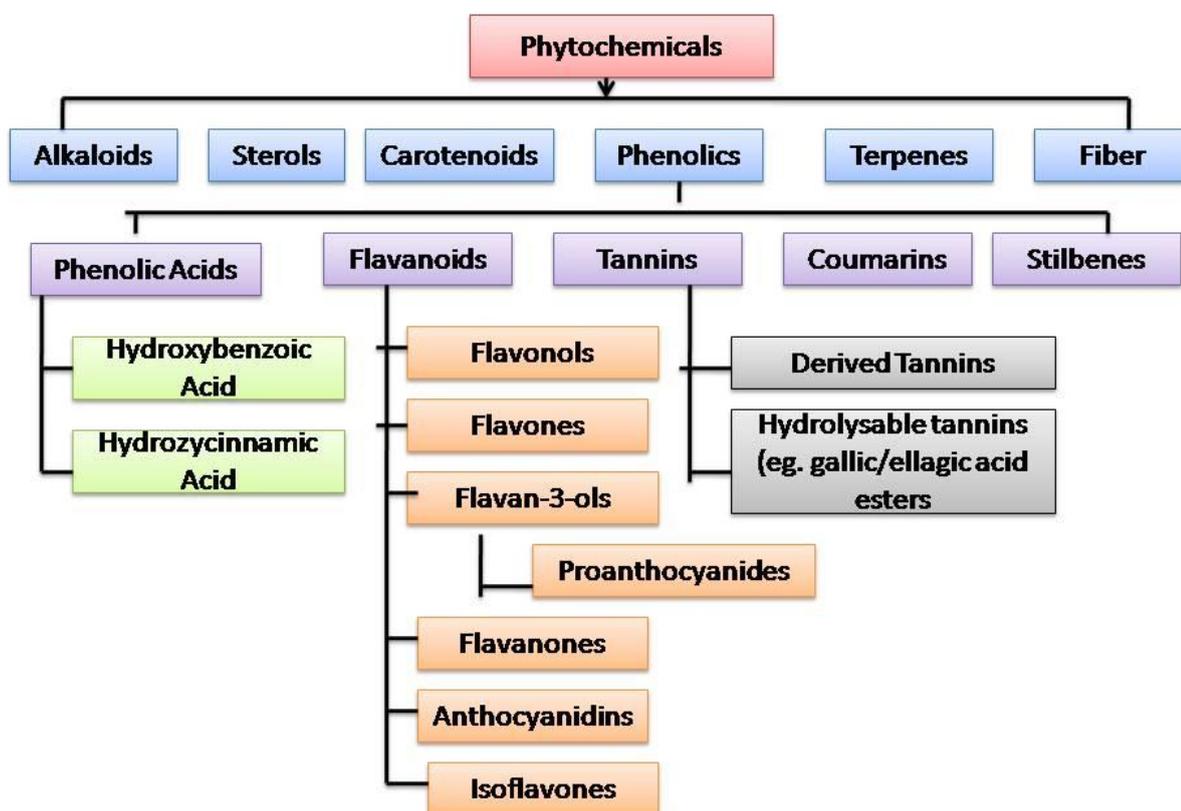


Figure 1 Classification of phytochemicals based on their chemical structure according to Liu RH<sup>[9]</sup>

It has been known since centuries that herbs and their extracts such as neem , aloevera , tulsi, Hawthorn, *Echinacea purpurea* etc have inherent potential to inhibit the growth of pathogenic bacteria thus reducing the periodontal problems. Hawthron is used for tightening gums as it is rich in bioflavonoid, *Echinacea* has been found to have good antimicrobial property , alovera has soothing effects on the gums and turmeric has best healing property.<sup>[8,9]</sup>

It is well known that progression of periodontal disease is caused by abnormal host response to predominantly gram negative anaerobic microorganisms within the subgingival biofilm. Periodontitis is characterized by excess production of free radicals or reactive oxygen species (ROS) by inflammatory cells chiefly polymorphonuclear neutrophils (PMNs) that induce oxidative stress resulting in periodontal breakdown and cell destruction.<sup>[10]</sup> Numerous studies have highlighted the role of ROS in the regulation of bone turnover and alveolar bone resorption with subsequent loss of teeth which is characteristic feature of periodontal disease.<sup>[10,11]</sup> Therefore, it is important to address the abnormal host response to prevent progression of periodontal disease and loss of teeth. Phytochemicals have protective effect on periodontal tissues by neutralizing ROS and nitrogen species thus controlling the periodontal destruction. Due to their unique antioxidant properties, these natural plant based products are gaining attention and are an active area of research. A literature search was performed using keywords such as “ayurveda”, “herbs”, “phytomedicine”, “phytochemicals”, “plant extracts” ‘plaque” and “periodontal diseases” using PubMed, Medline, EBESCO and Google Scholar. Most eligible articles were included in this review that highlights the potential benefits of phytomedicine in the management of periodontal diseases. Table 1 summarizes clinical trials conducted to elucidate the role of phytochemicals in the reduction of plaque related diseases.

