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## Use of Medicinal Plants in Oral Lesions

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### ABSTRACT

The progress of dentistry into an advanced science is a truly remarkable one. The importance and value of dental art and science as a humane service are well recognized. It was people of earlier periods who laid the foundations upon which current day dentistry has been built. The use of indigenous plants for the treatment of various health conditions has been documented since 6,000 BC throughout the Indian subcontinent. The popularity and widespread acceptance of this form of medicine stem from the easy accessibility to local herbs, lower cost, and the absence of any potential chemical additives which are present in conventional drugs. In dentistry, many of these have been studied for their cleansing action, antimicrobial, and antiplaque properties, due to their innate antioxidant and anti-inflammatory mechanisms. In this review, we intend to discuss the use of indigenous plants in treating various oral lesions. A literature review was conducted for finding a solution to show evidence on a meta-level. Two reviewers selected the articles to ensure the quality and reliability of the search protocol. Search engine like Google, Pubmed, Medline and Scopus were used with the key terms herbal extracts, alternative medicine, oral lesions, phytotherapy. Medicinal herbs have been found to possess anti-inflammatory properties and some even demonstrated to have anti-cancer properties. In developing countries still, herbal medicine is considered to be the main system in treating many diseases since it is affordable. But, the end-users should be given sufficient scientific evidence to use them which can be achieved by conducting scientific experiments to confirm their safety and efficacy.

**Key Words:** Herbal extracts, Alternative medicine, Oral lesions, Dental herb therapy, Antibacterial, Phytotherapy

### INTRODUCTION

Ayurvedic medicine has often been quoted as the oldest medical system in the world. The use of indigenous plants for the treatment of various health conditions has been documented since 6,000 BC throughout the Indian subcontinent. Traditional healers know over 2500 herbs and use almost 100 species of therapeutic plants in everyday practice.<sup>1</sup>

In recent years, a system of 'complementary and alternative medicine' (CAM) has been recognized by healthcare professionals all over the world. The National Centre for Complementary and Integrative Health (NCCIH, USA) has defined CAM as "a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine". Following this, the World Health Organization defined herbal medicine as 'plant-derived materials or preparations intended for human therapeutic use or other health benefits in humans' and cat-

egorized it based on the evolution, origin, and current usage into 4 subtypes:

1. Indigenous herbal medicine- used primarily by the members of a small local community and the knowledge is passed on over generations.
2. Herbal medicines in systems- the system of medicine that is widely documented and accepted by their respective countries, like Ayurveda, Siddha, and Unani.
3. Modified herbal medicines- plant extracts whose dose, chemistry, and administration have been modified to reach the safety standards of a regulatory body.
4. Imported products with a herbal medicinal base- include all forms of a herb and its extracts that are imported and approved by a national regulatory body.<sup>2</sup>

### USES OF HERBS IN DENTISTRY

Phytotherapy or phytomedicine is commonly defined as the study of the use of extracts of natural origin as medicines

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or health-promoting agents. The popularity and widespread acceptance of this form of medicine stem from the easy accessibility to local herbs, lower cost, and the absence of any potential chemical additives which are present in conventional drugs.

Although only a few herbs have been scientifically approved for their medicinal values, a large number of them have always been used as major staples in local cuisine. In dentistry, many of these have been studied for their cleansing action, antimicrobial, and antiplaque properties, due to their innate antioxidant and anti-inflammatory mechanisms. Besides, they have proven to be effective in specific conditions such as recurrent aphthous ulcers, gingivitis, oral infections of *Candida albicans*, etc.<sup>3,4</sup>

### ALOE VERA

*Aloe barbadensis miller*, commonly called Aloe vera, belongs to the *Asphodelaceae* family. It is a succulent plant, widely cultivated for its ornamental and medicinal properties. This succulence or fleshy nature of the leaves allows the plant to thrive in dry regions with low annual rainfall. The parenchymal tissue of the leaves contains three prominent layers

1. An inner layer of colourless mucilaginous gel that is primarily made of water (98-99%)
2. A middle layer of yellow sap or latex
3. A thick protective outer layer or rind

The leaves also contain important bioactive molecules such as aloesin, aloin, aloe-emodin, flavonoids, anthraquinones, etc.

