

Application of Alternative Medicine as a Curative Therapy of Oral Mucosal Lesions: A Comprehensive Review

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ABSTRACT

The term Alternative Medicine is used to denote a form of medicine that falls outside the mainstream of western medicine. These medicines exist in all cultures to some degrees and terms such as traditional medicines, indigenous medicines, holistic medicines, folk medicines and oriental medicines. When such medicines and related therapies are applied in the dental field, the term holistic dentistry is used. Alternative medicines or therapy encompasses a variety of disciplines such as acupuncture, chiropractic treatment, guided imagery, yoga, biofeedback, hypnosis, aromatherapy, herbal remedies, relaxation, massage etc. There is common patient belief that these therapies are safe to use. However, there is lack of sufficient scientifically proven data regarding their safety. The emphasis with most alternative therapies is based upon the natural healing capability of the body. This article emphasizes the use of various alternative therapies, their advantages, mechanism of actions, side effects and implications in dentistry.

Key words: Alternative Medicine, Anti-oxidant, Herbal Medicines, Holistic, Oral Mucosal Lesions.

Alternative therapy is a generalized term applied to all methods of treating a specific disease or condition. This therapy aims at co-operating with the natural forces and various defensive mechanism of the body against pathogens. World health organization (WHO) has identified more than 150 systems of alternative medicines. Most practiced ones are :Ayurveda, Homeopathy, Naturopathy, Unani medicine, Magneto therapy, Aroma therapy, Acupuncture, Yoga, Biofeedback Training, Mud Therapy, Massage therapy etc.

Complementary and alternative medicine (CAM), according to National Center for Complementary and Alternative Medicine (NCCAM), represents a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of the conventional medicine.

Complementary medicine is the one used together with conventional medicine. Example: Using aromatherapy to help reduce patient's discomfort following surgery.

Alternative medicine is the one used in place of conventional medicine. Example: Using a special diet to treat cancer instead of undergoing surgery, radiation, or chemotherapy that has been recommended by a conventional doctor.

NCCAM classifies CAM therapies into five categories [1,2].

1. **Alternative medical systems:** These systems are built as a result of various theories and consequently practice and expertise. They are evolved apart from and earlier than the conventional medical approach in treating various diseases. These systems are divided into therapies that fall into western culture (Homeopathic and Naturopathic medicine) and Non-Western cultures (Traditional Chinese medicine and Ayurveda) [1,2].

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2. **Mind-Body Interventions:** The connection between the mind and the body uses a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptoms. Example: Meditation, prayer and therapies that use creative outlets such as art, music, or dance [2].
3. **Biologically based therapies:** These therapies use natural substances such as herbs and vitamins to cure a disease. Example: Dietary supplements, herbal products and the use of other natural but as yet scientifically unproven therapies (Example- Using shark cartilage to treat cancer) [2].
4. **Manipulative and Body-Based Methods:** These methods are based on manipulation and/or movement of one or more parts of the body. Example: Chiropractic or osteopathic manipulation and massage [1].
5. **Energy therapies** - Energy therapies involve the use of energy fields. They are of two types:
 - a) **Bio-field therapies:** The bio-field therapies are intended to affect energy fields that surround and penetrate the human body. However, the existence of such fields has not yet been scientifically proven. Some forms of energy therapy manipulate bio-fields by applying pressure and/or manipulating the body by placing the hands in, or through, these fields. Examples include qigong, Reiki and therapeutic touch [2]
 - b) **Bio-electromagnetic based therapies:** Unconventional use of electromagnetic fields such as pulsed fields, magnetic fields, or alternating-current or direct-current fields [2].

The use of alternative medicine aims at prevention of a disease whereas traditional medicine tends to intervene once disease has occurred. Alternative medicines when compared with traditional medicine have lesser side effects and are less expensive, since most of them are manufactured using plant extracts. However, there is very little scientifically proven data regarding their safety when compared to traditional medical methods [3].

Alternative therapies commonly used in management of oral mucosal lesions.

ALOE VERA

The name Aloe vera derives from the Arabic word "Alloeh" meaning "shining bitter substance," while "vera" in Latin means "true." The botanical name of Aloe vera is *Aloe barbadensis miller*. It belongs to Liliaceae family.

