

## Review Article

### Curcumin as a Herbal Remedy for Oral Maladies- An Updated Review

<sup>1</sup>Gracelin Ranjitha. E, <sup>2</sup>G. Vinothini, <sup>3</sup>Pratheba, <sup>4</sup>Arivuselvi

<sup>1</sup>Senior Lecturer, Department of Oral Medicine and Radiology, Rajas Dental College and Hospital, Kavalkinaru, Tamil nadu, <sup>2</sup>Oral Physician, Pondicherry, <sup>3</sup>Oral Physician, Kalugumalai, Kovilpatti, <sup>4</sup>Oral Physician, Chidambaram

#### ABSTRACT:

Curcumin is a herbal polyphenol derived from a common dietary spice called turmeric. It has various divergent properties like anti-inflammatory, antioxidant, antimicrobial, antiseptic and anti- mutagenic which makes it appropriate for the treatment of oral disease like Oral sub mucous fibrosis, Lichen Planus, Precancers, cancers of oral cavity and also Recurrent aphthous ulcers. This review focuses on elaborating the therapeutic properties of curcumin which are the key for the healing potential of the magical herb. The efficacy of curcumin in oral lesions and the studies conducted to prove the same have also been detailed in this review. This review tries to highlight the natural properties of curcumin with less or no adverse effects better than the routine medicines or treatment used for oral lesions.

**Key words:** Curcumin, Herbs, Oral submucous fibrosis, Oral Lichen planus, Precancers.

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**Corresponding author:** Dr. Gracelin Ranjitha. E, Senior Lecturer, Department of Oral Medicine and Radiology, Rajas Dental College and Hospital, Kavalkinaru, Tamil nadu, India

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#### INTRODUCTION:

Herbs or phytochemicals are used for centuries to prevent and cure disease. Phytochemicals are naturally occurring substances found in plants. There has been considerable public and scientific interest in the use of phytochemicals derived from dietary components to combat human diseases. They are effective because they interact with specific biological receptors within the body. Herbal medicine excels in the treatment of chronic disease, and very effective as a first-aid, they believe in gentle, long-term support to enable the body's own innate powers to do the healing and have less adverse effects<sup>[1]</sup>

The most widely used home remedy which has been an area of focus in medicine and dentistry is turmeric (*Curcuma longa*). Turmeric is a ever growing plant with orange, oblong tubers 2 or 3 inches in length and one inch in diameter, pointed at one end. When dried, it is made into a yellow powder with a bitter, slightly acrid, with a slight sweet taste, similar to ginger. The active component of turmeric is curcumin. A member of the Zingiberaceae family, it is cultivated in several parts of the Indian subcontinent, South East Asia and South America. It has widely used in cooking, cosmetics, fabric dyeing and medicine for more than 2000 years<sup>[2]</sup>.

Due to adverse effects of conventional medicines, herbal medicines like curcumin have gained focus in the field of dentistry especially in treating oral diseases

#### Components of Curcumin:

Curcumin that is derived from the turmeric plant has three main components they are Curcumin (Curcumin I), demethoxycurcumin (Curcumin II), and bisdemethoxy curcumin (Curcumin III).<sup>1-6</sup> All the three Curcuminoids the active part of curcumin are equally effective in providing the curative actions. Hence, most of the studies refer Curcumin as a whole component rather than individual components. Additionally turmeric also contains several volatile oils like germacrone; termerone;  $\beta$ -termerones;  $\beta$ -bisabolene;  $\alpha$ - curcumene; zingiberene bisacurone; alkaloids and sterols. These Curcuminoids and essential oils have been reported to be the main components responsible for eliciting the medicinal properties to cure diseases.<sup>[3,4]</sup>

#### Therapeutic properties of curcumin:

Curcumin has many useful pharmacological properties, its role relevant in field of dentistry are

