

Phytotherapy: An Emerging Alternate Therapy in the Management of Common Oral Lesions- A Review

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ABSTRACT

Oral diseases are a rising concern for people all over the world with many treatment options being explored from time to time. The need for an effective, safe and economical alternative therapeutic system that can prevent development of resistant microorganisms, and opportunistic infections has become critical. Phytotherapy refers to the alternative system of medicine which uses plant products, herbs and shrubs for the management of diseases. Various clinical trials have been conducted in recent times that assess the efficiency of plant products in different lesions of the oral mucosa. Curcumin, aloe vera, propolis, honey, chamomile, calendula have been effective in many oral lesions including leukoplakia, lichen planus and recurrent aphthous stomatitis. Other herbs like catuama, satureja oil, myrrh, ginger, garlic, cannabinoids, Punica granatum are being evaluated for their effectiveness in reducing symptoms associated with various oral lesions. With the increase in the usage of these plant-based products, physicians have to be more aware about these herbs and the precautionary measures to be given while implementing such alternative therapy in our daily practice.

Keywords: Phytotherapy, alternative system, curcumin, aloe vera, honey.

INTRODUCTION

“All that man needs for health and healing has been provided by God in nature, the challenge of science is to find it.” Oral health is integral to general well being and relates to the quality of life that extends beyond the functions of the craniofacial complex. ^[1] The need for an effective, safe and economical alternative therapeutic system that can prevent development of resistant microorganisms, and opportunistic infections has become critical. The increases in adverse effects in conventional medicines have navigated researchers towards safe herbal medicinal products. Phytotherapy refers to the alternative system of medicine which uses plant products, herbs and shrubs for the management of diseases. In oral care, these plant and plant derived products have been used to reduce inflammation,

infection and aid in healing of premalignant lesions like leukoplakia, oral submucous fibrosis and lichen planus. About one - fourth of the drugs manufactured are derived from plant products. ^[2] This increased usage has implored health professionals to seek knowledge about these herbs, their origins and the adverse effects to guide their usage among patients.

HISTORY OF PHYTOTHERAPY:

Hippocrates was one of the earliest to have researched on the benefits of herbs. He had mentioned about 400 medicinal plants for various diseases in the 5th century B.C. Another massive publication was the De Materia Medica which is a prototype for modern pharmacopoeias which contained thousand of herbs and their uses in detail. In ancient India, the knowledge on medicinal plants has been accumulated in the course of

many centuries, based on different medicinal systems such as Ayurveda, Unani and Siddha. AYUSH states the use of 1250 medicinal plants for various diseases and the alternate medical practice of siddha has various valuable compilations of herbs including the “karpa mooligaigal” which is a group of 108 herbs for orofacial diseases. This whole different practice of using various medicinal plants and animal products to maintain healthy states of living is known as “Ethnobotany” or “Ethnopharmacology”. [3]

PLANT AND PLANT DERIVATIVES:

The components in plants that are having anti-inflammatory, analgesic,

astringent, antioxidant, antibacterial and anti-fungal properties are called phytochemicals and they have been tabulated here. (Fig 1) There are various methods of extraction by which these phytochemicals are derived from the leaves, stem and roots. They are ethanol or methanol extraction, aqueous fractionation, chromatography and radioimmunoassay. The plant products can be steeped in hot water to create teas, mixed with dilutions of alcohol to make tinctures, dried and mixed with petroleum or oil to make local applications. They can also be inhaled as steam or used as poultices. [4]

Fig 1: COMPONENTS OF PLANT SUBSTANCES

PHENOLICS AND POLYPHENOLS	Anti-fungal, anti-viral and anti-bacterial activity Eg: Cinnamon, caffeic acids
ESSENTIAL OILS	Anti-microbial, bacteriostatic and anti-fungal Eg: Eugenol in clove oil
FLAVONES, FLAVONOIDS, FLAVONOLS	Antimicrobial in nature Eg: Catechins- Inhibits <i>Vibrio cholerae</i> , <i>Strep. mutans</i> , <i>Shigella</i>
TANNINS	Anti-microbial property- inactivates microbial adhesins and cell envelope proteins Eg: Green teas and red wines
COUMARINS	Anti-thrombotic, anti-inflammatory, vaso-dilatory, anti-viral, anti-fungal Stimulates macrophages
ALKALOIDS	Anti-microbial properties, anti-diarrheal, Anti-HIV Eg: Morphine, berberine
LECTINS & POLYPEPTIDES	Forms ion channels, competitive inhibition of microbial proteins Anti-bacterial, anti-viral in nature