Constituents of Aloe vera

1. **Vitamins:** It contains antioxidant such as A, C and E. It also contains vitamin B12, folic acid, and choline.
2. **Enzymes:** It contains enzymes such as: Alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidase. Bradykinase helps to reduce excessive inflammation when applied to the skin topically, while others help in the breakdown of sugars and fats.
3. **Minerals:** It contains calcium, chromium, copper, selenium, magnesium, manganese, potassium, sodium and zinc. They are essential for the proper functioning of various enzyme systems in different metabolic pathways.
4. **Sugars:** It contains monosaccharides (glucose and fructose) and polysaccharides (glucomannans, Acemannan).
5. **Anthraquinones:** It has 12 anthraquinones, which are phenolic compounds traditionally known as laxatives. Aloin and emodin act as analgesics, antibacterials and antivirals [3].
6. **Fatty acids:** It provides 4 plant steroids; cholesterol, campesterol, β -sisosterol and lupeol. All these have anti-inflammatory action and lupeolin addition possesses antiseptic and analgesic properties [3]

Mechanism of action

- a) **Healing properties:** Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interacts with growth factor receptors on the fibroblast, thereby stimulating its activity and proliferation, which in turn significantly increases collagen synthesis [3].
- b) **Effects on skin exposure to UV and gamma radiation:** Topical application of aloe vera in gel form result in generation of metallothionein (Antioxidant) that scavenges hydroxyl radicals and prevents suppression of glutathione peroxidase and superoxide dismutase. This in turn decreases the production and release of IL-10 and thus prevents UV-induced suppression of delayed type hypersensitivity (**Figure 1**).
- c) **Anti-inflammatory action:** Aloe vera inhibits the COX pathway and reduces PGE₂ production from arachidonic acid.
- d) **Effects on the immune system:** Alprogen inhibits calcium influx into mast cells, thereby inhibiting the antigen-antibody mediated release of histamine and leukotriene from mast cells.
- e) **Antiviral and antitumor activity:** These actions may be due to indirect or direct effects. Direct effect is due to anthraquinones. The anthraquinone inactivates various

enveloped viruses such as herpes simplex, varicella zoster and influenza while indirect effect is due to stimulation of the immune system.³An induction of glutathione S-transferase and an inhibition of the tumor-promoting effects of phorbolmyristic acetate has also been reported which suggest a possible benefit of using aloe gel in cancer chemoprevention [4].

Indications in oral mucosal lesions: Aloe vera may be indicated in the management of recurrent aphthous stomatitis, Lichen planus, Radiation mucositis, OSMF and Leukoplakia.

a) **Oral lichen planus:** A randomized controlled trial study was conducted to check the efficacy of Aloe vera gel in the treatment of oral lichen planus (OLP). The authors concluded that Aloe vera gel is statistically more effective than placebo in inducing clinical and symptomatic improvement of OLP. Therefore, Aloe vera gel can be considered as a safe and alternative treatment for patients with OLP [5].

b) **Oral submucous fibrosis:** A study was conducted in 2012 to compare the efficacy of antioxidants and aloe vera in treatment of OSMF, where the subjects under the Aloe vera group showed a better treatment response compared to the antioxidants group. It reduced the burning sensation and also improved mouth opening [6].

c) **Recurrent aphthous stomatitis:** In a study the authors conducted a double-blind clinical trial to evaluate the efficacy of topically administered Aloe vera gel on minor aphthous ulcers. It was concluded that 2% Aloe vera oral gel was not only effective in decreasing the patient's pain score and wound size, but also decreased the wound healing period [7].

Side effects: Topical application may cause redness, burning, stinging sensation and rarely generalized dermatitis in sensitive individuals. Allergic reactions are mostly due to anthraquinones such as aloin. When administered orally it may cause abdominal cramps, diarrhea, constipation, red urine and hepatitis.