| <b>Author (Year)</b>                  | <b>Aims and Objectives</b>  | <b>Phytochemical / Herb</b> | <b>Comparison</b>  | <b>Outcome</b>  |
|---------------------------------------|---|-----------------------------|--------------------|---|
| Naitkari S et al (2014) <sup>13</sup> | Comparison of efficacy of triphala mouthwash with 0.2% chlorhexidine in hospitalized periodontal disease patients | Triphala mouthwash          | 0.2% CHX gluconate | Triphala mouthwash is as effective antiplaque antigingivitis agent as 0.2 % CHX (p<0.0001). |

|  |   |  |                           |  |
|--|---|--|---------------------------|--|
| Kudalkar et al (2014) <sup>16</sup>      | To evaluate inhibitory effect of neem and aloe vera by MMP-2 and MMP 9 activity   | Neem 1500 µg<br><br>Aloe vera 1000 µg          | Doxycycline<br><br>300 µg | Neem showed 53.5% and 52.5% reduction in MMP-2 and 9 respectively, for aloe vera it was 20.09 and 20.4%<br><br>Doxycycline showed 82.1 and 82.6 % reduction for MMP2 and MMP -9 respectively |
| Suhag A et al (2007) <sup>18</sup>       | To establish effectiveness of curcumin as subgingival irrigant  | 1% curcumin                                    | 0.2% CHX irrigant         | 1% curcumin as irrigant showed better reduction of gingivitis almost 96% to 100% and periodontal pocket depth.   |
| Behal R et al (2011) <sup>19</sup>       | To compare effect of 2 % turmeric gel to SRP on periodontal health  | 2 % turmeric gel                               | Conventional SRP          | Turmeric gel proved as an effective adjunct to SRP than SRP alone in reduction of periodontal pockets  |
| Mallikarjun S et al (2016) <sup>20</sup> | Antimicrobial efficacy of Tulsi leaf extract on periodontal pathogens: An invitro study                                   | Tulsi leaves extract 5% and 10 % concentration | Doxycycline               | Tulsi demonstrated effective antimicrobial activity against <i>A. actinomycetemcomitans</i> (p<0.001).   |
| Eswar P et al (2016) <sup>21</sup>       | To determine if <i>Ocimum sanctum L</i> has antibacterial activity against <i>Actinobacillus actinomycetemcomitans</i> in | Tulsi ( <i>Ocimum sanctum L.</i> )             | 0.2 % CHX                 | At 6 % concentration <i>Ocimum sanctum L.</i> showed wide zone of inhibition 22 mm comparable to CHX for which zone of   |

|   |   |                            |           |   |
|---|---|----------------------------|-----------|---|
|   | dental plaque   |                            |           | inhibition was 25 mm  |
| Gupta A et al (2016) <sup>23</sup>      | Efficacy of Babool Neem toothpaste in oral health care  | Babool neem toothpaste     | Placebo   | Babool neem toothpaste showed significant improvement in all the clinical parameters after 6 weeks  |
| Vangipuram S et al (2016) <sup>27</sup> | To evaluate the efficacy of aloe vera on periodontal health   | Aloe vera                  | 0.12 %CHX | Better reduction of plaque and gingival index was elicited with aloe vera (p=0.0000)  |
| Dobayan BAL et al (2019) <sup>30</sup>  | Effectiveness of punica granatum gel as an adjunctive to non surgical periodontal therapy in treatment of moderate , severe periodontitis | <i>Punica granatum</i> gel | placebo   | Significant reduction in bleeding, plaque and gingival index was seen after 15 days of gel application  |
| Kudva P et al (2011) <sup>32</sup>      | Evaluation of adjunctive use of locally delivered green tea catechin  | Green tea catechin chip    | SRP       | Green tea catechin was more effective in reducing pocket depth (p<0.001) after 21 days although significant difference was not seen between the groups for gingival index |
| Warad SB et al (2013) <sup>37</sup>     | Evaluation of the efficacy of locally delivered 2% lemongrass essential oil in gel form   | 2% lemongrass oil          | SRP       | Statistically significant reduction in probing depth and gingival index and gain in relative attachment level were noted after  |

|  |  |  |  |                          |
|--|--|--|--|--------------------------|
|  |  |  |  | 1 and 3 months (p=0.000) |
|--|--|--|--|--------------------------|

