



Treatment of Periodontal Disease – A Herbal Approach

Bhushan.S.Kala*, Chauhan Gunjan¹, Nagpal Disha², Prakash Shobha³

*MDS, Professor, Department of periodontics, College of Dental Sciences, Davangere, Karnataka, India

¹BDS, Post graduate student, Department of periodontics, College of Dental Sciences, Davangere, Karnataka, India.

²MDS, Post graduate student, Department of periodontics, College of Dental Sciences, Davangere, Karnataka, India.

³MDS, Professor and head, Department of Periodontics, College of Dental Sciences, Davangere, Karnataka, India.

*Corresponding author's E-mail: tanmay5634@yahoo.co.in

Accepted on: 12-06-2015; Finalized on: 31-07-2015.

ABSTRACT

Periodontitis, or gum disease, affects millions of people each year. Periodontitis is a serious gum infection that damages periodontium (the soft tissues and bones present around tooth for support). The disease mainly occurs when bacteria in dental plaque infect the gums and bones that anchor the teeth. Periodontal diseases, if left unchecked, can lead to major health problems. Over the last decade, herbal and Ayurvedic drugs has become a subject of world importance, with both medicinal and economical implications. Herbal excipients are non-toxic and compatible they have a major role to play in pharmaceutical formulation. Herbal medicines have been widely used all over the world since ancient times and have been recognized by physicians and patients for their better therapeutic value as they have fewer adverse effects as compared to modern medicines. The aim of the present article is to present overall view of the current strategies adopted for the formulation and application of traditional herbal remedies. This review article summarizes the current data on the effect of natural products like Acaciacatechu, Aloe vera, Azadirachata indica, Ocimum sanctum, Punica granatum & other important herbs on management of various periodontal diseases together with their biological activities.

Keywords: Herbal drugs, periodontitis, gingivitis, dental plaque

INTRODUCTION

Periodontal disease is one of the most important concerns for dentists and patients.¹ It is recognized as a major public health problem throughout the world and is the most common cause of tooth loss in adults.² The word "periodontitis" comes from peri ("around"), odont ("tooth") and -itis ("redness"). Periodontitis is a set of diseases which usually attacks the periodontium. The periodontium is the specialized tissues that both surround and support the teeth, maintaining them in the maxillary and mandibular bones. Periodontitis in comparison with gingivitis is a more severe inflammation, because not only it affects the tissues, but also, it affects the bottom of the teeth. If it is not treated at all, it may lead to a loss of teeth.^{3,4}

A variety of triggering factors like bacterial causes, dyscrasias, avitaminosis etc cause inflamed gums leading to gingivitis. Salivary tartar has an additive effect to these causative factors in causing gingivitis. Aggressive periodontitis, chronic periodontitis and those resulting from conditions like HIV, diabetes, malnutrition and immunosuppression are the other types of periodontitis.⁵ Researchers found that Actinobacillus actinomycetemcomitans and Porphyromonas gingivalis these two bacteria appear to be likely to cause aggressive periodontal disease. Both P. gingivalis and A. actinomycetemcomitans, along with multiple deep pockets in the gum, are associated with resistance to standard treatments for gum disease.⁶ Other bacteria associated with periodontal disease are Treponema

denticola, T.socranskii, and P. intermedia. These bacteria, together with P. gingivalis, are frequently present at the same sites, and are associated with deep periodontal pockets.⁷

Morris reported that in the United Kingdom 40-45% of adults have moderate destructive periodontal disease and 5-10% has a severe form of the disease. They also reported that 72% of adults have visible plaque; which is the main causative factor of periodontal disease. In the United States 50% of adults have gingivitis affecting at least 3-4 teeth; two-thirds of the population has sub gingival calculus, and about a one-third have periodontitis.^{1,8}

Pain, discomfort and cosmetic considerations are some of the factors that demonstrate severity of the problems associated with dental diseases and hence, it is of utmost importance to minimize and control dental diseases.⁹ Periodontal treatment aims to cure inflamed tissue, reduce the number of pathogenic bacteria and eliminate the diseased pockets. Mechanical therapy, chemotherapy and systemic administration of antibiotics are some of the clinical methods being utilized currently. Conventional therapy includes scaling – removal of the calculus and the plaque, curettage clearing the inflamed soft tissue, and root planning - removal of necrotic tissues on the root surface. Periodontal diseases are associated with bacterial infections; therefore antibacterial treatment seems to be an appropriate method of improving the condition of the inflamed tissues. One of the major problems associated with conventional treatment of



systemic administration of antibiotics is the distribution of drug throughout the body, which is not required and it can also give rise to toxicity problems.¹⁰

One method of minimizing the distribution of therapeutic agents in the body is through the use of local drug delivery system.

Many antibacterial are applied directly to the mouth for the treatment of periodontal diseases. Mouth rinses, irrigating solutions and sustained release devices are some of the local delivery systems.

Periodontal local delivery devices that have been used for the targeted delivery of antimicrobial agents include: fibers (hollow and monolithic), strips and compacts, films, microparticles, gels and nanoparticles.¹¹

Despite several chemical agents being commercially available, these can alter oral microbiota and have undesirable side-effects such as vomiting, diarrhoea and tooth staining.^{12,13}

Hence, the search for alternative products continues and natural phytochemicals isolated from plants used in traditional medicine are considered as good alternatives to synthetic chemicals.¹⁴

Herbal and natural products of folk medicine have been used for centuries in every culture throughout the world. "Let food be your medicine and let medicine be your food" was advised by Hippocrates, over two millennia ago. It's still true today that "you are what you eat."¹⁵

The practice of medicine has evolved over many centuries to reach its current state.

A recent survey conducted by the World Health Organization estimated that almost 70–80% of the population in the developing world has resorted to traditional practices for treatment of a variety of ailments.¹⁶

The populations of the two most populous countries in the world, China and India, have practised traditional medicine for the management of oral diseases, including periodontal disease, for well over 2000 years.¹⁷

With respect to diseases caused by microorganisms, the increasing resistance in many common pathogens to currently used therapeutic agents, such as antibiotics and antiviral agents, has led to renewed interest in the discovery of novel anti-infective compounds.

As there are approximately 5,00,000 plant species occurring worldwide, of which only 1% has been phytochemically investigated, there is great potential for discovering novel bioactive compounds from these sources.¹⁸

Plants and natural products from time immemorial used for their pharmacological applications viz., antiulcerogenic, wound healing, anti-inflammatory, antimicrobial, antioxidant properties etc. Here is a list of few of these in Table 1.

The purpose of this review is to present some recent examples of traditional medicinal plant extracts or phytochemicals that have been shown to inhibit the growth of oral pathogens, reduce the development of dental plaque and reduce the symptoms of oral diseases.

Various plants and their immense potential in management of dental health :

1. *Acacia catechu* Wild

Acacia catechu Wild. (AC)(Family: Fabaceae and subfamily: Mimosoideae) known as Black Khair. AC is commercially used to obtain Katha (a concentrated filtered extract) in North India.

AC is used as mouthwash for mouth, gum and throat diseases like gingivitis, stomatitis. Cutch and katha is cooling, digestive and a very valuable astringent, especially in chronic diarrhoea and dysentery, bleeding piles, uterine haemorrhages, leucorrhoea, gleet, atonic dyspepsia, chronic bronchitis, etc.