Aloe vera gel (AVG), extracted from the fleshy leaves, and has been proven to be a potent antibacterial, antifungal, antioxidant and immune-boosting agent. As a result, AVG has been studied in the treatment of various oral lesions such as recurrent oral ulcers, oral lichen planus, and oral candidiasis. Besides, AVG gel has also shown positive outcomes in aiding wound healing when used over-extraction sockets.

In an in vitro study comparing various dilutions of AVG with standard drugs such as Ciprofloxacin and Ofloxacin, it was found that at higher concentrations (50%, 100%) the gel showed significant potency as an antibacterial agent. However, at concentrations below 50%, no antibacterial effect was reported.<sup>5</sup>

Following this, the effect of aloe vera on colonies of cariogenic and periodontal pathogens was studied by disc diffusion assays and reported based on the zone of inhibition produced by various concentrations. It was found that the minimum inhibitory concentrations (MIC) were much lesser for strains of *Streptococcus mutans* when compared to *Aggregatibacter actinomycetemcomitans* and *Porphyromonas*

*gingivalis*. The antibacterial properties of aloe vera against specific pathogens such as *Escherichia coli*, *Salmonella typhi*, *Klebsiella*, *Pseudomonas*, etc. have also been studied.<sup>6</sup>

### TURMERIC

*Curcuma longa* (*C. longa*), commonly used as a household ingredient turmeric, has been used for its therapeutic properties in Ayurveda, Siddha, and Unani medicine. It contains a class of phytochemicals known as curcuminoids, namely curcumin, dimethoxy curcumin, and bisdemethoxycurcumin.

Curcuminoids have shown significant anti-inflammatory, antioxidant, and anticancer properties in in-vivo and ex-vivo studies. This anti-inflammatory action is attributed to its inhibitory effect on enzymes such as Cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and inducible nitric oxide synthase enzymes (iNOS). It also blocks the release of cytokines such as tumour necrosis factor (TNF), and interleukins (IL) 1, 2, 6, 8, and 12. The immunomodulatory effect of curcumin has also been correlated to its activation of host macrophages and natural killer cells and regulation of lymphocyte-mediated function.<sup>7</sup>

A study comparing the effect of 1% curcumin oral gel with 0.1% paste of triamcinolone acetonide was conducted in patients with oral lichen planus (OLP), and it was found that the pain and burning sensation was significantly reduced with the use of the natural alternative. It was concluded that although turmeric gel cannot be used independently in the management of OLP, it could be used in the maintenance phase of treatment, following the initial phase of standard corticosteroid therapy.<sup>8</sup> Similarly, when higher doses of curcuminoids were administered systemically in patients with OLP, greater control of the symptoms was observed.

In a randomized controlled trial conducted among known cases of Oral submucous fibrosis (OSMF), leukoplakia, and OLP, it was found that curcumin produced a marked reduction in the pain scores, as well as the extent of the mucosal lesions, and an increased mouth opening was observed in patients with OSMF. This effect of curcumin on these potentially malignant conditions was associated with a rise in vitamin C and E, and subsequent inhibition of damage to DNA or lipid peroxidation.<sup>9</sup>

### TULSI

*Ocimum sanctum* (*O. sanctum*), commonly known as holy basil or Tulsi is an aromatic plant used for religious and traditional medicinal practices. The main phytochemical components of tulsi are saponins, flavonoids, triterpenoids, and tannin. Other bioactive molecules include oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linoleic acid, and  $\beta$ -caryophyllene.

In an experimental study conducted on rats, the combined antioxidant, anti-inflammatory and analgesic properties of

tulsi have shown positive results in aiding wound healing. Ethanolic extracts of *O. sanctum* have shown greater wound breaking strength, a faster rate of epithelialization with the substantial rise in wound contraction.<sup>4</sup>

Herbal mouth rinses containing extracts of tulsi have shown antibacterial activity specifically against strains of *Streptococcus mutans*. In a comparative evaluation of a herbal mouth rinse containing tulsi and a standard sodium fluoride mouth rinse, it was found that this inhibitory effect on the pathogen was achieved employing increasing salivary pH levels resulting in reduced virulence of the bacteria.<sup>10</sup> Clinical trials conducted with a tulsi mouth rinse and 0.2% Chlorhexidine mouth rinses have provided similar results, and patients have shown to favour the natural alternative due to better taste and convenience.