SRP , scaling and root planning; CHX , chlorhexidine; MMP , matrix metalloproteinases

Table 1: Literature studies demonstrating clinical effectiveness of various herbal products/phytochemicals for the treatment of periodontal diseases

## TRIPHLA

Triphala is most ancient powder preparation in Indian culture with various medicinal properties. It is combination of three plant species namely *Haritaki (Terminalia chebula)* , *Bahera (Terminalia belerica)* and *Amalaki Phyllanthus emblica (Emblica officinalis)*. *Emblica officinalis* , *Amalaki* is one of the most important ingredient consisting of amlaki, vitamin C, carotenoids, nicotine and tannins.<sup>[5]</sup> It is one of the well known ayurvedic medicament used as anti-aging, immune enhancer, gastro protective , analgesic , antipyretic , antioxidant agent and is beneficial against gastrointestinal tract (GIT) problems, cancer , diabetes and liver diseases. *Terminalis belerica* in indian ayurveda is known as ‘behera’ which has potent anti-inflammatory, anti-oxidant, analgesic and cardio-protective antihypertensive properties. *Terminalia chebula*, *Haritaki* is well recognized unani ayurvedic medicine that is anti-microbial, immunomodulatory, radioprotective , and cytoprotective in nature.<sup>[12]</sup>

Various randomized controlled clinical trials have shown the beneficial effects of triphala in the reduction of oral bacteria, dental plaque and gingivitis. It strengthens the periodontal matrix due to its anti-collagenase activity and presence of antioxidants protects it from degradation by the free radicals. Naitkari SR et al<sup>13</sup> found the efficacy of Triphala mouth rinse comparable to gold standard 0.2 % chlorhexidine (CHX) in controlling periodontal diseases with no reported side effects. In their another study antibacterial substantivity

of triphala was found to last for 3-4 hours after a single rinse that was less in comparison to 7-8 hours for CHX gluconate. Hence for maximum therapeutic benefits, triphala mouthwash should be used three times a day. Further trials should be carried out to emphasize the effect of triphala on gram negative organisms and to determine its substantivity in prevention of periodontal diseases.

### **NEEM (*Azadirachta indica*)**

*Azadirachta indica* commonly known as Neem has been extensively used in ayurveda in India and South African countries as astringent, insecticidal, antiseptic and anti-ulcer medicament for treatment of oral and periodontal diseases. Phytochemicals present in neem leaves imbidin, nimbin, nimbolide, azadirachtin, gallic acid, epicatechin, catechin, and margolone are responsible for its antimicrobial, antioxidant and anti-inflammatory actions. Azadirachtin is a potent antibacterial constituent that destroys bacterial cell wall and inhibits the growth of bacteria.<sup>[14]</sup> It is also a good anti gingivitis agent due to its anti-inflammatory action that is explained by its ability to inhibit inflammatory mediators' prostaglandin and 5HT thus reducing gingival inflammation.<sup>[14,15]</sup> Kudalkar MD et al <sup>[15]</sup> demonstrated inhibitory activity of neem on matrix metallo –proteinases MMP-2 and MMP-9 at 1500 µg/ml concentration that play a key role in tissue destruction in periodontitis.

Neem dental care products are available in form of tooth pastes and mouthrinses containing neem leaf or bark extract that help in elimination of aerobic and anaerobic bacteria present in the oral cavity. Several studies has shown reduction of plaque index score, salivary bacterial count and gingivitis by regular use of these neem products. Neem extract mouthrinse has been found to be more effective in reducing bacterial loads when compared to 0.2 % CHX and could be used as an adjunct in treatment of plaque induced gingivitis.<sup>[14-16]</sup>