The decoction of bark mixed with milk is taken to cure cold and cough.²³⁻²⁷



Figure 1: *Acacia catechu*

The extracts of AC have been reported to have various pharmacological effects like antipyretic, anti-inflammatory, anti diarrhoeal, hypoglycaemic, hepatoprotective, antioxidant and antimicrobial activities.^{23,25-29}

The important chemical constituents reported in the heartwood are catechin, catechutannic acid, epicatechin, catechin tetramer, dicatechin, galocatechin, kaempferol, taxifolin, isorhamnetin, (+)Afzelechin, L-arabinose, D-galactose, D-rhamnose and aldobiuronic acid. Catechin is highly active. It is used as a haemostatic.³⁰

Table 1

Plants with antiulcerogenic property ¹⁹	Plants with antimicrobial property ²⁰	Plants with antioxidant property ²¹	Plants with analgesic property ²²	Plants with anti-inflammatory property ²²
Ocimum sanctum, Allophylus serratus, Desmodium gagicum, Azadirachta indica, Hemidesmus indicus, Asparagus racemosus and Musa sapientum.	Aloe (<i>Aloe barbadensis</i> , <i>Aloe vera</i>), Apple (<i>Malus sylvestris</i> , <i>Withania somniferum</i>), Ashwagandha (<i>Withania somniferum</i>), Bael tree (<i>Aegle marmelos</i>), Basil (<i>Ocimum basilicum</i>), Betel pepper (<i>Piper betel</i>), Black pepper (<i>Piper nigrum</i>), Buttercup (<i>Ranunculus bulbosus</i>), Cashew (<i>Anacardium pulsatilla</i>), Castor bean (<i>Ricinus communis</i>), Ceylon cinnamon (<i>Cinnamomum verum</i>), Chili peppers, paprika (<i>Capsicum annum</i>), Clove (<i>Syzygium aromaticum</i>), Coriander, (<i>Coriandrum sativum</i>), Eucalyptus (<i>Eucalyptus globules</i>), Garlic (<i>Allium sativum</i>), Gotu kola (<i>Centella asiatica</i>), Turmeric (<i>Curcuma longa</i>), Green tea (<i>Camellia sinensis</i>), Henna (<i>Lawsonia inermis</i>), Licorice (<i>Glycyrrhiza glabra</i>), Marigold (<i>Calendula officinalis</i>), Olive oil (<i>Olea europaea</i>), Onion (<i>Allium cepa</i>), Papaya (<i>Carica papaya</i>), Peppermint (<i>Mentha piperita</i>), Poppy (<i>Papaver somniferum</i>), Potato (<i>Solanum tuberosum</i>)	Spinach, pepper, black tea, broccoli, green tea, carrot, potato tomato, blackberry, grape, olive, pineapple, strawberry, orange	Anicillo (<i>Piper</i>) species, Arnica (<i>Arnica Montana</i>), Betle (<i>Piper betle</i>), Capsicum (<i>Capsicum annum</i>), Chile (<i>Capsicum annum</i>), Clove (<i>Eugenia caryophyllus</i>), Coca (<i>Erythroxylum coca</i>), Feverview (<i>Tanacetum parthenium</i>), Ginger (<i>Zingiber officinale</i>), Marijuana (<i>Cannabis sativa</i>), Menthol (<i>Mentha piperata</i>), Myrrh (<i>Commiphora myrrha</i>), Peppermint (<i>Mentha piperita</i>), Poppy (<i>Papaver somniferum</i>), Tobacco (<i>Nicotiana tabacum</i>), Willow bark (<i>Salix alba</i>), Wintergreen (<i>Gaultheria procumbens</i>)	Aloe (<i>Aloe vera</i>), Anesthesia (<i>Ottonia frutescens</i>), Angelica (<i>Angelica archangelica</i>), Anisillo (<i>Piper auritum</i>), Piperaceae Anisillo (<i>Piper marginatum</i>), Arnica (<i>Arnica Montana</i>), Calendula (<i>Calendula officinalis</i>), Camptotheca (<i>Camptotheca acuminata</i>), Celery seeds (<i>Apium graveolens</i>), Chamomile (<i>Anthemis nobilis</i>), Chickweed (<i>Stellaria media</i>), Chicle (<i>Manilkara sapota</i>), Chilcuague (<i>Heliopsis longipes</i>), Chilmecatl (<i>Heliopsis longipes</i>), Chinchillia (Anicillo) (<i>Tagetes minuta</i>), Dandelion (<i>Taraxacum officinale</i>), Garlic (<i>Allium sativum</i>), Ginger (<i>Zingiber officinale</i>), Gotu kola (<i>Centella asiatica</i>), Hierba mora (<i>Solanum nigrum</i>), Jaborandi (<i>Pilocarpus jaborandi</i>), Licorice (<i>Glycyrrhiza glabra</i>)

Role of *Acacia catechu* on Management of Periodontal disease

A herbal tooth powder which removed plaque, stain or patches and cleaned and polished tooth surfaces without any abrasive action, comprised the powder of *Acaciacatechu*, Menthol and camphor in the proportion of 91%, 2.7% and 6.3% respectively. The powder of *Acacia catechu* was used to remove tarter, plaque and stain and in cleansing and polishing tooth surface without any abrasionaction.

The powders of menthol and camphor were used as a flavouring agent. A clinical study on this dentifrice herbal tooth powder reported 87-95%, 70-72% and 80-95% reductions in plaque, gingivitis and dental calculus respectively, about 15 days of treatment.³¹

2. *Aloe vera* (*Aloe barbadensis miller*)

The botanical name of *Aloe vera* is *Aloe barbadensis miller*. It belongs to Asphodelaceae (Liliaceae) family, and is a shrubby orarborescent, perennial, xerophytic, pea-green color plant. It grows mainly in the dry regions of Africa, Asia, Europe and America. In India, it is found in

Rajasthan, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu.

The species is frequently used in herbal medicine. Many scientific studies of the use of extracts of *Aloe vera* have been undertaken.³³⁻³⁶ *Aloe vera* contains 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids.³⁷⁻³⁹

Aloe vera is found to possess good wound healing activity.⁴⁰ *Aloe Vera* contains 6 antiseptic agents: Lupeol, salicylic acid, urea, nitrogen, cinnamonic acid, phenols and sulfur. They all have inhibitory action on fungi, bacteria and viruses. *Aloevera* has been found to be useful in cancer prevention, aphthous stomatitis, mucositis, and radiation dermatitis.⁴¹⁻⁴⁴

Aloe vera is a potent anti inflammatory agent it inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid.⁴⁵ *Aloevera* is a potent laxative,⁴⁶ it exhibits potent anti viral and anti tumoractivity.⁴⁷ *AloeVera* possess good anti bacterial and anti fungal activity, *Streptococcus pyogenes* and *Streptococcus faecalis* are two microorganisms that have been inhibited by *aloe veragel*.^{48,49} Using a rat model, in a study it was suggested that the antibacterial effect of the



aloe vera gel *in vivo* could enhance the wound healing process by eliminating the bacteria that contributed to inflammation.⁴⁹

It was proposed that a glycoprotein, alectin A, which was isolated from *Aloe arborescens*, markedly inhibits arthritis in rats and carrageenan-induced edema in rats.⁵⁰ Hutter identified an anti-inflammatory agent as C-glucosyl chromone from *Aloe barbadensis*.⁵¹ It is recently reported that aloe vera leaf pulp extract was effective in reducing blood sugar, suggesting that it might be useful in the scavenging of free radicals.⁵² It was reported that treatment with aloe vera increased antioxidant enzymes and significantly reduced lipid peroxidation products in streptozotocin induced diabetic rats, showing the relationship between antioxidant activity and the onset of diabetes.⁵³⁻⁵⁵