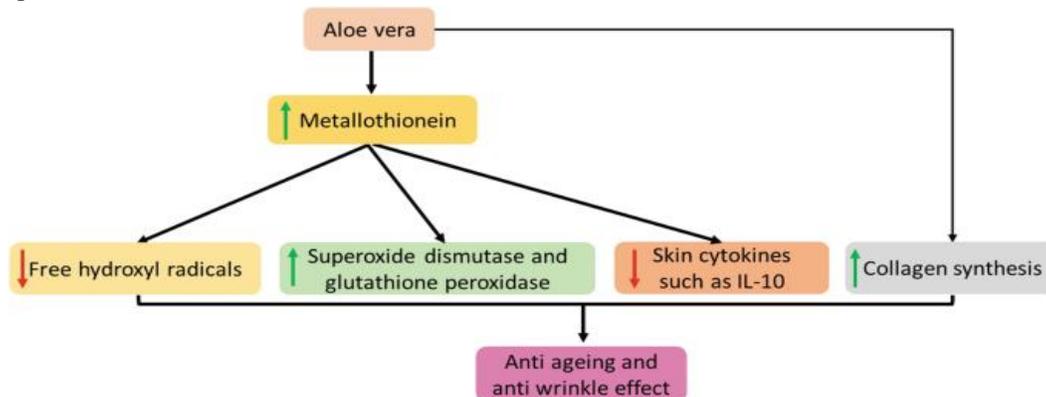


Figure 1: Showing the possible effects of topical application of aloe vera gel on skin.

CURCUMIN

Curcumin (diferuloylmethane) is the chief component of the spice turmeric and is derived from the rhizome of the East Indian plant *Curcuma longa*. Turmeric contains a class of compounds known as the curcuminoids, comprised of curcumin, demethoxycurcumin and bisdemethoxycurcumin. Curcumin has anti-oxidant, antiseptic, analgesic, antimalarial and anti-inflammatory properties.

1. **Antioxidant Activity:** Curcumin has been shown to inhibit lipid peroxidation using linoleate, a polyunsaturated fatty acid that can be oxidized to form a fatty acid radical. It also scavenges various reactive oxygen species (ROS) produced by macrophages

(superoxide anions, hydrogen peroxide and nitrite radicals) [8]. It also down regulates the Nitric oxide synthase (iNOS) activity in macrophages, thus reducing the amount of ROS generated in response to oxidative stress [9].

2. **Anti-inflammatory Activity:** Curcumin suppresses the activation of NF- κ B, an inducible transcription factor that regulates the expression of a host of genes involved in the inflammation such as COX-2, TNF- α , Cyclin -D1, ICAM-1 [10].

Indications

a) **Recurrent aphthous stomatitis:** Eight studies involving 439 subjects were reviewed. The efficacy of curcumin

was compared with 1% triamcinolone in four studies, glycerin vehicle in one study, placebo in one study, and honey in one study. Overall, these studies reported a good efficacy of curcumin in reducing pain and ulcers size in patients with RAS [11].

- b) **Pre- cancerous lesions:** Curcumin has a crucial role in the management of precancerous conditions like lichen planus, oral submucous fibrosis and leukoplakia. Various in vitro and in vivo animal experiments activities of turmeric extract oil have demonstrated that symptoms of pain and burning sensation declined and mouth opening was also partially reversed [11].

Dosages: Doses of 500-8,000 mg of powdered turmeric per day have been used in human studies. Standardized extracts are typically used in lower amounts in the 250-2,000 mg range [12].

Adverse effects: May cause gastric irritation, stomach upset, nausea, diarrhea, allergic skin reaction, and anti-thrombosis activity interfering with blood-clot formation in some patients.

ALLICIN

The word Allicin is derived from the Latin name of the garlic plant, *Allium sativum*.

1. **Anti-microbial action:** Allicin has been reported to inhibit the growth of gram positive, gram-negative, and acid-fast bacterium, including multidrug-resistant bacterium especially the oral bacteria by its chemical reaction on thiol groups of various enzymes in vitro [13]. It also possess some degree of immunomodulatory effect by increasing the activity of natural killer cell. It inhibits TNF-alpha -induced secretion of IL-1, IL-8, IFN- γ in a dose dependent manner. It also suppresses the expression of IL-8 and IL-1 [14].

2. Indications

- a) **Recurrent aphthous ulcer:** Oral adhesive tablets (5 mg allicin): It adhere to the oral mucosa and release allicin slowly at the site of the ulcer in 3 to 4 hours. In this way, a higher drug concentration and a longer-lasting release period could be achieved at the affected site to increase the efficacy [15].

Side effects-Increases bleeding- should be stopped 2 weeks before surgery. It can irritate GI tract -should be used in caution in patients with digestive problem. It was also found to decreases Blood pressure in some patients [16].

GREEN TEA

Green tea is made from un-oxidized leaves and is one of the less processed types of tea and therefore contains one of the most amounts of antioxidants and beneficial polyphenols mainly catechins.