PHYTOTHERAPY IN ORAL LESIONS: APHTHOUS ULCERS:

Aloe vera has many chemical constituents like anthraquinones, saccharides, prostaglandins and fatty acids. It is analgesic, antibacterial, anti-inflammatory and immunomodulatory in nature. It stimulates complement linked to polysaccharides in recurrent aphthous ulcers. It can be given as a juice or as topical oil or ointment. Chamomile (*Matricaria recutita*) has 1-2% volatile oils, chamazulene, alpha-bisabolol, apigenin, flavonoids and quercetin. Its potent anti-inflammatory and anti-bacterial properties can be used and prescribed as a mouth wash for recurrent aphthous stomatitis (RAS).

Myrrh (*Commiphora molm*) has resins, gums and volatile oil. It has 20% proteins and 65% carbohydrates. A mixture of 200 to 300mg of myrrh extract with warm water is beneficial for aphthous

ulcers. [5] Propolis is a secretory product from honey bees and it has 50% resins, 30% waxes, 10% essential oils, 5% pollens. It has anesthetic, antibacterial, antifungal, antioxidant, antithrombotic properties. It is used as a cream, oral capsules, or as an alcoholic topical solution in propyleneglycol vehicle. [6]

Ginger officinale can be used as a mucoadhesive with alcohol base for RAS relieved pain with significant reduction in ulcer diameter, erythema and healing time according to a randomized double blind placebo controlled trial done in 30 patients by Haghpanah et al. Jhiang et al evaluated the effectiveness of allicin in garlic when used as a mouth wash for aphthous ulcers. The author concluded that it was effective in controlling pain and prevented recurrence of aphthous stomatitis as it reduces the migration of neutrophils, antagonizes oxidation and regulates immunity. [7] Myrtle

communis, honey, nigella sativa, licorice root and echinacea purpurea were other alternate therapies which were effective in healing and prevention of recurrence in RAS.

ORAL CANDIDIASIS:

Nigella sativa is also called black cumin. It belongs to the family of Ranunculaceae. It contains 28-36% fixed oils, saponins and alkaloids. It has anti-inflammatory, anti-microbial, histamine release inhibitor and antioxidant properties. This natural product when combined with other herbal ingredients is effective against oral candidiasis.

A study conducted by Fareid et al assessed the in vitro inhibitory activity of Zinger officinale, Cinnamomum, Nigella sativa, Syzgium aromaticum, Piper nigrum and chamomile against 65 Candida isolates. The highest inhibitory effect was seen in Cinnamon and clove extracts. [8]

Vasconcelos et al proved the efficacy of Punica granatum (pomegranate) when used as a mouthwash against Candidal infections in 60 patients. It showed satisfactory and good response in all study groups. [9]

Isoquinoline alkaloid berberine is a compound found in all berries. They are anti cancerous, anti-diabetic, anti-microbial in nature. Dhamgaye et al in his study provides evidence that the treatment of Candida cells with berberine extracts in ethanol compromises the cell wall integrity via the calcineurin pathway leading to cell death. The study also assigns a new role to HSF1 in combating Multi drug resistant species. [10]

HERPES:

Saller et al conducted a double-blind clinical trial with aqueous extracts of Salvia officinalis (sage) leaf and Rheum palmatum (Chinese rhubarb) root which was given to patients with herpes labialis. It proved as effective as topical acyclovir. [11]

Mellisa officinalis or the common lemon balm leaf contains rosmarine alkaloids, caffeine, ferulic acid and terpenoids. These substances inhibit the HSV-1, 2 replications. It has been shown to

be effective when used as a concentrated extract in a cream base for relieving symptoms of acute herpes labialis in a double-blinded clinical trial conducted by Wolbling et al. [12]

Tea tree oil is a volatile oil of Melaleuca alternifolia. It is a potent blocker of HSV. It has tepinen-4-ol and terpenoids which reduce its water solubility significantly. A preliminary, single-blind clinical trial was carried out by Carson et al who evaluated the effect of a gel product containing 6% tea tree volatile oil in immune-competent patients with recurrent herpes labialis. There was significant healing and reduction of pain in the patients. [13] Other herbs like Mentha piperata (mint) and Ocimum basilicum Lineo (basil) when used as a suspension, displayed strong activity in vitro when studied against strains of herpes virus.