Role of *Aloe Vera* in Management of periodontal disease



Figure 2: Aloe vera

The aloe vera plant contains anthraquinone glycosides (especially in the latex form, which is different from the gel), polysaccharides, aloeresins, glucomannans, and β-sitosterol.⁵⁶ Antioxidative phenolic compounds were recently isolated from *Aloe barbadensis* and identified as aloeresin derivatives.⁵⁷ These properties, along with the ease of availability, no known adverse effects, and cost effectiveness, make aloe vera an ideal candidate for plaque control, thereby reducing gingivitis and most likely eventual periodontitis.⁵⁸

Treatment of inflammation is still the key effect for most types of healing, and immunomodulatory properties of the gel polysaccharides, especially the Acetylated mannans from aloe vera, seem to play a key role. Antidiabetic, anticancer, and antibiotic activities of aloe vera have also been reported, indicating wider use of this gel.⁵⁶

Studies observed a significant reduction in plaque and gingivitis after a 30-day use of mouth rinse containing aloe vera with toothbrushing.⁵⁹ It was found out that both dentifrice containing aloe vera and fluoride resulted in significant reduction of plaque and gingivitis, but no

statistical significant difference was observed between them that inactivates bradykinin *in vitro*, salicylates, and a substance that inhibits thromboxane formation.⁶⁰ Compositions that were safe and effective for preventing and treating oral disease and for maintaining good oral health for both humans as well as animals has been described. The composition contains a herbal ingredient such as olive leaf extract, black walnut green hulls, clove leaf, thyme herb, grapefruit seed extract, Aloe vera, Calendula flower, Echinacea purpurea, gota kola extract, chamomile flower, green tea leaf, oregano leaf, peppermint oil, cinnamon bark, eucalyptus leaf, lavender oil etc.⁶¹

The aloe vera extract treatment has also resulted in a significant increase in reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase, and glutathione S transferase in the liver and kidney of diabetic rats, showing the antioxidant property of aloe vera gel extract.⁶² Thus, it can be hypothesized that aloe vera extracts can be useful in the control and treatment of periodontal diseases by virtue of their antioxidant properties as well.

3. Neem (*Azadirachta indica*)

Azadirachta indica (syn. *Melia azadirachta*) is well known in India and its neighbouring countries for more than 2000 years as one of the most versatile medicinal plants having a wide spectrum of biological activity. Every part of the tree has been used as traditional medicine for household remedy against various human ailments, from antiquity.⁶³⁻⁶⁸

More than 135 compounds have been isolated from neem. The main active ingredients are named nimbin, nimbinin, and nimbidin. All parts of the plant yield β-sitosterol.⁶⁹ The leaves contain 6-desacetylnimbinene, nimbandiol, nimbolide and quercetin, n-hexacosanol and nonacosane. The diterpenoids margolone, nimbogone, nimbonolone and nimbolinin have also been isolated from the plant. Various parts of the neem tree have been used as traditional Ayurvedic medicine in India from time immemorial.⁷⁰

Neem oil, bark and leaf extract have been therapeutically used as folk medicine to control leprosy, intestinal helmenthesis, respiratory disorders, constipation and as health promoter.⁶⁸ Studies indicate that neem leaf extract possess antiarrhythmic, antiarthritis, antiviral, antioxidant, hepatoprotective and antidiabetic activity.⁷¹⁻⁷³

Role of Neem in management of periodontal disease

The ancient Ayurvedic practise of using Neem to heal and rejuvenate gum tissue and to prevent cavities and gum disease is verified in modern clinical studies.⁷⁴

Some of the observed anti-plaque activity of neem chewing sticks is attributed to the fibrous nature of these sticks resulting in mechanical plaque removal; however, neem plant also contain chemotherapeutic antiplaque

agents. The presence of gallotannins during the early stages of plaque formation could effectively reduce the number of bacteria available for binding to the tooth surface by increasing their physical removal from the oral cavity through aggregate formation. Additionally, the effective inhibition of glucosyl transferase activity and the reduced bacterial adhesion to SHA, as seen with the presence of gallotannin extracts, suggest some potential anti-plaque activity.⁷⁷ The microorganisms found in inflamed gums are resistant to penicillin and tetracycline but are not resistant to antibacterial plant extracts like neem. Unlike antibiotics, antibacterial plant extracts produced no allergy in the gingiva that could inhibit their effectiveness.⁷⁸

In a clinical study, 50 patients with confirmed gingivitis were selected, 40 showed severe bleeding and pustular discharges from the gums. After just three weeks of brushing twice a day with paste including neem leaf extracts, eight out of ten patients showed significant improvement. The patients also showed a reduction in bacterial populations and elimination of halitosis (bad breath) with no side effects.⁷⁸



Figure 3: Neem leaves & twigs

A synergistic herbal formulation comprising of active fractions from *Azadirachta indica*, *Citrullus colocynthis* and *Cucumis sativus* extract and a carrier or additive was developed. The composition was found to be useful for teeth and gums as mouthwash or mouth rinse. This herbal formulation was described to be useful for preventing dental plaque and gingivitis in humans and also as an antimicrobial agent for preventing periodontal diseases.⁷⁹

A clinical study conducted on 60 volunteer subjects to evaluate the efficacy of fraction from neem, fraction from *Citrullus colocynthis* and a mixture of them on the reduction of dental plaque led to significant reductions of dental plaque.⁷⁹

4. Tulsi (*Ocimum sanctum*)



Figure 4: Tulsi leaves

Botanical name is *Ocimum sanctum*, Tulsi was recognized thousands of years ago as one of the India's greatest healing herb.⁸⁰ It is an erect soft, hairy aromatic herb or undershrub found throughout India.⁸¹

Several medicinal properties have been attributed to *Ocimum sanctum*. Different parts of Tulsi plant e.g. leaves, flowers, stem, root, seeds etc. are known to possess therapeutic potentials and have been used by traditional medical practitioners as expectorant, analgesic, anticancer, antiasthmatic, antiemetic, diaphoretic, anti-diabetic, antifertility, hepatoprotective, hypotensive, hypolipidemic and antistress agents. Tulsi has also been used in treatment of fever, bronchitis, arthritis, convulsions etc.⁸²

In an *in-vitro* study the various concentrations of the Tulsi extracts have been assessed against streptococcus mutans and concluded that the Tulsi extract 4% has a maximum antimicrobial potential.⁸³

Tulsi can act as COX-2 inhibitor, like modern analgesics due to its significant amount of Eugenol (1 - hydroxyl - 2methoxy - 4 allyl benzene). *Ocimum sanctum* leaves contain 0.7% volatile oil comprising about 71% eugenol and 20% methyl eugenol.⁸⁴

Ocimum sanctum at a dose of 100 mg/kg was found to be effective antiulcer agent in a study. Anti-ulcer effect of *Ocimum sanctum* may be due to its cytoprotective effect rather than antisecretory effect.⁸⁵ Due to its immunomodulating property *Ocimum sanctum* may find its potential use in treating immunologically mediated mucosal condition like pemphigus.⁸⁶

Role in the management of periodontal disease

Tulsi leaves are quite effective in treating common oral infections. Also few leaves chewed help in maintaining oral hygiene. Carracrol and Tetpene are the antibacterial agents present in this plant. Sesquiterpene bicyclic sesquiterpene also serves the same purpose. This

constituent is FDA approved food additive which is naturally present in Tulsi.⁸³

Tulsi leaves dried in sun and powdered can be used for brushing teeth.⁸⁷ It can also be mixed with mustard oil to make a paste and used as toothpaste. Tulsi has also proven to be very effective in counteracting halitosis. Its anti-inflammatory property makes it a suitable remedy for gingivitis and periodontitis, and it can be used for massaging the gingiva in these conditions.⁸⁸

Tulsi contains Vitamin A and C, calcium, zinc and iron. It also has chlorophyll and many other phytonutrients. Deficiency of these nutrient has been associated with variety of oral diseases.⁸⁹