The antibacterial action of extracts of *O. sanctum* has been attributed to the nature of the formulation. While aqueous extracts have shown a greater inhibitory effect on *Klebsiellapneumoniae*, *Escherichiacoli*, *Candida albicans*, and *Staphylococcus aureus*, the alcoholic extracts showed greater antagonistic effects on *Vibrio cholerae*.

An experiment conducted on hamsters with 7,12-dimethyl benza-anthracene (DMBA) induced buccal pouch carcinogenesis highlighted the anticancer property of *O. sanctum* extracts. Simultaneous topical application of aqueous extracts along with oral administration of ethanolic extracts, showed substantially lesser development of oral papillomas and squamous cell carcinomas.<sup>11</sup>

## POMEGRANATE

*Punicagranatum* (*P. granatum*), commonly called pomegranate, is a shrub that is native to the Indian subcontinent. It is abundant with phytochemicals like tannins, flavones, and anthocyanins (like delphinidin and cyanidin) which produce the bright red colour of the fruit extracts. These molecules have been studied for their chemopreventive and anti-inflammatory effects on cells. Besides, the seeds are a rich source of puniceic acid, oleic and linoleic acid, palmitic acid, and stearic acid.

These phytochemicals have shown a substantial inhibitory effect on inflammatory mediators. Punicic acid has shown an antagonistic effect on prostaglandin synthesis, while pomegranate seed oil has shown suppression of cyclooxygenase and lipoxygenase enzymes. The presence of tannins has led researchers to believe that *P. granatum* can promote wound healing and enhance collagen stabilization due to the inherent affinity of these molecules for proteins, and hence reduce tissue destruction in periodontal disease. The combined effect of tannins and polyphenols has also been attributed to the greater proliferation of fibroblasts and collagen formation, along with faster wound healing and angiogenesis.

The anaesthetic effect of tannins has also been under study. Topical application of extracts of *P. granatum* have elicited lower gag reflex in the soft palate and in the tonsillar region. Methanolic extracts obtained from the peel of the *P. granatum* fruit (MEPGP) have shown antibacterial properties under various concentrations. While the growth of *Staphylococcus aureus* and *Staphylococcus epidermidis* was inhibited at all concentrations between 4-12 mg/mL, significant inhibition of *Streptococcus sanguinis*, *Lactobacillus acidophilus*, *Streptococcus mutans*, and *Streptococcus salivarius* were observed at concentrations between 8-12 mg/mL.<sup>12</sup>

## PAPAYA, FENUGREEK, CINNAMON

*Carica papaya* (*C. papaya*), commonly known as papaw or papaya fruit is a rich source of vitamins A, C, and E, along with magnesium, potassium, folate and pantothenic acid. The seeds contain phenolic compounds like benzyl isothiocyanate and carotenoids, while the extracts of papaya leaves are high in food fibres and flavonoids.

In an experimental study conducted on mice (*Mus musculus*) with gingival ulcerations to verify the therapeutic properties of papaya leaf extract at various concentrations, it was found that at all concentrations between 25-75% the extract acted as a potent antioxidant and allowed wound healing and contraction. At 75% concentration, the rate of epithelialisation was accelerated with better fibroplasia and wound contraction.<sup>13</sup>

In an in vitro study of alcoholic extracts obtained from *Carica papaya*, *Trigonella foenum-graecum* (fenugreek), and *Cinnamomum verum* (cinnamon), all of the herbal alternatives showed significant anti-fungal activity against Fluconazole resistant *Candida albicans*.<sup>4</sup> Additionally, in an evaluation of the antifungal activity of cinnamon bark oil, it was found that along with the fungicidal properties, aqueous extracts of cinnamon showed the potential to reinforce the oral epithelial barrier and prevent the formation of biofilms by *Candida albicans*.<sup>14</sup>

## CRANBERRY

Cranberries are *Vaccinium macrocarpon* (*V. macrocarpon*) and contain proanthocyanidins (PACs) and anthocyanidins. It was used to prevent recurrent urinary tract infections and has been postulated to inhibit bacterial adherence due to the presence of proanthocyanidin.<sup>15</sup> Cranberry flavonols have shown an inhibitory effect on the enzymes of *Streptococcus mutans*. A comparison of these biomolecules on their antibacterial effects demonstrated that the highest inhibition of *Streptococcus mutans* was exhibited by PACs, followed by the flavonols. Extracts of *V. macrocarpon* have shown the highest antibacterial properties on periodontal pathogens like *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Aggregatibacter actinomycetemcomitans* at bactericid-

al concentrations of 0.25 mg/mL. Other oral microbes like *Veillonellaparvula* and *Streptococcus oralis* were inhibited at concentrations above 1mg/mL.<sup>16</sup>

### NEEM

*Azadirachtaindica* (*A.indica*), known as neem or Indian lilac, has been cultivated for its herbal properties for over two millennia. While the most significant biomolecules of *A.indica* are azadirachtins, the leaf extracts also contain Nimbolinin, Nimbin, Nimbidin, Nimbanene, Quercetin, Gedunin, and Salannin.