### **TURMERIC (*Curcuma longa*)**

Since pre-historic time in India, China and many other countries use this benchmark medicament turmeric (haldi), a rhizome of *Curcuma longa* in daily medicine practice and since time of Sushrut in India it became a famous healing agent. The active constituent of turmeric are three curcuminoids: Curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (turmerone, atlantone, and zingiberone), sugars, proteins, and resins. Curcumin possess high antioxidant, anti-inflammatory, hepato-protective, antiplatelet aggregation, antimutagenic, antimicrobial properties. It is a good scavenger, reduces chemical mediators of inflammation, levels of histamine, down regulates the activity of cyclooxygenase 2 (COX 2), lipooxygenase, and protects liver from oxidative damages of drugs and other free radicals. Its antiplatelet effects are explained by its ability to inhibit the synthesis of thromboxane. It has a potential to inhibit the growth of bacteria, fungi and viruses, hence it is a good germicidal drug.<sup>[17]</sup> Studies have concluded that both turmeric and CHX mouthwash have comparable efficacy as antiplaque, anti-inflammatory and antimicrobial agent. Suhag et al<sup>18</sup> found that as a subgingival irrigant, inflammatory signs were better resolved by 1 % curcumin solution as compared to normal saline and CHX.

Now a days local drug delivery systems containing 2 % turmeric is gaining attention to treat deep periodontal pockets. Local administration by means of injectable syringe allows easy insertion into the periodontal pocket and is retained there for longer duration due to the bioadhesive nature leading to enhanced antimicrobial activity. Clinical trials have found local delivery of 1 % curcumin gel to be more effective in inhibition of growth of oral bacteria when used as an adjunct to scaling and root planning (SRP) in chronic periodontitis.<sup>[19]</sup>

### **TULSI (*Ocimum sanctum*)**

In India tulsi (*Ocimum sanctum*) is considered as a sacred plant known as “holy basil” and “the mother medicine of nature” It is a medicinal plant with diverse applications in medicine, and hence commonly referred as “Queen of Herbs”. Beneficial effects of tulsi has been studied on a large scale and it has been found to have antimicrobial, anti-inflammatory, immunomodulatory, hypoglycaemic, chemoprotective and analgesic

properties.<sup>[20,21]</sup> However few in vitro studies have reported in literature that showed its maximum antimicrobial effect at different concentrations on the periodontal pathogens. Mallikarjun S et al <sup>[20]</sup> demonstrated that 5 % and 10 % tulsi extracts have potent antimicrobial activity against *A. actinomycetemcomitans*, *P. gingivalis* and *P. intermedia* and could be used as an adjunct along with standard therapy in the treatment of periodontitis. In another invitro study, Eswar P et al <sup>[21]</sup> observed widest zone of inhibition of 25 mm for *ocimum sanctum* at 6 % concentration against *A. actinomycetemcomitans*. More clinical trials should be encouraged to explore the pharmacological effects of this medicinal herb on periodontal health.

### **BABOOL (*Aracia arabica*)**

*Aracia Arabica* commonly known as babool in India has many cyanogenic glycosides and enzymes like oxidase, pectinase, peroxidase that exhibit antimicrobial actions. Its bark contain tannins (24-42%) responsible for its anti-inflammatory and analgesic effect. Its formulations available as gels, tooth powders and toothpastes and have active ingredients that play an important role in prevention of plaque related diseases.<sup>[22]</sup> Babool Neem tooth paste consisting of extracts both of neem(*Azadirachta indica* A. Juss) and babool (*Acacia Arabica* Willd) have been found to reduce halitosis, gingivitis, plaque, and clinical attachment loss.<sup>[23]</sup> Many studies revealed that using babool is clinically equally effective for treatment of gingivitis as other gum paints and even mouthwash containing babool is equally effective for reducing gingivitis as 0.2% CHX gluconate.<sup>[22,23]</sup>

### **Coriander (*Coriandrum sativum* L.) and Persian Oak (*Quercus brantii* L.)**

Coriander locally known as “dhanya” is one of the widely cultivated herbs and its use is popular in folk medicine especially in Egypt due to its therapeutic potential. *Coriandrum sativum* extract is commonly used for the treatment of various gastrointestinal problems such as flatulence. Literature studies have shown that *coriandrum sativum* contain tannin that cause increase in antioxidant levels in the saliva.<sup>[24,25]</sup> In addition it has good anti-inflammatory and antibacterial activity against periodontal pathogens. Another tannin containing herb *querus branii* native to Western Asia exhibits potent anti-inflammatory, analgesic,

astringent, antibacterial and antioxidant properties. It has been used traditionally in the treatment of diarrhoea, gastrointestinal and inflammatory diseases. Many commercially available mucoadhesive gel formulations namely Carbopol 940, Sodium CMC ,HPMC gel consisting of extracts of both ingredients have been found to be clinically effective in reducing microbial count in deep periodontal pockets.<sup>[24]</sup>