5. Turmeric (*Curcuma Longa*)



Figure 5: Turmeric

It is a rhizomatous herbaceous perennial plant of family Zingiberaceae. It is native to tropical South Asia and needs temperatures between 20 °C and 30 °C. It is a perennial plant with orange, oblong tubers 2 or 3 inches in length and one inch in diameter, pointed or tapering at one end. When dried, it is made into a yellow powder with a bitter, slightly acrid, yet sweet taste. Ancient Indian medicine has touted turmeric as an herb with the ability to provide glow and luster to the skin as well as vigor and vitality to the entire body. Since turmeric has antimicrobial, antioxidant, astringent, and other useful properties, it is quite useful in dentistry also.^{91,92}

The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils including tumerone, atlantone, and zingiberone. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3-5.4% of raw turmeric. Curcumin has been used extensively in ayurvedic medicine for centuries, as it is nontoxic and has a variety of therapeutic properties including antioxidant, analgesic, anti-inflammatory, antiseptic activity, and anticarcinogenic activity.⁹³ Its role in the treatment of various precancerous conditions like oral submucous fibrosis, leukoplakia, and lichen planus has also been studied. Turmeric extract and turmeric oil

have demonstrated oncopreventive activity in *in vitro* and *in vivo* animal experiments.⁹⁴

Role in the management of periodontal disease

Massaging the aching teeth with roasted, ground turmeric eliminates pain and swelling.⁹³ A study concluded that chlorhexidine gluconate as well as turmeric mouthwash can be effectively used as an adjunct to mechanical plaque control methods in prevention of plaque and gingivitis. The effect of turmeric observed may be because of its anti-inflammatory action. Reduction in total microbial count was observed in both the groups. It is reported that the local drug delivery system containing 2% whole turmeric gel can be used as an adjunct to scaling and root planing. There was a significant reduction in the trypsin-like enzyme activity of "red complex" microorganisms.⁹⁶

Another study it was seen that, 1% curcumin solution can cause better resolution of inflammatory signs than chlorhexidine and saline irrigation as a subgingival irrigant. Mean PPD reduction was significantly greater for the curcumin group than all other groups on all post-treatment days.⁹⁷

6. Pomegranate (*Punica granatum*)

Punica granatum (family Punicaceae), generally known as "pomegranate," is a shrub or small tree native to Asia where several of its parts have been used as astringent, and for hemostatic as well as diabetic control.

The fruit of this tree is used for the treatment of throat infections, coughs, and fever due to its anti-inflammatory properties.⁹⁹

The constituents of pomegranate have been thoroughly investigated, however, clinical trials are in progress to explore the therapeutic potential of pomegranate products, particularly determining preventive efficacy of pomegranate extracts in cancer, cardiovascular diseases, inflammation diabetes and ultraviolet radiation-induced skin damage.

The most therapeutically beneficial pomegranate constituents are ellagic acid, ellagitannins (including punicalagins), punicic acid, flavonoids, anthocyanidins, anthocyanins, and estrogenic flavonols and flavones.¹⁰⁰

Pomegranate extracts have been shown to scavenge free radicals and decrease macrophage Oxidative stress and lipid peroxidation in animals and increase plasma antioxidant capacity in elderly humans. Also pomegranate extracts (juice, seed oil, peel) potently inhibit prostate cancer cell invasiveness and proliferation, cause cell cycle disruption, induce apoptosis, and inhibit tumour growth.¹⁰¹

Role in the management of periodontal disease

Research showed that pomegranate extract was more effective against the adherence of biofilm

microorganisms than a pharmaceutical antifungal, when three or four microorganisms were involved.¹⁰²

Investigators noted that pomegranate's active components, including polyphenolic flavonoids (e.g., punicalagins and ellagic acid), are believed to prevent gingivitis through a number of mechanisms including reduction of oxidative stress in the oral cavity,¹⁰³⁻¹⁰⁵ direct antioxidant activity; anti-inflammatory effects,^{106,107} antibacterial activity,¹⁰⁸ and direct removal of plaque from the teeth.¹⁰⁹



Figure 6: Pomegranate

In a study evaluating the effects of pomegranate on gingivitis, results showed a significant reduction in gingival bleeding after using a dentifrice containing the pomegranate extract.¹¹⁰ Yet in another similar study with a control group the effect of a gel with a pomegranate extract was tested on a group with experimental gingivitis which hardly mimics the naturally occurring gingivitis.⁹⁹

Pomegranate rinsing also lowered saliva activities of alpha-glucosidase, an enzyme that breaks down sucrose (sugar),¹¹¹ while it increased activities of ceruloplasmin, an antioxidant enzyme.¹¹² "The pomegranate extract-induced increase in ceruloplasmin activity can be expected to strengthen antioxidant defences," noted investigators. Subjects who rinsed with placebo solution did not experience any of these changes.¹¹³ Taken together, researchers concluded that these changes in saliva content indicated that routine rinsing with a pomegranate mouthwash, could promote oral health, including affecting processes related to gingivitis.¹¹³

Other Herbs

1. Drynaria

One of the traditional Korean medicine, *Drynaria fortunei* (D. fortunei; Gol-Se-Bo in Korean and Gu-Sui-Bu in Chinese) is one of candidates known to be effective for the treatment of inflammation, hyperlipidemia, arteriosclerosis, rheumatism, and gynaecological diseases such as osteoporosis and bone resorption in oriental

medicine.¹¹⁵⁻¹¹⁷ *D. fortunei* is also commonly used to manage disorders of orthopedics and has been claimed to have therapeutic effects on bone healing.^{115,116} Liu has shown that *D. fortunei* has an antioxidant effect on rat osteoblasts from hydrogen peroxide-induced death and may promote bone recovery under similar pathologic conditions.¹¹⁸ Liu reported that *D. fortunei* increases the attachment and growth of human gingival fibroblasts on *in vitro*.¹¹⁹ The water extract of *D. fortunei* has been reported to significantly protect against ototoxicity caused by streptomycin, streptomycin and kanamycin in human and the progression of bone loss induced by ovariectomy in rats.^{120,121} Moreover, it was also shown that *D. fortunei* extracts are shown to be potent inhibitors of the degradation of denaturated collagen by cathepsin K and of bone resorption in an *in vitro* model.¹²²

2. Garlic (*Allium sativum*)

Historically, garlic was used in China to lower blood pressure, in Egypt to increase physical strength, in Europe to prevent the plague and in India as a home remedy for various minor ailments like flu and cough. Garlic has been used not only to flavour food but also because it contains a sulfur-rich derivative of cysteine felt to have medicinal benefits. Its anticarcinogenic actions may be explained by particular organo-sulfur compounds. Diallyl sulfide, for example, which is responsible in part for its strong taste and odor, has been shown to selectively inhibit as well as induce certain P-450 enzymes.¹²³

As *S. mutans* is one of the primary etiological organisms in dental caries development, and in this study garlic extract has been shown to be effective against *S. mutans*, garlic extract mouth rinse might be used as an effective remedy in the prevention of dental caries.¹²⁴

In a study it was found that the garlic has antimicrobial properties *in vitro* against streptococci and anticariogenic properties against oral microorganism.¹²⁵

Allicin is considered the most therapeutic constituent of garlic. Research performed using broth dilution method revealed that planktonic growth of the cariogenic, gram-positive species *S. mutans*, *S. sobrinus*, and *Actinomyces oris* was inhibited by various allicin concentrations. Planktonic growth of the tested gram-negative periopathogenic species *A.* and *Fusobacterium nucleatum* was also inhibited by allicin.¹²⁶