**I. Anti-inflammatory property:**

Curcumin has the ability to suppress the acute and chronic inflammation. It reduces inflammation by lowering histamine levels and by possibly increasing the production of natural cortisone by adrenal glands. They also reduce pain from arthritis, bursitis, tendonitis, stiffness of joints. It also inhibits the biosynthesis of inflammatory prostaglandins from the arachidonic acid and neutrophil function. Anti-inflammatory action of curcumin is exhibited by stabilizing the lysosomal enzymes Srivastava R et al done a study by comparing Curcumin and ibuprofen showed Serum phosphatase activity increased from 7.26 to 15.4 units due to inflammation. Thus the study concluded that Curcumin prevented the increase by 50% and hence, showed lysosomal membrane stabilization effect<sup>[5]</sup>

**ii. Antibacterial property:**

Curcumin inhibits the growth of variety of bacteria like Streptococci, Staphylococci, Lactobacillus, etc and also prevents Helicobacter pylori. It is also effective against Enterococcus faecalis, and will serve to be useful as root canal medicaments in endodontics. It also acts as antifungal agent which is active against Aspergillus flavus, A. parasiticus, Fusarium moniliforme, Penicillium digitatum. It has antiprotozoan activity against E. histolytica, Leishmania, Plasmodium falciparum. The most pronounced antibacterial effect of curcumin is by inhibiting the cellular dynamics of the bacteria. Kaur S et al conducted a study to evaluate the inhibitory effect against FtsZ on E. coli and B. subtilis. They concluded that Curcumin could suppress the FtsZ assembly leading to disruption of both the prokaryotic cell division causing the bacterial cell death<sup>[6]</sup>.

**iii. Antiviral property:**

Curcumin has a wider range of antiviral effect by effects of reduction of viral RNA expression, protein synthesis, and virus proteasus. In addition, it was found to have a protective effect on cells against virus-induced apoptosis and cytopathic activity. In addition, it was found to have a protective effect on cells against virus-induced apoptosis and cytopathic activity Divya CS et al conducted a study to evaluate antitumor action of Curcumin in human papillomavirus. They concluded that Curcumin showed inhibitory activity against the expression of E6 and E7 genes of HPV-16 and HPV-18 that are highly oncogenic human papilloma viruses<sup>[7]</sup>.

**iv. Antifungal property:**

Down regulation of desaturase leading to significant reduction in ergosterol of fungal cell Reduction in ergosterol results in accumulations of biosynthetic precursors of ergosterol causing cell death by generation of ROS and reduction in proteinase secretion are other possible critical factors for antifungal activity of Curcumin. A study by Khan N et al demonstrated anti-Candida activity of Curcumin against 38 different strains of Candida including some fluconazole resistant strains and clinical isolates of C. albicans, C. glabrata, C. krusei,

C. tropicalis, and C. guilliermondii. Combination of Curcumin with amphotericin exhibited synergistic activity, suggesting that combination treatment of Curcumin with existing fungicidal agents provided significant effect against systemic fungal infections<sup>[8]</sup>

**v. Anticarcinogenic property:**

Curcumin potentially helps to prevent the new cancers that are caused by chemotherapy or radiation used to treat existing cancers. Studies had proved that curcumin induces cell-cycle arrest and apoptosis in a variety of cancer cell lines grown in culture. Its potent anti-mutagenic property helps prevent new cancers that are caused by chemotherapy or radiotherapy which is used to treat existing cancers. It effectively inhibits metastasis in skin cancers<sup>[9, 10]</sup> and may be especially useful in deactivating the carcinogens in cigarette smoke and chewing tobacco which is of great value in the field of dentistry.