### **ALOE VERA (*Aloe barbadensis*)**

Aloe vera is jelly like fleshy plant the inside of which contains the liquidish jelly that has soothing effect and is widely accepted species for medicinal and pharmaceutical purpose in many countries. Aloe vera is having high contents of salicylic acid, vitamins, minerals, sugars, enzymes, lignin, saponins, and amino acids. Antimicrobial activity especially against *candida albicans*, *streptococcus pyogenes* and *streptococcus faecalis* is because of its protein inhibiting property in bacterial cell wall. It has been used to treat oral lesions such as acute gingival lesion of herpes virus, denture stomatitis ,and now researches are exploring its effect on peri-implantitis.<sup>[26]</sup> Several researchers have found it effective in reducing gingival index scores which can be attributed to its anti-inflammatory action by inhibition of COX and prostaglandins.<sup>[27]</sup> Commercially available gel form has been investigated to improve periodontal condition due to its excellent healing, anti inflammatory and antibacterial properties.<sup>[26]</sup> Although its plaque reduction action is well elucidated, but few studies have found it to be less efficacious than other mouthwashes or gels. de Oliviera et al <sup>[28]</sup> suggested that dentifrices containing aloe vera did not show any additional effect on plaque and gingivitis in comparison to fluoridated dentifrice. Therefore further randomized controlled trials should be encouraged to validate the anti gingivitis effect of this herbal medicine.

### **POMEGRANATE (*Punica granatum*)**

*Punica granatum* known as pomegranate common edible fruit with medicinal properties in Iran. Pomegranate is referred as the “ Nature's power fruit “ and “ pharmacy unto itself” due to the presence of various phytochemicals such as ellagic acid, punicalagin, pedunculagin, quercetin, rutin, ellagic acid, polyphenol, tannic acid, anthocyanins , and catechins. It has been proven to possess excellent antioxidant, anti-inflammatory and antibacterial properties that reduces the gingivitis and improves oral health of an

individual.<sup>[29]</sup> Studies have suggested pomegranate extract mouthrinse as an effective adjunct to conventional plaque control measures in the treatment of gingivitis. Dobayan BAL et al<sup>[30]</sup> found *Punica granatum* gel to have better anti-inflammatory and antigingivitis effects on the periodontium than topical chemotherapeutics.

### **GREEN TEA ( *Camellia sinensis* )**

Green tea made from plant *camellia sinensis* contains large amount of catechin' that has antioxidant, antimutagenic, antioxidant properties. It also contains caretenoids, beta carotene, and ascorbic acid that make it a potent free radical scavenger. It can prevent alveolar bone resorption, characteristic feature of periodontal disease by reducing the expression of MMP-9 in osteoblasts and decreasing the activity of osteoclasts.<sup>[31]</sup> Numerous in vitro studies have suggested that green tea catechins with steric structures of 3- galloyl radical, EGCG, ECg and galocatechin gallate inhibits the growth of *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Prevotella nigrescens* , decreases the microbial counts of soft tissue in periodontal pocket wall and also affects the adherence of *P.gingivalis* onto the buccal epithelial cells. The use of green tea catechin chips is gaining popularity in improving periodontal status of patients. Studies have demonstrated it as a good locally delivered agent as peptidase activity is maintained at its minimal level in the gingival crevicular fluid.<sup>[32-34]</sup> Besides maintaining healthy periodontium it has also been implicated in reduction of oral malodour due to its disinfectant and deodorant activities.

The main concern is amount of consumption of green tea for beneficial effects. Studies have demonstrated that excessive consumption of green tea is associated with risk of periodontal disease due to presence of caffeine in it which has been reported to stimulate osteoclasts enhancing periodontal destruction. In consideration to above consumption of one cup of green tea (250 ml) a day is found to be adequate for positive effects on the periodontium.<sup>[35]</sup>