3. Onion (*Allium cepa*)

Onion has the distinction of being the king of vegetables. Its extensive use in various forms due to the antibacterial and antifungal properties is well documented. It promotes good heart health because it facilitates the thinning of the blood which helps to prevent clot formation. Onion extracts possess an effect on all test bacterial strains (*S. mutans* JC-2, *S. sobrinus* OMZ176, *P. gingivalis* ATCC 33277 and *P. intermedia* ATCC 25611), and the effects were bactericidal against cultured and resting bacterial cells.¹²⁷

Studies of experimental carcinogenesis in animal models and in cell culture systems indicate that several allium-derived compounds exhibit inhibitory effects and that the underlying mechanisms may involve both the initiation and the promotion phases of carcinogenesis.¹²⁸ The potential anticarcinogenic action of onions may also be related to their high content of organosulfur compounds or to their high antioxidant activity, which is principally due to their wide content of flavonoids.¹²⁹

Allium cepa juice (0.4g/100g b.w. for 4 weeks) exhibited anti-hyperglycemic and antioxidant effect in alloxan induced diabetic rats, it also repaired hepatic and renal damage caused by alloxan.¹³⁰

4. Grape Seed Extract

Grape seed extract contains proanthocyanidins (PA) which are potent antioxidants and are known to possess anti-inflammatory, antibacterial and immune-stimulating effects. It has been reported to strengthen collagen based tissues by increasing collagen cross-links.¹³¹ In a study conducted to determine re-mineralizing effects of grape seed extract on artificial root caries, results showed that it is a promising natural agent for non-invasive root caries therapy.^{131,132}

5. Cloves (*Syzygium aromaticum*)

The dried flower buds of an East Indian evergreen tree, cloves are popularly used as a spice.

They also yield a volatile oil used medicinally and in perfumes. Cloves have antiseptic, stimulant, and antiemetic (vomiting preventive) properties and are used to treat the mouth, stomach, intestines, circulation, and lungs.¹³³

Eugenol extracts from clove have often been used in dentistry in conjunction with root canal therapy, temporary fillings, and general gum pain, since eugenol and other components of clove (including beta-caryophyllene) combine to make clove a mild anaesthetic as well as an anti-bacterial agent.

Eugenol, the primary component of clove's volatile oils, functions as an anti-inflammatory substance. Clove also contains a variety of flavonoids, including kaempferol and rhamnetin, which also contribute to clove's anti-inflammatory (and antioxidant) properties.¹³⁴

6. Mango (*Mangifera indica*)

Mango leaf contains ascorbic and phenolic acids which are known to possess antibacterial properties. Studies have shown that mango leaves (*mangifera indica*) possess antibacterial properties against anaerobic dental microflora such as *P. intermedia* and *P. gingivalis* and can effectively be used as adjunct for maintenance of oral hygiene.¹³⁵

CONCLUSION

Pharmacologically active phytochemicals useful for the prevention, treatment and maintenance of periodontal

diseases have been widely identified. They may be tannins, terpenoids, flavanoids, alkaloids etc. Antimicrobial activities of these have been found to be particularly useful for periodontal diseases. Clinical trials for assessment of safety and efficacy of these herbal remedies are in its infant stage. These herbal remedies are expected to be a widely used in future. The herbal remedies have an edge over conventional antibiotic treatment which suffer the limitation of low benefit to high risk as compared to herbal treatment which possess high benefit to low risk ratio.¹³⁶

As traditional plant preparations have significant historical background, it may be ethical to clinically evaluate these first and then collect modern toxicological data. Important classes of compounds essential for biologic activity must be delineated. All of this knowledge will be essential for proper standardization of a product. Therapeutic approaches with herbal medicine are often staggered due to lack of data on safety and efficacy and meticulous clinical trial evidence. It is recommended that more researches should be undertaken.¹³⁷

Standardization and quality assurance of these herbal remedies is also a key area to be focused in future and efforts have been initialized towards this target. There are much more opportunities for further research in the utility of herbal remedies for periodontal diseases. More organized and long-term research is to be carried out to support the use of established remedies. Development of novel drug delivery systems for these herbal ingredients is likely to be one of the thrust areas of research in future. Research on colloidal drug delivery systems such as nanoparticles, nanoemulsion etc seems to be promising.¹³⁶

REFERENCES

1. Oliver RC, Brown LJ, and Loe H, Periodontal diseases in the United States population, *Journal of Periodontics*, 69, 1998, 269-278.
2. Schwach-Abdellaoui K, Vivien-Castoni N, Gurny R, Local delivery of antimicrobial agents for the treatment of periodontal diseases, *Eur J Pharm Biopharm*, 50, 2000, 83-99.
3. Reddy PD, Satyanarayana T, Purushothaman M, Local Drug Delivery of Herbs for Treatment of Periodontitis, *Journal of Innovative trends in Pharmaceutical Sciences*, 1, 2010, 245-251.
4. Kornman KS, Controlled release local delivery - Antimicrobials in Periodontics. Prospects for the future, *Journal of Periodontology*, 64, 1993, 782-791.
5. Pirmal S.A., Jathar S.R., Sirwani R.P., Malhotra P.: WO2008001325, 2008.
6. De Oliveira RR, Schwartz-Filho HO, Novaes AB Jr, Taba M Jr, Antimicrobial photodynamic therapy in the non-surgical treatment of aggressive periodontitis: a preliminary randomized controlled clinical study, *J Periodontol*, 78, 2007, 965-73.
7. Mosby's medical dictionary, 8th edition. © 2009, Elsevier
8. Morris AJ, Steele J, and White DA, The oral cleanliness and periodontal health of UK adults in 1998, *British Dental Journal*, 191, 2001, 186-192.
9. Friedman M, Golomb G, New sustained release dosage form of chlorhexidine for dental use, *J Periodontal Res*, 17, 1982, 323-328.
10. Steinberg D, Friedman M, Sustained release drug delivery devices for treatment of dental diseases; In: Tyle P, Ed. Drug delivery