**vi. Antioxidant property:**

Curcumin serves to be a potent anti-oxidant comparable to vitamin C and E which is proved by extensive research done in vivo and vitro studies. Curcumin through ROS-dependent mechanism disorganizes multiple cell signaling molecules is known to exert its anticancer effect either by scavenging or by generating reactive oxygen species (ROS). Thus reporting a better correlation between anti-inflammatory and superoxide scavenging property. Balasubramanyam et al demonstrated that Curcumin abolished ROS generation in cells from control and diabetic subjects. The pattern of these ROS inhibitory effect by Curcumin proves it to be a potent Antioxidant. Priyadarsini et al evaluated the antioxidant mechanism of Curcumin and dimethoxy Curcumin by radiation-induced lipid peroxidation in rat liver microsomes. They concluded that at equal concentration, the efficiency to inhibit lipid peroxidation is changed from 82% with Curcumin to 24% with dimethoxy Curcumin<sup>[5, 6]</sup>

**Effects of curcumin on oral diseases:**

Curcumin plays a vital role in treating various oral lesions effectively in line with other conventionally used allopathic drugs. Many studies have been conducted and proved the same which are summarised below:

**1. Role of curcumin in treating oral sub mucous fibrosis:**

Oral submucous fibrosis (OSF) is a chronic inflammatory disease, and has been defined by WHO as one of the precancerous conditions (International Agency for Research on Cancer, 2005). The main clinical symptoms include the stiffness of oral mucosa, restriction of mouth opening, atrophy of tongue papillae, blisters, and intolerance to hot and spicy food. Malignant transformation rate in OSF is high, reaching 7-13%<sup>[11]</sup>.

Management of OSF is always critical and the therapeutics improvement is a way minimal.

Curcumin has some important biological properties such as anti-inflammatory, antioxidant and antitumor activity as

mentioned earlier in the review. Recently, many studies have reported curcumin's role in the prevention and reduction of fibrosis caused by harmful factors. They are

- I. **Deepa Das et al** conducted a Comparative study of the efficacy of curcumin and turmeric oil as chemopreventive agents in OSMF in 2010. 48 patients with OSMF, Group I 1g of curcumin capsules / day, group II 600 mg drops of turmeric oil / day, group III tab mutinal 1000mg /day. Significant improvement with the use of curcumin in 3 months, turmeric oil had long term effect than the multinal tablets was achieved<sup>[12]</sup>
- II. **Shan- Shan Zhang et al** did a study on Antifibrotic Effect of Curcumin in TGF- $\beta$ 1-Induced Myofibroblasts from Human Oral Mucosa in 2012 by doing Cell culture from 3 patients of 1-3 years undergoing cheiloplasty. Myofibroblast treated with curcumin for 24 hours. Significant antifibrotic effect- curcumin inhibits the proliferation of fibroblast, myofibroblast, type I and III collagen was proved<sup>[13]</sup>.
- III. **Nithin Agarwal et al** in 2014 did a study on the efficacy of turmeric in management of oral submucous fibrosis. 30 subjects diagnosed with OSMF were included in this study. The patients were administered commercially available turmeric; their mouth opening and burning sensation on VAS scale were evaluated at regular intervals, and the data was then compared and concluded that Treatment of OSMF with turmeric is an affordable and effective treatment methodology; however, further research needs to be done.<sup>[14]</sup>
- IV. **Hazarey et al in 2015** conducted a study on the effect of curcumin in the treatment for oral submucous fibrosis - A randomized clinical trial. 30 clinically diagnosed OSF patients were divided into two groups, test group patients were treated with Longvida (curcumin) lozenges and control group with Tenovate ointment (clobetasol propionate (0.05%). The treatment was given for 3 months duration and follow-up was done for 6 months. The study concluded that hat combination strategies for the management of OSF which include the stoppage of causative ill habits, appropriate medicinal and physiotherapy management is more efficient than single therapeutic modality. It was evident from the study that curcumin holds a good promise in the treatment of OSF in future<sup>[15]</sup>.