### **LEMONGRASS OIL ( *Cymbopogon citratus* )**

Lemongrass (*Cymbopogon citratus*) oil is an essential oil used as potent antibacterial, antifungal, antioxidant, anti-inflammatory, analgesic, astringent and antiseptic agent. Its antimicrobial action is considered to be equally effective as penicillin. [36] It has been hypothesised that lemongrass oil interferes with bacterial adhesion plaque formation at a concentration less than or equal to 2 % because of its high viscosity and presence of terpenes that alter the cell permeability by penetrating between the fatty acyl chains of lipid bilayer. Many recent researches are going on in India for its efficacy as mouth rinse in concentration of 0.25% and suggested that it could be used as an adjunct to mechanical measures in order to prevent plaque formation and gingivitis.[37]

### **CLOVE OIL (*Syzygium aromaticum*)**

Clove (*Syzygium aromaticum*) is a plant derived spice from dried flower bud of the clove tree *Eugenia caryophyllata*. Clove oil is extracted from the leaves, buds and stem of the tree *Syzygium aromaticum* by steam distillation. It is one of the oldest natural medicine used to relieve dental pain in India. Eugenol a primary component of clove oil possess remarkable antioxidant and anti-inflammatory properties.[38] Clove oil has been shown to exhibit antibacterial activity against anaerobic periodontal pathogens such as *P.gingivalis* and *P. intermedia*. It reduces periodontal inflammation and periodontal bone loss by suppression of inflammatory mediators interleukin -6, COX 2 and TNF  $\alpha$ . Clove oil based gum paints and mouth rinses are found to be highly biocompatible with potent analgesic and anti inflammatory effects for prevention and treatment of periodontal diseases.[38,39]

### **MISWAK (*Salvadora persica*)**

Herbal chewing sticks, commonly known as Miswak or Siwak is one of the popular oral hygiene aid since ancient times in India, Pakistan, most Arabian and African countries. It has dual action on plaque control first is mechanical by friction between the plant fibres and the tooth surfaces and second is chemical by its

chemical composition. Each of its constituent has specific role in promoting oral health. Silica is an abrasive material that helps in removal of stains from the tooth surfaces, fluorides prevents the development of dental caries, tannic acid serves as an astringent and is good antiplaque and anti gingivitis agent. Resins form layer over the enamel and protect it from oral microbes, alkaloids have bactericidal action, vitamin C helps in healing and repair and lastly essential oils gives it a pungent taste that stimulates the salivary flow.<sup>40</sup> It has been found to have good antimicrobial activity against *P.gingivalis*, *Aggegatibacter actinomycetemcomitans*, and *H. influenza*. It has been found to have antidiabetic, antiulcerative, antihyperlipidemic and anticonvulsant effects. Miswak is being used as an important ingredient in tooth pastes, mouthwashes and irrigation solutions. Now a day's tooth pastes and tooth powders containing *Salvadora persica* miswak extract are commercially available.<sup>[41]</sup>

Miswak should be used in preventive dental programs as it is economical, simple to use, readily available for the rural area inhabitants but children require special instructions and supervision regarding its proper use. Although studies have demonstrated that regular use of miswak reduces dental plaque more effectively than conventional tooth brush but it has certain disadvantages as excessive use may result in gingival recession, gingival bleeding and oral ulcerations due to mechanical trauma.<sup>[41]</sup> Moreover its bristles lie in the long axis of the stick that limits its access to the lingual tooth surfaces. More clinical trials should be focussed on the comparison of effectiveness of miswak in relation to conventional tooth brushing as an oral hygiene measure in both urban and rural population.

### **Safety of the phytochemicals**

These natural plant based products are generally considered safe; still no clear evidence has been obtained regarding the potential risks associated with the use of phytochemicals. Side effects have been reported to occur at larger doses or they may show adverse drug reactions due to presence of certain impurities e.g. allergens, pollens etc. Unlike allopathic medications, herbal products are not tested for the purity; therefore physicians should be aware of the mechanism of action and various drug interactions of the natural products. Patients should take phytochemical supplementation only on physician's prescription.<sup>[1,3]</sup>

## CONCLUSION

With advancement in allopathic medication we forgot the importance of natural home based easy and biocompatible less expensive phytomedicines. Emerging antimicrobial resistance and side effects which we are facing time to time with these allopathic medicines recapitulate the need of phytomedicine in treatment of periodontal infections. Many researchers have found absolute results for the eradication of microbes in the deep periodontal pockets with the herbal extracts. More evidence based trials should be carried out to establish phytomedicine as a reliable treatment adjunct to SRP in the treatment of periodontitis. These should also focus on standardization and quality assurance of the herbal remedies. Novel drug delivery systems for herbal products are going to become a promising approach for the treatment of chronic and aggressive periodontitis in near future.