- devices: Fundamentals and applications. New York: Marcel Dekker, 1998, 491-515.
11. Lakshmi T, Geetha RV, Jai Ganesh Ramamurthy, Rummilla Anand VA, Anitha roy, Vishnu priya V & Ananthi T, Unfolding Gift of Nature - Herbs for the Management of Periodontal disease: A Comprehensive Review, *Journal of Pharmacy Research*, 4, 2011, 2576-2580
 12. Park KM, You JS, Lee HY, Baek NI, Hwang JK, Kuwanon G: an antibacterial agent from the root bark of *Morus alba* against oral pathogens, *Journal of Ethnopharmacology*, 84, 2003, 181–85.
 13. Chung JY, Choo JH, Lee MH, Hwang JK, Anticariogenic activity of macleignan isolated from *Myristica fragrans* (nutmeg) against *Streptococcus mutans*. *Phytomedicine*, 13, 2006, 261–66.
 14. Prabhu GR, Gnanamania, Sadulla S, Guajjaverin—a plant flavonoid as potential antiplaque agent against *Streptococcus mutans*, *Journal of Applied Microbiology*, 101, 2006, 487–95.
 15. Zhu YP, Woerdenbag HJ, Traditional Chinese herbal medicine, *Pharm World Sci*, 17, 1995, 103-12.
 16. World Health Organization. WHO Traditional Medicine Strategy 2002–2005, Document WHO / EDM / TRM /2002.1. Geneva, Switzerland: World Health Organization, 11, 2002.
 17. Zhu L, Petersen PE, Wang JY, Bian JY, Zhang BX, Oral health knowledge, attitudes and behaviour of adults in China, *Int Dent J*, 55, 2005, 231–241.
 18. Bhardwaj A, Bhardwaj SV, ROLE OF MEDICINAL HERBS IN PREVENTION AND TREATMENT OF DENTAL DISEASES, *Ann Ayurvedic Medicine*, 1, 2012, 95-101.
 19. Dharmani P, Palit G, Exploring Indian medicinal plants for antiulcer activity, *Indian J Pharmacol*, 38, 2006, 95-9.
 20. Cowan MM, Plant Products as Antimicrobial Agents, *Clin Micro Rev*, 12, 1999, 564–582.
 21. Petti S, Scully C, Polyphenols, oral health and disease: A review, *J Dent*, 37, 2009, 413–423.
 22. Colvard MD, Cordell GA, Villalobos R, Sancho G, Soejarto DD, Pestle W, Survey of medical ethnobotanicals for dental and oral medicine conditions and pathologies, *Journal of Ethnopharmacology*, 107, 2006, 134–142.
 23. Anonymous, Indian Herbal Pharmacopoeia, Revised new edition 2002, Indian Drug Manufacturer's Association, Mumbai, 2002, 1-11.
 24. Wallis TE, Textbook of Pharmacognosy, 5th Edition, CBS Publishers and Distributors, New Delhi, 2005, 461-463. Anonymous, the Wealth of India, Raw Material, Vol 1, CSIR, New Delhi, 2004.
 25. Singh KN, Lal B, Note on traditional uses of Khair (*Acacia catechu* Wild.) by inhabitants of shivalik range of western Himalaya, *Ethnobotanical Leaflets*, 10, 2006, 109-112.
 26. Qadry JS, Shah's and Qadry's Pharmacognosy, 12th edition, B.S Shah Prakashan, Ahmedabad, 2008, 302-303.
 27. Ray D, Sharatchandra KH, Thokchom IS, Antipyretic, anti diarrhoeal, hypoglycaemic and hepatoprotective activities of ethyl acetate extract of *Acaciacatechu* Wild. In albino rats, *Indian Journal of Pharmacology*, 38, 2006, 408-413.
 28. Jayasekhar P, Mohanan PV, Hepatoprotective activity of ethyl acetate extract of *Acacia catechu*, *Indian Journal of Pharmacology*, 29, 1997, 426-428.
 29. http://www.himalayahealthcare.com/herbfinder/h_acaciac.htm
 30. Harborne J.B 1999 phytochemical Dictionary, Tylor & francis Ltd., London
 31. Ernst E, Adverse effects of herbal drugs in dermatology, *The British journal of dermatology*, 143, 2000, 923–929.
 32. <http://de.wikipedia.org/wiki/Gerber-Akazie>
 33. Marshall JM (2000). "Aloe vera gel: what is the evidence?". *Pharm J*, 244: 360–362.
 34. Boudreau MD, Beland FA, An evaluation of the biological and toxicological properties of *Aloe barbadensis* (Miller), *Aloe vera*, *Journal of environmental science and health. Part C, Environmental carcinogenesis & ecotoxicology reviews* 24, 2006
 35. Vogler BK, Ernst E, Aloe vera: a systematic review of its clinical effectiveness, *The British journal of general practice : the journal of the RoyalCollege of General Practitioners* 49, 1999, 823–8.
 36. Atherton P, Aloe vera revisited, *Br J Phytother*, 4, 1998, 76-83.
 37. Shelton M, Aloe vera, its chemical and therapeutic properties, *Int J Dermatol*, 30, 1991, 679-83.
 38. Atherton P, The essential Aloe vera, The actions and the evidence, 2nd ed, 1997.
 39. Chithra R, Sajithlal GB, Chandrakasan G, Influence of aloe vera on collagen characteristics in healing dermal wounds in rats, *Mol Cell Biochem*, 181, 1998, 71-6.
 40. Hegggers J, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, Beneficial effect of aloe on wound healing In an excisional wound model, *J Altern Complement Med*, 2, 1996, 271-7.
 41. Furukawa F, Nishikawa A, Chihara T, Shimpo K, Beppu H, Kuzuya H. Chemopreventive effects of *Aloe arborescens* on N-nitrosobis (2-oxopropyl) amine-induced pancreatic carcinogenesis in hamsters, *Cancer Lett*, 178, 2002.
 42. Fenig E, Nordenberg J, Beery E, Sulkes J, Wasserman L, Combined effect of aloe-emodin and chemotherapeutic agents on the proliferation of an adherent variant cell line of Merkel cell carcinoma, *Oncol Rep*, 11, 2004, 213–7.
 43. Garnick JJ, Singh B, Winkley G, Effectiveness of a medicament containing silicon dioxide, aloe, and allantoin on aphthous stomatitis, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 86, 1998, 550–6.
 44. Su K, Mehta V, Ravikumar L, Shah R, Pinto H, Halpern J. Phase II double-blind randomized study comparing oral aloe vera versus placebo to prevent radiation-related mucositis in patients with head-and-neck neoplasms, *Int J Radiat Oncol Biol Phys*, 60, 2004, 71–7.
 45. Michael. G. Newman, Henry H. Takei, Fermin A, Carranza. *Clinical periodontology*, 22, 347, 6, 97.
 46. Sydiskis RJ, Owen DG, Lohr JL, Rosler KH, Blomster RN, Inactivation of enveloped viruses by anthraquinones extracted from plants. *Antimicrob Agents Chemother*, 35, 1991, 2463-6.
 47. West DP, Zhu YF, Evaluation of aloe vera gel gloves in the treatment of dry skin associated with occupational exposure, *Am J Infect Control*, 31, 2003, 40-2.
 48. Robson MC, Hegggers JP, Hagstrom WJ, Myth, magic, witchcraft or Fact? Aloe vera revisited, *J Burn Care Rehab*, 3, 1982, 157-163.
 49. Cera LM, Hegggers JP, Robson MC, Hagstrom WJ, The therapeutic efficacy of aloe vera cream (Dermaide Aloe) in thermal injuries. Two case reports, *J Am Animal Hosp Assoc*, 16, 1980, 768-772.
 50. Saito H, Ishiguro T, Imanishi K, Suzuki I, Pharmacological studies on a plant lectin aloctin A. II. Inhibitory effect of aloctin A on experimental models of inflammation in rats, *Jpn J Pharmacol*, 32, 1982, 139-142.
 51. Hutter JA, Salman M, Stavinoha WB, Antiinflammatory C-glucosyl chromone from *Aloe barbadensis*, *J Nat Prod*, 59, 1996, 541-543.
 52. Okyar A, Can A, Akev N, Baktir G, Su' tlu' pinar N, Effect of Aloe vera leaves on blood glucose level in type I and type II diabetic rat models, *Phytother Res*, 15, 2001, 157-161.
 53. Rajasekaran S, Sivagnanam K, Subramanian S, Antioxidant effect of Aloe vera gel extract in streptozotocin induced diabetes in rats, *Pharmacol Rep*, 57, 2005, 90-96.
 54. Nwanjo HU, Antioxidant activity of the exudate from *Aloe barbadensis* leaves in diabetic rats. *Biokemistri*, 18, 2006, 77-81.
 55. Ozsoy NR, Yanardag R, Can A, Akev N, Okyar A, Effectiveness of Aloe vera versus glibenclamide on serum lipid parameters, heart