An in vitro study using the chloroform based crude extracts of *A.indica*, demonstrated a significant antioxidant potential of the leaves. Azadirachtin has shown to antagonise the development of buccal pouch carcinogenesis and prevent Deoxy Ribonucleic Acid damage with chemopreventive effect in hamsters. Further, the leaf extracts have been associated with the induction of apoptosis in target organs.<sup>17</sup> Inactivation of viral strains by interruption of the replication mechanism by the leaf extracts has also been observed. *A.indica* mouth rinses have also shown positive outcomes in controlling periodontal pathogens comparable to standard chlorhexidine mouth rinses. Both aqueous and ethanolic extracts have inhibited strains of *Fusobacterium nuceatum*.<sup>18</sup>

### CHAMOMILE

Chamomile tea obtained from the leaves of *Matricaria chamomilla* (*M.chamomilla*), is widely consumed for its therapeutic properties. It is a rich source of sesquiterpenes, flavonoids, and coumarins. The powdered form of chamomile leaves has been used topically to treat perioral inflammation, skin eruptions, and infections of the mouth. This topical application has shown to accelerate wound healing and also have an analgesic effect.

In a double-blind clinical study analysing the rate of wound healing, the topical application of *M.chamomilla* extracts allowed faster wound drying with re-epithelialisation. Chamomile has also exhibited antioxidant properties in inhibition of lipid peroxidation and blocking the formation of reactive chemical entities in tissue. Apigenin, found in *M.chamomilla* has shown chemopreventive effects in Oral Squamous Cell Carcinoma due to its inherent potential to interfere with the cell cycle at several stages of carcinogenesis.<sup>19</sup>

### CLOVE

Clove oil, obtained from *Syzygiumaromaticum* (*S.aromaticum*), is rich in thymol, eugenol, carvacrol, cinnamaldehyde, and  $\beta$ -caryophyllene. The eugenol component has an inherent affinity for free radicals, and hence clove oil acts as a potent antioxidant. Besides, eugenol has also demonstrated the alteration of ergosterol structure, which is the main component of fungal cell membranes. Studies have also correlated

the antifungal potency of eugenol with the inhibition of germ tube formation in strains of *Candida albicans*.<sup>20</sup>

### TOXICITY OF HERBAL EXTRACTS

Herbal medicine has received criticism due to its potential to cause side-effects or toxicities when consumed without regulation. This is attributed to the lack of standardization of doses and form of administration in various communities. Toxicities also arise due to adulteration or inappropriate processing of dietary herbal supplements, interactions of these extracts with conventional drugs, as well as the inherent toxins associated with some plant species. Metabolomics is the study of bioactive molecules or metabolites in tissues, biofluids, etc. The most recent approach in the management of herbal toxicities involves a metabolomic analysis of the phytochemical constituents present in each medicinal plant. This is done via phytochemical profiling and fingerprinting.<sup>21</sup> While 'phytochemical profiling' involves a targeted analysis to detect the presence of known biomolecules in a plant extract, 'phytochemical fingerprinting' refers to the identification of all molecular species found in a sample. A holistic analysis of the phytochemicals in herbal extracts can allow better control over manifestations of toxicities and negate side effects.

### CONCLUSION

Traditional medicine has played a key role in the prevention and treatment of various diseases since time immemorial. The use of indigenous medicinal plants is widely being used independently, and as an adjunct to conventional forms of treatment in the management of many oral lesions. Herbal extracts of *Aloe vera*, *Ocimumtenuiflorum* (Tulsi), *Curcuma longa* (turmeric), etc, have shown positive outcomes in the management of gingivitis, oral ulcers, and other mucosal lesions. In developing countries still, herbal medicine is considered to be the main system in treating many diseases as it is affordable and it is the responsibility of the practitioner to use them ethically.

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