## 2. Role of curcumin in treating Oral Lichen Planus [OLP].

Lichen planus is a T – cell mediated immune response mediated disease which affects the skin and mucous membrane of humans. It presents frequently in the fourth decade of life with women predilection. Although its etiology remains an enigma various evidence indicates

that a dysregulation of T-cell mediated immunity, which leads to the attack of activated CD8+ lymphocytes on basal keratinocytes, has an important role in the pathogenesis of OLP<sup>[15]</sup>. Cortico steroids along with other drugs like Calcineurin inhibitors, retinoids, dapson, hydroxychloroquine, mycophenolatemofetil and enoxaparin are also applied for OLP treatment . Side effects like high blood pressure, adrenal suppression, etc., may occur through corticosteroids therapy, thus usage of drugs which are of natural or herbal origin has gained importance. Curcumin is safe even given at very high doses. Curcumin mediates its anti-inflammatory effects through the down regulation of inflammatory transcription factors, enzymes (such as cyclooxygenase 2 and 5, lipoxygenase) and cytokine. Furthermore, curcumin produces its antioxidant effect through inhibition of free radicals and nitric oxide which can be very well used in treating OLP<sup>[17]</sup>. Studies conducted to prove the efficacy of curcumin in treating OLP are

- I. **Vibha Singh et al** in 2013 conducted a study on Turmeric - A new treatment option for lichen planus: A pilot study with 10 patients with OLP. Crude extracts of curcumin applied in the form of ointment. Improvement in clinical symptoms , 9 patients OLP healed completely in 3 months<sup>[18]</sup>
- II. **Sumanth Prasad et al** in 2014 conducted a study on the magic of herbal curcumin therapy in recurrent OLP . Case report of 22 year male with recurrent OLP who was first treated with Kenocart, later was treated with systemic 500 mg and topical curcumin. After using curcumin there was no recurrence after a follow up of 3 months even after withdrawal of medication<sup>[19]</sup>
- III. **SeidJavadKia et al** in 2015 did a study on Comparative Efficacy of Topical Curcumin and Triamcinolone for Oral Lichen Planus: A Randomized, Controlled Clinical Trial. In this study, 50 patients (36 women and 14 men) in the age range of 38 to 73 years with OLP were randomly divided into two groups. Each group received 0.1% triamcinolone or 5% curcumin oral paste three times a day for four weeks and concluded that Application of curcumin is suggested for treatment of OLP because of its desirable anti-inflammatory effects and insignificant side effects<sup>[20]</sup>.
- IV. **Maryam et al in 2016** conducted a study on Evaluation of the Efficacy of Curcumin in the Treatment of Oral Lichen Planus: A Randomized Controlled Trial. 20 OLP patients were divided into two groups, each treated with curcumin tablets at a dose of 2000 mg/day or placebo for a period of four weeks. Furthermore, the patients of both groups received routine treatment for OLP (i.e. Mouthwash Dexamethasone 0.5 mg and suspension Nystatin 100,000 Units). The study concluded that ,curcumin had no detectable effect in the treatment of OLP. However, a higher dose of

curcumin administration and other forms of curcumin with improved bioavailability may be considered in future studies.<sup>[21]</sup>

### 3. Role of curcumin in treating oral precancers and cancers

Oral cancer is the 6<sup>th</sup> most common cancer worldwide particularly high in India and other Asian countries. Oral squamous cell carcinoma occurs due to multiple factors like genetic, epigenetic and changes in metabolism. Presence of a precursor lesion leads to the progression of cancer<sup>[22]</sup>. Curcumin with its anti-oxidant and anti-mutagenic property has been proved in various research to be effective in treating cancers and precancers they are

- I. **Balwant Rai et al in 2010** conducted a study on Possible action mechanism for curcumin in precancerous lesions based on serum and salivary markers of oxidative stress. 100 patients, 25 with oral leukoplakia, 25 with OSMF, 25 with OLP, 25 healthy persons. Curcumin 1 g capsule was given. Curcumin significantly increases anti-oxidant status and the levels of vitamin C and E and decreases lipid peroxidation and DNA damage<sup>[23]</sup>
- II. **N.Vijayalaxmi et al in 2012** conducted a study on Efficacy of curcumin in treating palatal changes associated with reverse smoking. 20 reverse smoking patients, 10 given curcumin gel 3-4 times / day, 10 patients asked to quit the habit. Evident improvement in the reduction in size and severity of lesion in 1 month for patients under the treatment of curcumin<sup>[24]</sup>.
- III. Study by **Duvoix A et al in 2005** proved that curcumin induces cell-cycle arrest and apoptosis in a variety of cancer cell lines grown in culture<sup>[23]</sup>.
- IV. **Somasundaram et al in 2002** found that curcumin inhibited apoptosis induced by several chemotherapeutic agents in cultured breast cancer cells<sup>[25]</sup>.