- and skin lipid peroxidation in type II diabetic rats, *Asian J Chem*, 20, 2008, 2679-2689.
56. Reynolds T, Dweck AC, Aloe vera leaf gel: A review update, *J Ethnopharmacol*, 68, 1999, 3-37.
 57. Yagi A, Kabash A, Okamura N, Haraguchi H, Moustafa SM, Khalifa TI, Antioxidant, free radical scavenging and anti-inflammatory effects of aloesin derivatives in Aloe vera, *Planta Med*, 68, 2002, 957-960.
 58. Grindlay D, Reynolds T, The Aloe vera phenomenon: A review of the properties and modern uses of the leaf parenchyma gel, *J Ethnopharmacol*, 16, 1986, 117-151.
 59. Villalobos OJ, Salazar CR, Sa´nchez GR, Effect of a mouthwash made of Aloe vera on plaque and gingival inflammation, *Acta Odontol Venez*, 39, 2001, 16-24.
 60. de Oliveira SM, Torres TC, Pereira SL, Mota OM, Carlos MX, Effect of a dentifrice containing Aloe vera on plaque and gingivitis control. A double-blind clinical study in humans, *J Appl Oral Sci*, 16, 2008, 293-296.
 61. Garnick JJ, Singh B, Winkley G, Effectiveness of a medicament containing silicon dioxide, aloe, and allantoin on aphthous ulcers, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 86, 1998, 550-556.
 62. Rajasekaran S, Sivagnanam K, Subramanian S, Antioxidant effect of Aloe vera gel extract in streptozotocin induced diabetes in rats, *Pharmacol Rep*, 57, 2005, 90-96.
 63. Chopra RN, Nayer SL and Chopra IC, *Glossary of Indian Medicinal Plants*, CSIR, New Delhi, 1956.
 64. Chopra RN, Chopra IC, Handa KL and Kapur LD (eds), *Indigenous Drugs of India*, U.N. Dhur and Sons, Kolkata, 1958, 51-595.
 65. Kirtikar KR and Basu BD, in *Medicinal Plants* (eds Blatter E, Cains, JF, Mhaskar, KS.), Vivek Vihar, New Delhi, 1975, 536.
 66. Thakur RS, Singh SB and Goswami A, *Curr. Res. Med. Aromat. Plants*, 3, 1981, 135-140.
 67. Koul O, Isman M B and Ketkar CM, *Can. J. Bot.*, 68, 1990, 1-11.
 68. Chatterjee A and Pakrashi S (eds), *The Treatise on Indian Medicinal Plants*, 3, 1994, 76.
 69. Siddiqui S., *Curr. Sci.*, 11, 1942, 278-279.
 70. Varma G S, *Miracles of Neem Tree*, Rasayan Pharmacy, New Delhi, 1976.
 71. Mitra CR, Garg HS, Pandey GN, *Phytochemistry*, 10, 1971, 857-864.
 72. Rao AR, Kumar S, Paramshivam TB, Kamalaksi S, Parashuram AR, *Indian J. Med. Res.*, 57, 1969, 495-502.
 73. Murty KS, Rao DN, Murty LB, *Indian J. Pharmacol.*, 10, 1978, 247-250.
 74. <http://www.gits4u.com/agri/agri5a.htm>
 75. http://en.wikipedia.org/wiki/Aloe_vera
 76. <http://www.healthtipsexpress.com>
 77. Wolinsky LE, Mania S, Nachnani S, and Ling S, The inhibiting effect of aqueous azadirachta indica (neem) extract upon bacterial properties influencing *in vitro* plaque formation, *J Dent Res*, 75, 1996, 816-822.
 78. <http://www.neemamerica.com/research.asp>
 79. Behl HM., Sidhu OP, Pushpangadan P, Singh SC, WO2004084852, 2004.
 80. Cox SD, Mann CM, Markham J, The mode of antimicrobial action of the essential oil of *Melaleuca alternifolia* (tea tree oil), *J Appl Microbiol*, 88, 2000, 170-176.
 81. Fine DH, Furgang D, Barnett ML, Drew C, Steinberg L, Charles CH, Vincent JW, Effect of an essential oil-containing antiseptic mouthrinse on plaque and salivary *Streptococcus mutans* levels, *J Clin Periodontol*, 27, 2000, 157-161.
 82. Rai Y. *Holy Basil: Tulsi (A Herb)*, Navneet Publications India Ltd., 2002.
 83. Agarwal P, Nageshi L, Murlikrishnan, Evaluation of the antimicrobial activity of various concentrations of Tulsi (*Ocimum sanctum*) extract against *Streptococcus mutans*, *Ind J Dent Res*, 21, 2010, 357-59.
 84. Singh SA, Majumdar DK, Rehan HMS, Evaluation of anti inflammatory potential of fixed oil of *Ocimum sanctum* (Holybasil) and its possible mechanism of action, *J Ethnopharmacol*, 54, 1996, 19-26.
 85. Dharmani P, Evaluation of anti-ulcerogenic and ulcer-healing properties of *Ocimum sanctum* Linn. *J Ethnopharmacol*, 93, 2004, 197-206.
 86. Mediratta PK, Evaluation of immunomodulatory potential of *Ocimum sanctum* seed oil and its possible mechanism of action, *J Ethnopharmacol*, 80, 2002, 15-20.
 87. Prakash P, Gupta N, Therapeutic uses of *ocimum sanctum* linn (tulsi) with a note on eugenol and its pharmacological action: A short review, *Indian J Physiol Pharmacol*, 49, 2005, 125-31.
 88. Sen P, Therapeutic potential of Tulsi: from experience to facts. *Drugs News and views*, 1, 1993, 15-21.
 89. Tulsi Medicinal Ingredients. Available at <http://www.tulsiherbalte>
 90. <http://www.wildflowerapothecary.com>, The Health Benefits Of Tulsi Tea
 91. Ramirez S, Bosca A, Soler A, Gutierrez MA, Antioxidant curcuma extracts decrease the blood lipid peroxide levels of human subjects: *Age*, 18, 1995, 167-169.
 92. Kiso Y, Suzuki Y, Watanbe N, Oshima Y, Hikino H, Antihepatotoxic principles of *Curcuma longa* rhizomes: *Planta Med*, 49, 1983, 185-7.
 93. Çıkrıkçı S, Mozioglu E, Yılmaz H, Biological activity of curcuminoids isolated from *Curcuma longa*. *Rec Nat Prod*, 2, 2008, 19-24.
 94. Deepa DA, Anita B, Sreelatha KT, Comparative study of the efficacy of curcumin and turmeric oil as chemoprotective agents in oral submucous fibrosis: A clinical and histopathological evaluation, *JIAOMR*, 22, 2010, 88-92.
 95. Waghmare PF, Chaudhary AU, Karhadkar VM, Jamkhande AS, Comparative evaluation of turmeric and chlorhexidine gluconate mouthwash in prevention of plaque formation and gingivitis: A clinical and microbiological study. *J Contemp Dent Pract*, 12, 2011, 221-2.
 96. Behal R, Mali MA, Gilda SS, Paradkar AR, Evaluation of local drug delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planning in chronic periodontitis: A clinical and microbiological study, *J Indian Soc Periodontol*, 15, 2011, 35-8.
 97. Suhag A, Dixit J, Dhan P, Role of curcumin as a subgingival irrigant: A pilot study. *PERIO: Periodontal Pract Today*, 2, 2007, 115-21.
 98. <http://dailyayurvedanews.com>, Turmeric facts
 99. Salgado AD, Maia JL, Pereira SL, de Lemos TL, Mota OM, Antiplaque and antigingivitis effects of a gel containing *Punica granatum* Linn extract. A double-blind clinical study in humans, *J Appl Oral Sci*, 14, 2006, 162-6.
 100. Pomegranate. www.crfp.org/pubs/ff/pomegranate.html
 101. Jurenka K. et al, Therapeutic Applications of Pomegranate (*Punica granatum* L.): A Review. *Alt Med Rev*, 13, 2008, 128-144.
 102. Vasconcelos LC, Sampaio FC, Sampaio MC et al, Minimum inhibitory concentration of adherence of *Punica granatum* Linn (pomegranate) gel against *S. mutans*, *S. mitis* and *C. albicans*, *Braz Dent J*, 17, 2006, 223-7.
 103. Seeram NP, Adams LS, Henning SM et al, *In vitro* antiproliferative, apoptotic and antioxidant activities of punicalagin, ellagic acid and a total pomegranate tannin extract are enhanced in combination with other polyphenols as found in pomegranate juice, *J Nutr Biochem*, 16, 2005, 360-7.