## REFERENCES

1. Agrawal N, Gupta N.D, Garg A.K, Sharma V, Singh R. Resurgence of Phytomedicine Use in Dentistry. *Am J Phytomed Clin Ther* 2014;3:322-33.
2. Dzink JL, Socransky SS, Haffajee AD. The predominant cultivable microbiota of active and inactive lesions of destructive periodontal diseases. *J Clin Periodontol* 1988; 15:316–23.
3. Kim J, Amar S. Periodontal disease and systemic conditions. A bidirectional relationship. *Odontol* 2006; 94: 10-21.
4. Sorsa T, Ingman T, Suomalainen K, Haapasalo M, Kontinen YT, Lindy O, et al. Identification of proteases from periodontopathogenic bacteria as activators of latent human neutrophil and fibroblast-type interstitial collagenases. *Infect Immun* 1992; 60:4491–5.
5. Prakash S, Shelke AU. Role of Triphala in dentistry. *J Indian Soc Periodontol* 2014;18:132-5.
6. Carr C, Wigmore T. The side effects of chemotherapeutic agents. ***Curr Anaesth Crit Care* 2008;19:70-9.**

7. [Bhat N](#), [Mitra R](#), [Oza S](#), [Mantu VK](#), [Bishnoi S](#), [Gohil M](#), et al. The antiplaque effect of herbal mouthwash in comparison to chlorhexidine in human gingival disease: a randomized placebo controlled clinical trial. *J Complement Integr Med* 2014;11:129-37.
8. Cao C.F, Sun X.P. Herbal medicine for periodontal diseases. *Int Dent J* 1998;1: 31 6-322.
9. Liu RH. Potential synergy of phytochemicals in cancer prevention: mechanism of action. *J Nutr* 2004;12:3479-85.
10. Tomofuji T, Irie K, Sanbe T, Azumba T, Ekuni D, Tamaki N, et al. Periodontitis and increase in circulating oxidative stress. *Japanese Dent Sci Rev* 2009;45:46-51.
11. Cherian DA, Peter T, Narayanan A, Madhavan SS, Achammada S, Vynat GP. Malondialdehyde as a marker of oxidative stress in periodontitis patients. *J Pharm Bioall Sci* 2019;11:297-300.
12. Mourya DK, Mittal N, Sharma KR, Nath G. Role of triphala in management of periodontal disease. *Ancient Sci Life* 1997;17:120-7.
13. Naitkari 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; 44:134–40.
14. Lakshmi T, Krishnan V, Rajendran R, Madhusudhanan N. *Azadirachta indica*: A herbal panacea in dentistry – An update. *Pharmacogn Rev* 2015 ; 9: 41–4
15. Chatterjee A, Saluja M, Singh N, Kandwal A. To evaluate the antigingivitis and antiplaque effect of an *Azadirachta indica* (neem) mouthrinse on plaque induced gingivitis: A double-blind, randomized, controlled trial. *J Indian Soc Periodontol.* 2011 ;15(4):398-401.
16. Kudalkar MD, Nayak A, Bhat KS, Nayak RN. Effect of *Azadirachta indica* (*Neem*) and Aloe vera as compared to subantimicrobial dose doxycycline on matrix metalloproteinases (MMP)-2 and MMP-9: An in-vitro study. *Ayu* 2014; 35(1): 85–9.
17. Nagpal M, Sood S. Role of curcumin in systemic and oral health: An overview. *J Nat Sci Biol Med* 2013 Jan-Jun;4(1):3-7.
18. Suhag A, Dixit J, Dhan P. Role of Curcumin as a sub gingival irrigant: a pilot study. *Perio* 2007;4:115-21.