### 4. Role of curcumin in Recurrent Aphthous Stomatitis [RAS]:

It is a mucosal disorder which is multifactorial in etiology like behavioral factor in smoking and stress, trauma, food and nutrients deficiency, systemic disease (e.g: anemia, Behcet's disease, Chron's disease), and medication (e.g. NSAIDs,  $\beta$ -blockers, Nicorandil, Alendronate). The possible mechanism of action of curcumin involves the decreased rate of release and metabolism of arachidonic acid involving diminished activities of phospholipase A2, cyclooxygenase, lipooxygenase, and also by inhibiting the production of reactive oxygen and nitrogen species, which act as intermediates in many signal transduction pathways helps in treating RAS<sup>[26]</sup>. The studies conducted to prove the use of curcumin in RAS are

- I. **Daddy Suradi Halim et al in 2013** conducted a study on Novel Material in the Treatment of

Minor Oral Recurrent Aphthous Stomatitis. 20 patients with minor RAS, divided into 2 groups. Turmeric was equally effective to relieve ulcer pain and size like triamcinolone acetonide<sup>[27]</sup>.

- II. **Manifer .S et al in 2012** conducted a study on Curcumin Gel in the Treatment of Minor Aphthous Ulcer: a Randomized, Placebo-Controlled Trial. 28 patients treated with 2% curcumin gel. 29 patients treated with placebo gel. Curcumin gel significantly reduced pain and ulcer size than placebo in 2 weeks<sup>[28]</sup>.
- III. **Deskmukh R. A et al in 2014** compared the effectiveness of curcumin with triamcinolone acetonide in the gel form in treatment of minor recurrent aphthous stomatitis: A randomized clinical trial. 60 patients of either sex with clinically diagnosed RAS were randomly divided into 2 groups-Curcumin gel group (Group I) and Triamcinolone Acetonide gel group (Group II). Patients in either group were asked to apply the gel three times a day on each ulcer. Assessment of efficacy of gel was done on the basis of time required for regression in pain, size, and number of the ulcers. The results showed significant difference in size, pain, number, and duration of ulcers in Group I and Group II within a period of 7 days. However, no significant difference was noted in both the groups in the treatment of RAS. Curcumin has strong antioxidant, with anti-inflammatory, immunomodulatory and analgesic properties, which according to the results obtained from the present study, can be used as an effective alternative to steroids in treatment of RAS<sup>[29]</sup>.
- IV. **Yogesh S. Thorat et al in 2015** conducted a study for treatment of mouth ulcer by curcumin loaded thermoreversible mucoadhesive gel [TMG]: A Technical Note. Formulations were prepared by using Pluronic F68 and Pluronic F127 as thermoreversible agent along with carbomers and Xanthan gum as bioadhesive polymers. The formulations were characterized for gelation temperature, pH, gel strength, spreadability, in vitro mucoadhesion and in vitro drug release. The obtained results show that the residence time as well as the contact area of curcumin at the ulcer can be enhanced along with a sustained release. It can be concluded that TMG of Curcumin can be ideal candidate for mouth ulcer<sup>[30]</sup>.

### CONCLUSION:

Curcumin not only helps in treating Oral Lesions and conditions but also used for periodontal problems, for subgingival irrigation, as a pit and fissure sealant, as an intra-canal medicament and even as a cure for dental pain. Herbal medicines like curcumin believe in gentle, long-term support to enable the body's own innate powers to do the healing. Many studies have proved that curcumin have the properties which are beneficial in treating oral

mucosal lesions and improving the oral health. More studies with high level of evidence are needed in order to know their maximum dosage and their adverse effects. Therefore in future dentist should be encouraged to make use of Mother Nature's naturally occurring herbs in treating oral lesions which has more cure and less adverse effect.

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