104. Chidambara Murthy KN, Jayaprakasha GK, Singh RP, Studies on antioxidant activity of pomegranate (*Punica granatum*) peel extract using *in vivo* models. *J Agric Food Chem*, 50, 2002, 4791-5.
105. Battino M, Bullon P, Wilson M, Newman H, Oxidative injury and inflammatory periodontal diseases: the challenge of antioxidants to free radicals and reactive oxygen species, *Crit Rev Oral Biol Med*, 10, 1999, 458-76.
106. Madianos PN, Bobetsis YA, Kinane DF, Generation of inflammatory stimuli: how bacteria set up inflammatory responses in the gingiva, *J Clin Periodontol*, 32, 2005, 57-71.
107. Aggarwal BB, Shishodia S, Suppression of the nuclear factor-kappaB activation pathway by spice-derived phytochemicals: reasoning for seasoning, *Ann NY Acad Sci*, 1030, 2004, 434-41.
108. Badria FA, Zidan OA, Natural products for dental caries prevention, *J Med Food*, 7, 2004, 381-4.
109. Menezes SM, Cordeiro LN, Viana GS, *Punica granatum* (pomegranate) extract is active against dental plaque, *J Herb Pharmacother*, 6, 2006, 79-92
110. Pereira JV, Sampaio FC, Estudos com o extrato da *punica granatum* linn (roma): Efeito antimicrobiano *in vitro* e avaliacao clinica de um dentifricio sobre microorganismos do biofilme dental [abstract], *Journal da Aboprev* 2003; Fev-abr:8.
111. Beighton D, Radford JR, Naylor MN, Glycosidase activities in gingival crevicular fluid in subjects with adult periodontitis or gingivitis, *Arch Oral Biol*, 37, 1992, 343-8.
112. Bielli P, Calabrese L, Structure to function relationships in ceruloplasmin: a 'moonlighting' protein, *Cell Mol Life Sci*, 59, 2002, 1413.
113. DiSilvestro R, DiSilvestro D, DiSilvestro D, Pomegranate extract Pomella® Mouth Rinsing Effects on Saliva Measures Relevant to Gingivitis Risk, Manuscript Submitted 12-07.
114. <http://www.health-study.com>, Amazing Health Benefits of Pomegranate
115. Huang HF, You JS, The use of Chinese herbal medicine on experimental fracture healing, *Am J Chin Med*, 25, 1997, 351-356.
116. Sun JS, Lin CY, Dong GC, Sheu SY, Lin FH, Chen LT, Wang YJ, The effect of Gu-Sui-Bu (*Drynaria fortunei* J Sm) on bone cell activities, *Biomaterials*, 23, 2002, 3377-3385.
117. Wong RW, Rabie AB, Systemic effect of crude extract from rhizome of *Drynaria fortunei* on bone formation in mice, *Phytother Res*, 20, 2006, 313-315.
118. Liu HC, Chen RM, Jian WC, Lin YL, Cytotoxic and antioxidant effects of the water extract of the traditional Chinese herb gusuibu (*Drynaria fortunei*) on rat osteoblasts, *J Formos Med Assoc*, 100, 2001, 383-388.
119. Liu B, Zhonghua Kou Qiang Yi Xue Za Zhi, Effects of *Lycium barbarum* and *Drynaria fortunei* on *in vitro* attachment and growth of human gingival fibroblasts on root surfaces, 27, 1992, 159-161.
120. Long M, Smouha EE, Qiu D, Li F, Johnson F, Luft B, Flavanoid of *Drynaria fortunei* protects against gentamicin ototoxicity. *Phytother Res*, 18, 2004, 609-614.
121. Wang Z, Zhonghua Er Bi Yan Hou Ke Za Zhi. Experimental study of *Rhizoma drynariae* (Gusuibu) in the treatment of streptomycin ototoxicity, 24, 1989, 79-81.
122. Jeong JC, Kang SK, Yoon CH, Jeong CW, Kim HM, Lee YC, Chang YC, Kim CH, Inhibition of *Drynariae Rhizoma* extracts on bone resorption mediated by processing of cathepsin K in cultured mouse osteoclasts, *Int Immunopharmacol*, 3, 2003, 1685-1697.
123. Yang CS, Chhabra SK, Hong JY, Smith TJ, Mechanisms of inhibition of chemical toxicity and carcinogenesis by diallyl sulfide (DAS) and related compounds from garlic, *J Nutr*, 131, 2001, 1041S-5S.
124. Chavan SD, Shetty NL, Kanuri M, Comparative evaluation of garlic extract mouthwash and chlorhexidine mouthwash on salivary *Streptococcus mutans* count - an *in vitro* study. *Oral Health Prev Dent*, 8, 2010, 369-74.
125. Groppo FC, Ramacciato JC, Motta RH, Ferraresi PM, Sartoratto A, Antimicrobial activity of garlic against oral streptococci, *Int J Dent Hyg*, 5, 2007, 109-15.
126. Bachrach G, Jamil A, Naor R, Tal G, Ludmer Z, Steinberg D, Garlic Allicin as a Potential Agent for Controlling Oral Pathogens, *J Med Food*, 6, 2011.
127. Kim JH, Anti-bacterial action of onion (*Allium cepa* L.) extracts against oral pathogenic bacteria, *J Nihon Univ Sch Dent*, 39, 1997, 136-41.
128. Shirin H, Pinto JT, Kawabata Y, Antiproliferative effects of S allylmercaptocysteine on colon cancer cells when tested alone or in combination with sulindac sulphide, *Cancer Res*, 61, 2001, 725-31.
129. Yang J, Meyers KJ, van der Heide J, Liu RH, Varietal differences in phenolic content and antioxidant and antiproliferative activities of onions, *J Agric Food Chem*, 52, 2004, 6787-93.
130. El-Demerdash FM, Yusef MI and El-Naga NI, Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats, *Food Chem. Toxicol*, 43, 2005, 57-63.
131. Wu CD: Grape products and oral health, *J Nutr*, 139, 2009, 1818S-1823S.
132. Xie Q, Bedran-Russo AK, Wu CD, *In vitro* remineralization effects of grape seed extract on artificial root caries, *J Dent*, 36, 2008, 900-906.
133. Wahlquist ML, and Dalais FS, Phytoestrogens: emerging multifaceted plant compounds, *Med J Aust*, 167, 1997, 199-200.
134. Amrutesh S, Dentistry & Ayurveda V - An evidence based approach, *Int Journal of Clinical dental science*, 2, 2011, 3-9.
135. Evaluation of Antibacterial activity of *magnifera indica* on anaerobic dental microflora based on *in vivo* studies, *Indian J Pathology Microbiol*, 45, 2002, 307-310.
136. Kumar P, Ansari SH and Ali J, Herbal Remedies for the Treatment of Periodontal Disease - A Patent Review, *Recent Patents on Drug Delivery & Formulation*, 3, 2009, 221-228.
137. Agrawal N, Gupta R, Gupta I, Mehrotra V, HERBCRAFT: BOON TO THE PERIODONTAL THERAPY, *Int J Dent Health Sci*, 1, 2014, 47-62.

Source of Support: Nil, Conflict of Interest: None.