Constituents: Catechins (30 %), Caffeine, Vitamins (A, B2, E, Folic acid, B-carotene), Saponins, γ - aminobutyric acid, Minerals (Potassium, calcium, phosphorus, manganese) and Chlorophyll.

Actions

1. **Antioxidant:** It has antioxidant activity either directly by scavenging of reactive oxygen and nitrogen species or indirectly by inhibition of redox sensitive transcription factors, and induction of antioxidant enzymes [17].
2. **Antitumor effect:** EGCG (epigallocatechingallate) has shown to induce apoptotic cell death and cell cycle arrest in tumor cells [18].
3. **Antimicrobial activity:** Catechins constitute the most important antibacterial agents on methicillin resistant *Staphylococcus aureus*, *Helicobacter pylori* and α -Hemolytic streptococcus [19].

Indications in Dentistry

- a) **Oral lichen planus:** Green tea, especially epigallocatechin-3-gallate, possesses anti-inflammatory and chemopreventive properties. It can inhibit antigen presentation, T-cell activation, proliferation and migration, keratinocyte apoptosis, nuclear factor-kappaB (NF- κ B) activation and MMP-9 activity and can modulate the imbalance between TGF- β and interferon- γ signaling, all of which are involved in the pathogenesis of OLP [20].
- b) **Candidiasis:** These results indicate that EGCG enhances the antifungal effect of amphotericin B or fluconazole against antimycotic-susceptible and resistant *C. albicans*. Combined treatment with catechin allows the use of lower doses of antimycotics and induces multiple antifungal effects [21].

Side effects: Drinking more than 5 cups a day is unsafe. It can cause side effects because of the caffeine. These side effects can range from mild to serious and include headache, nervousness, sleep problems, vomiting, diarrhea, irritability, irregular heartbeat, tremor, heartburn, dizziness, ringing in

the ears, convulsions, and confusion [22]. It increases the excretion of calcium in the urine leading to osteoporosis. Caffeine should be limited to less than 300 mg per day (2-3 cups) [22].

HONEY

Honey, a thick sweet liquid made by bees from the nectar of flowers, is one of the oldest known medicines.

Properties

- Hygroscopic properties:** This effect is based on high osmotic properties so it can extract water from bacterial cells and cause them to die. It has been shown that wounds infected with *Staphylococcus aureus* are quickly rendered sterile by honey
- Acidic pH:** Honey is characteristically quite acidic, its pH being between 3.2 and 4.5, which is low enough to be inhibitory to many animal pathogens
- Increased lymphocyte and phagocytic activity:** Honey (at a concentration of 1%) stimulates monocytes in cell culture to release cytokines like tumour Necrosis Factor (TNF)-alpha, interleukin (IL)-1 and IL-6, which activate the immune response to infection [23].

USES OF HONEY

- Recurrent aphthous stomatitis:** In a study, honey application can significantly reduce inflammation, accelerate healing process and increase pain free days in those lesions with resolution of the erythema or ulceration without need for steroid therapy. The mean

healing period in RAS was 4 days which is lower than the previous reported studies. In the same study, application of honey in the prodromal period, in one case, accelerated healing process with resolution of erythema and tingling sensation and prevented vesicular eruption. When it was applied after eruption of vesicles, in other cases, there was rapid resolution of the vesicles with no crust formation within 8 days [24].

- Denture stomatitis:** A study was conducted to evaluate the clinical efficacy of a new Brazilian propolis gel in the treatment of denture stomatitis. The results of the study showed that all patients treated with Brazilian propolis gel and Daktarin had complete clinical remission of palatal edema and erythema [25].
- Anti-tumor effects of honey:** A study had reported that Sangju honey (Simdanjeong, Sangju, Korea) could suppress cellular migration, metastasis, and cell proliferation in Oral squamous cell carcinoma (OSCC). The study results further indicated that Sangju honey could also induce apoptosis and suppress OSCC growth (Figure 2) [26]. Wang et al. studied the anti-mutagenic effects of different types of honey against a commonly encountered dietary mutagen Trp-p-1 and found that all honeys exhibited significant inhibition of mutagenicity against this compound [27]. A study done on tumour development and metastasis in murine tumour models using various honey-bee products showed an important role in controlling tumour growth and metastasis in mammary carcinoma and a methylcholanthrene-induced fibrosarcoma in mouse [28].