ORAL LICHEN PLANUS:

Aloe vera and turmeric have found to be very effective in managing oral lichen planus. Reddy et al conducted double blind randomized trial on 40 patients of OLP and all the patients were asked to apply aloe vera gel 3times daily for 2 months. Result showed that there was reduction in pain scores and burning sensation after 18weeks of therapy. [14] Sing V et al conducted a study on 10 patients of clinically and histologically diagnosed OLP. Turmeric ointment was given for application 2times a day for 3 months and significant improvement was observed in clinical symptoms. Other herbs used for oral lichen planus are raspberry leaf, licorice root, jasmine, propolis, lycopene extracts, tormentillo, Eleagnus angustifolia.

Honey is a natural product that is rich in antioxidants. It inhibits the release of TNF, IL-1,6 nitric oxide and induces apoptosis by activating mitochondrial pathway. It releases cytochrome c protein which forms apoptosome complex leading to depolarization and inhibits cellular proliferation. Sanathkhar et al conducted study on 50 patients of OLP with use of 20ml of cedar honey 3 times daily via swish

and swallow technique and concluded that efficacy of topical honey was great with no adverse effects. [15]

LEUKOPLAKIA:

The common neem (*Azadirachta indica*) is rich in nimbin, nimbidin, nimbolide, quercetin, beta sitosterol. These phytochemicals regulate cell signalling pathways, modulates activity of tumour suppressor genes like p53, pTEN, VEGF, transcription factors and induces apoptosis by acting on bcl2 gene. Ethyl acetates and methanol ethyl acetate inhibit tumorigenesis by modulating xenobiotic- metabolizing enzyme. The efficacy of neem extracts in leukoplakia was evaluated by Permal et al in 2017. They concluded that ethanolic neem leaf extract induced apoptosis by both extrinsic and intrinsic pathway and inhibits IGF signal and thus acting as a chemotherapeutic agent in cancer. [16]

Another important herb in the management of leukoplakia is curcumin (turmeric). Curcumin has a potent anti-tumour activity by increasing vitamin c levels locally and decreases the lipid peroxidation which causes DNA damage resulting in apoptosis of tumour cells. Cheng A, conducted prospective stage I-study on patient with oral leukoplakia and these patients took 500mg of curcumin powder /day for 5months and found that there was significant reduction in burning sensation.

Another surprising herb found helpful in managing leukoplakia is green tea. Green tea is derived from the plant *Camellia sinensis* and contains polyphenols, leucoanthocyanins and phenolic acid. The epigallocatechin-3-gallate is a polyphenol that acts as a chemo preventive agent. It binds to many cellular proteins and activates the mitogenic activator protein kinase (MAPK) and inhibits tumorigenesis. Li et al conducted double blind study on 59 oral leukoplakic patients using mixed tea products (3g mixed tea capsule oral administration along with mixed tea ointment topical) for 6months. Results

showed reduction in size of lesion in 37.9% of patients. [17-18]

In photodynamic therapy for management of premalignant lesions, many plant derived products like 0.1% chlorophyll gel (Mono-L-aspartyl chlorine), essential oils and margarine can be used as potent herbal photosensitizers.