19. Behal R, Mali AM, Gilda SS, Paradkar AR. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. J Indian Soc Periodontol 2011 ; 15: 35–8.
20. Mallikarjun S, Rao A,Rajesh G, Shenoy R, Pai M.Antimicrobial efficacy of Tulsi leaf (*Ocimum sanctum*) extract on periodontal pathogens: An invitro study. Indian Soc Periodontol 2016;20:145-50.
21. Eswar P, Devaraj CG, Agarwal P. Anti-microbial Activity of Tulsi {*Ocimum Sanctum (Linn.)*} extract on a periodontal pathogen in human dental plaque: An invitro study J Clin Diagn Res 2016;10:53-6.
22. Tangade PS, Mathur A, Tirth A,Kabasi S.Anti-gingivitis effects of Acacia Arabica-containing toothpaste. Chinese J Dent Res 2012;15:49-53.
23. Gupta A,Bhowate R, Srivastava R,Kumar K, Devasthale SV, et al. Clinical evaluation of babool neem toothpaste in oral hygiene and dental care. Int J Pharmaceut Res 2016;8:57-61.
24. Yaghini J, Shahabooei M, Aslani A, Zadeh MR, Kiani S, Naghsh N. Efficacy of a local-drug delivery gel containing extracts of *Quercus brantii* and *Coriandrum sativum* as an adjunct to scaling and root planing in moderate chronic periodontitis patients. J Res Pharm Pract 2014 ;3:67-71.
25. Pawar VA, Bhagat TB, Toshniwal MR, Mokashi ND, Khandelwal KR. Formulation and evaluation of dental gel containing essential oil of coriander against oral pathogens. Int Res J Pharm 2013;4:48-54.
26. Bhat G,Kudva P, Dodwad V. Aloe vera: Natures soothing healer to periodontal disease. J Indian Soc of Periodontol 2011;15:205-9.
27. Vangipuram S, Jha A,Bhashyam M. Comparative efficacy of aloe vera mouthwash and chlorhexidine on periodontal health: A randomized controlled trial. J Clin Exp Dent 2016;8:442-7.
28. deoliveira SMA, Torres TC, da Silva Pereira SL,de Lima Mota OV, Carlos MX. Effect of a dentifrice containing Aloe vera on plaque and gingivitis control. A double-blind clinical study in humans. J Applied Oral Sci 2008;16:293-6.
29. Prasad D, Kunnaiah R. *Punica granatum*: A review on its potential role in treating periodontal disease J Indian Soc Periodontol. 2014 ; 18: 428–32.

30. Dobayan BL, Ayeid FAL, Guraid IAL, Bassiouny G, Nasser SAL. The Effect of Punica Granatum Gel as An Adjunctive Therapy in Patients with chronic Periodontitis: A Clinical, Microbiological and histological Study. *J Am Sci* 2015;19:12-15.
31. Rashika V. Healthy benefits of green tea. *Asian J Phytomed Clin Res* 2013;1:203-6.
32. Kudva P, Tabasum ST, Shekhawat NK. Effect of green tea catechin, a local drug delivery system as an adjunct to scaling and root planing in chronic periodontitis patients: A clinic microbiological study. *J Indian Soc Periodontol.* 2011 ;15:39-45.
33. Sakanaka S, Aiwaza M, Kim M, Yamamoto T. Inhibitory effects of green tea polyphenols on growth and cellular adherence of an oral bacterium, *Porphyromonas gingivalis*. *Biosci Biotechnol Biochem* 1996;60:745-9.
34. Yun JH, Pang EK, Kim CS, Yoo YJ, Cho KS, Chai JK. Inhibitory effects of green tea polyphenol (-)-epigallocatechin gallate on the expression of matrix metalloproteinase-9 and on the formation of osteoclasts. *J Periodontal Res* 2004;39:300-7.
35. Han K, Hwang E, Park PB. Excessive Consumption of Green Tea as a Risk Factor for Periodontal Disease among Korean Adults. *Nutrients.* 2016 ; 8: 408
36. Abdelmagyd H.A, Shetty S.R. Herbal medicine as adjunct in periodontal therapies- A review of clinical trials in past decade. *J Oral Biol Craniofac Res* 2019;2:135-45.
37. Warad SB, Kolar SS, Kalburgi V, kalburgi NB. Lemongrass essential oil gel as a local drug delivery agent for the treatment of periodontitis. *Anc Sci Life* 2013 ; 32: 205–211.
38. Pulikotill SA, Nath S. Potential of clove of *Syzygium aromaticum* in development of a therapeutic agent for periodontal disease. A review. *J south Afr Dent Assoc* 2015;70:108-15.
39. Cao C.F, Sun X.P. Herbal medicine for periodontal diseases. *Int Dent J* 1998;1: 316-322.
40. Dahiya P, Kamal R, Luthra RP, Mishra R, Saini G. Miswak: A periodontist's perspective. *J Ayurveda Integr Med.* 2012 Oct-Dec; 3(4): 184–187.
41. Poureslami HR, Makarem A, Mojab F. Paraclinical Effects of Miswak Extract on Dental Plaque. *Dent Res J* 2007; 4(2): 106-110

42. Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med* 1993;328:246–52.