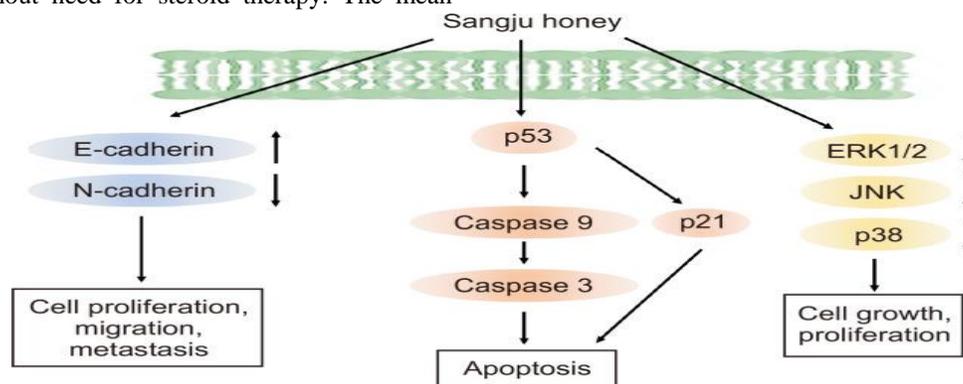


Figure 2- Proposed mechanisms underlying inhibition of oral cancer cell growth by Sangju honey.

SPIRULINA

Spirulina, or *Arthrospira platensis*, is blue - green algae which appear as long, thin, spiral threads. Spirulina contains

a rich supply of protein (60-70 % dry weight), Carbohydrates, Iron, Vitamins (A, K and B complex), Carotenoids (β carotene, Zeaxanthin, Cryptoxanthin, Phycocyanin, Lutein, Xanthophylls). The nutrients present in

Spirulina boost the immune system and enhance the body's ability to generate new blood cells to prevent disease and cancer [29].

Mechanism of action

β -carotene has antioxidant and anti-inflammatory activities – it inhibits the production of nitric oxide and PGE2 and suppresses the expression of COX-2, TNF- α and IL-1. Phycocyanin inhibits proinflammatory cytokine formation of TNF α , suppresses COX-2 expression and decreases PGE2 production [30].

Indications in dentistry

- a) **Oral submucous fibrosis:** A study was conducted on a group of patients with OSMF. The subjects were given spirulina 500 mg along with triamcinolone 0.1%. After the end of 3 months the subjects showed significant improvement in burning sensations, mouth opening and painful ulcerations [31].
- b) **Leukoplakia:** The evaluated the chemopreventive activity of Spirulina fusiformis (SF) (1 g/day for 12 mos) in reversing oral leukoplakia in pan tobacco chewers in Kerala, India. Complete regression of lesions was observed in 20 of 44 (45%) evaluable subjects supplemented with SF, as opposed to 3 of 43 (7%) in the placebo arm ($p < 0.0001$) [32].
- c) **Homeopathy:** The term homeopathy comes from the Greek word homoios, meaning similar, and pathos, meaning suffering or sickness. The basic law of homeopathy is "The law of similars." The law states that disease represents a disturbance in the body's ability to heal itself. "Remedies" are determined by noting the symptoms produced by large doses of a substance in a healthy individual and applying these substances in highly diluted doses to relieve the same symptoms [33].
- d) **Ignatia:** It is a homeopathic medicine that is derived from the bean of a small tree that is native to the Philippine Islands and China. The tree belongs to the Loganiaceae family, and has long, twining, smooth branches. Ignatia homeopathic 30C in management of oral lichen planus (OLP). A Single blind randomized control clinical trial was done on 30 consecutive patients with oral lesions consistent clinically and histologically with erosive and/or atrophic OLP were recruited. The patients were randomly divided into two groups to receive Ignatia or placebo. They were treated for 4 months. Mean lesion sizes and mean pain measures

differed between control and treatment groups favouring Ignatia [34].

CONCLUSION

The complementary and alternative medicines along with various other extracts from the plants together along with main stream of western medicines can be used as preventive or treatment modalities for oral mucosal and precancerous lesions. The dental health care workers needs to be informed regarding the use of herbal products that may have an impact the delivery of safe and effective dental treatment. In addition, the use of such treatments in dentistry should be based on evidence of effectiveness and safety as demonstrated in randomized clinical trials.

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