ORAL SUBMUCOUS FIBROSIS:

Many authors have assessed the efficiency of spirulina in patients with oral submucous fibrosis in various studies. Spirulina is a blue-green algae with high protein and carotenoid content. It has antioxidant properties due to the presence of beta carotene and superoxide dismutase. Mulk et al studied effects of spirulina (0.5gram capsules) with pentoxifylline in 40 OSMF patients. Reduction in burning, improvement in mouth opening and tongue protrusion was significant. The common house hold spice, the black pepper was also effective in improving the mouth opening in patients with oral submucous fibrosis. Annigeri et al studied the effects of black pepper and *Nigella sativa* (as a paste) in 40 OSMF patients. Significant improvement was seen after 3 months. [19] Srivastava A et al conducted a study by using 1 gram of tulsi paste and 1 gram of turmeric in base of glycerine. The authors instructed the patients to apply the mixture 4-5times a day for 15min. There was significant reduction in burning sensation with improved mouth opening. [20]

XEROSTOMIA:

Primrose (Efamol-omega-6 fatty acid) has many chemical constituents like cis - linoleic acid and gamma linolenic acid (GLA). They help to alter immunity by increasing cytokine production along with interferon-gamma (IFN-gamma), monocyte chemotactic protein-1 (MCP-1), and tumour necrosis factor-alpha (TNF-alpha). These phytochemicals increase the concentrations of essential fatty acids and reduce the inflammatory eicosanoids like leukotrienes, prostacyclins, prostaglandins and thromboxanes. Thus, the gland atrophy is prevented. A clinical trial concluded that the

combination of primrose and vitamin B complex was found to have a positive effect on Sjogren's syndrome after 8 weeks of treatment. [21]

Cannabinoids and ginger also have been useful in management of xerostomia and Sjogren's syndrome. Cannabinoids are natural compounds found in plants like hemp. They contain cannabidiol (CBD), tetrahydrocannabinol (THC) and other agents. These products are psycho active in nature and they bind to the body's cannabinoid receptors (CB₁ and CB₂).

Studies have found both CBD and THC to be effective in alleviating symptoms caused by Sjogren's syndrome. [22]

BURNING MOUTH SYNDROME:

Spanenberg, studied the effects of Catuama herb condensed as a capsule for the management of burning mouth syndrome in 72 subjects, where significant reduction in symptoms was obtained after a period of 8weeks. [23] Other herbs like curcumin and the dried leaves of Hibiscus rosa sinensis are also being evaluated for their efficacy in managing burning mouth syndrome.

DENTURE STOMATITIS:

Punica granatum also known as pomegranate has anti-oxidant, anti-carcinogenic, anti-inflammatory properties. It has been found to be effective when used topically for denture stomatitis. [24]

Satureja oil belonging to family Lamiacea is a flavouring agent. Its anti-nociceptive, anti-inflammatory, anti-fungal and anti-microbial properties are helpful in managing denture stomatitis. [25]

DESQUAMATIVE GINGIVITIS:

Marigold (*Calendula officinalis*) is a homeopathic remedy used for many decades. It has many carotenoids, flavonoids, triterpene saponins and coumarins. It has anti-inflammatory properties and accelerates wound healing. Machado et al conducted a study in which 2 cases of desquamative gingivitis were treated with calendula officinalis and clobetasol gel, which provided good remission of symptoms in patients. [26]

Antioxidant properties of honey was also used in the treatment of desquamative gingivitis lesions where pure, un boiled, commercially available honey was topically applied.

ORAL MUCOSITIS:

Various herbs and spices like neem, cloves, chamomiles when given in the form of mouthwashes are effective against oral mucositis. Topical application of honey was equally effective. According to a randomised control trial done by Susan et al, maximum improvement in Mean Mouth and Throat Soreness (MTS) Score was observed in subjects who used the mouthwash made from neem and cloves. Fidler et al studied the effects of 5FU chamomile as a mouth wash in 164 patients who received radiotherapy. A good number of patients did not develop any clinically noticeable mucositis. [27]

CONCLUSION

With conventional therapeutics having various adverse effects and developing microbial resistance over a period of usage, a paradigm shift is taking place towards complementary and alternative medical system. With more and more clinical trials and research being explored regarding the usage and safety levels of herbal therapeutics, conventional therapeutics may soon become history. A careful insight into the useful herbs, their preparation, dosages and precautions will help the oral physicians in guiding the patients during management of various oral lesions. Also, numerous research opportunities lie in these hidden herbs and their products which can be analysed in clinical trials.

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How to cite this article: Gauthaman J, Ganesan A. *Phytotherapy: an emerging alternate therapy in the management of common oral lesions- a review*. *International Journal of Research and Review*. 2019; 6(5):101-106.
