

Literature Review

Curcumin in turmeric (*Curcuma longa L.*) for treatment of oral lichen planus: A narrative review

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ABSTRACT

Background: Turmeric (*Curcuma longa L.*) has long been used as a traditional medicine. The primary active component of turmeric is curcumin. It has potential anti-inflammatory effects and high antioxidant activity. Curcumin contained in turmeric has been reported as an effective treatment for Oral lichen planus (OLP). OLP is a chronic autoimmune, inflammatory disease of the oral mucosa associated with systemic disease. This disease involves the skin and mucous membranes (mucocutaneous) of stratified squamous epithelium. **Purpose:** This narrative review conducted on Google Scholar, PubMed, Research Gate, and ScienceDirect databases aims to study the effectiveness of curcumin contained in Turmeric (*C. longa L.*) in OLP treatment. **Review:** OLP is a condition of the oral mucosa that is a chronic autoimmune mucocutaneous disease. As many as 0.5% to 2.2% of cases of OLP occur in the adult population. Systemic and topical corticosteroid drugs are usually used to treat OLP. However, the use of these drugs has many side effects, so it needs searching for a new active substance to treat OLP. Curcumin is a hydrophobic polyphenol extracted from the rhizome of the herb *Curcuma longa* (turmeric), which has a low molecular weight. The repeated use of steroids can cause side effects that cause atrophy of the mucosa and candidiasis. One natural product that is superior to corticosteroids is curcumin. This is due to curcumin's anti-inflammatory, antioxidant, and chemopreventive properties in several diseases. **Conclusion:** This review suggests that OLP treatment using curcumin in Turmeric (*C. longa L.*) is effective because curcumin exhibits antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic activities, as well as immunomodulatory properties.

Keywords: turmeric; curcumin; Oral Lichen Planus (OLP); medicine; non-communicable disease; autoimmune

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INTRODUCTION

Oral lichen planus (OLP), is a chronic inflammatory oral disease of stratified squamous epithelium that involves the skin and mucous membrane (mucocutaneous).¹ The clinical features of OLP are classified into two types of lesions, namely non-erosive (papular, reticular, and plaque) and erosive (atrophic, erosive, and bullous).² The type of non-erosive lesion (reticular) in OLP is often asymptomatic. While this type of erosive lesion (atrophic) is usually accompanied by symptoms such as roughness in the mouth, burning sensations in the sensations in the mouth, and pain in the oral mucosa.³ OLP on the tongue with a type of erosive lesion has the potential to become malignant. Malignant

transformation is also characterized by the histological appearance of aneuploidy.⁴ Several types of OLP can occur in patients simultaneously.⁵

OLP cases globally are estimated at around 2%. Compared to skin diseases, OLP tends to be more chronic. OLP is more common in women than men, with an average age of 60 years old.⁶ The prevalence of OLP increases significantly and progressively in people over the age of 40, especially in the 50s and 60s. In Indonesia, more than 10% of OLP cases are found mainly in female patients aged 40 years and over.² The etiology of OLP is still unclear.⁷ OLP occurs when an abnormal T-cell responds to foreign bodies in the basal membrane epithelium.¹ OLP oral lesions are symmetrical and bilateral in distribution.

Histopathologic features of OLP are characterized by hyperkeratosis (hyperorthokeratosis or hyperparakeratosis) with thickened granular cell layers, sawtooth epithelial protrusions, hydropic degeneration of basal epithelial cells, lymphocytic infiltration of the superficial lamina propria, lymphocyte infiltration, Civatte bodies (colloid, cytoid, hyaline), or keratinocytes. degeneration of the connective tissue and epithelial tissue.⁵

OLP is a multifactorial disease such as Genetic factors, psychological autoimmune reactions, and infectious factors such as hepatitis C infection act as causative agents. OLP has been associated with systemic diseases such as diabetes, hepatitis C infection, and liver disease. OLP can be associated with other immune-mediated diseases, including dermatomyositis, lichen sclerosis et atrophic, myasthenia gravis, vitiligo, ulcerative colitis, morphea, primary biliary cirrhosis, and alopecia areata. Other factors have also been identified as causative factors for OLP, including systemic medication, tobacco chewing, chronic liver disease, dental materials, and stress.⁶⁻⁸ The buccal mucosa, tongue, and gingiva were the most common oral sites of OLP, followed by the lip mucosa and vermilion of the lower lip. Lesions of OLP in the floor of the mouth, upper lip, and palate are rare. Approximately 10% of patients with OLP have gingival abnormalities, such as desquamative gingivitis. However, apart from focal periodontal disease, OLP in one location is rare. Based on the clinical picture, OLP is divided into six types. The six types are reticular, plaque, atrophic, papular, bullous, and erosive. A simpler classification based on clinical features divides OLP into three types. The three types are reticular, erosive, and erythematous.⁶

OLP is one of the most common pathological conditions encountered in dentistry. There is still no therapy that can completely cure patients with OLP. Some of the therapies used to treat OLP still have side effects, both local and systemic. If treatment is stopped, then the lesions may reappear. Treatment of OLP is aimed at relieving pain symptoms, healing ulcerative and atrophic lesions, and reducing the risk of OLP transforming into malignancy. Generally, the use of topical corticosteroids, with or without a combination of other immunomodulators, is used for the treatment of OLP and achieves its treatment goals. Some cases of OLP are not only treated with the use of corticosteroids but also sometimes require systemic therapy. Laser therapy for OLP shows satisfactory results, and this therapy is chosen as the last treatment for OLP. Treatment for OLP is considered to reach the late stages of healing of the erythema and ulceration of the mucosa, with remaining asymptomatic reticular or papular lesions.⁹ One of the treatments for OLP is to use herbal plants such as Turmeric (*Curcuma longa L.*) Turmeric has been shown to have benefits for various pathological conditions. Turmeric can be used as an anti-inflammatory, antioxidant, antibacterial, antimutagenic, and anticancer agent. Turmeric (*C. longa L.*) has been used for hundreds of years as a food spice, food coloring, and preservative. Turmeric (*C. longa L.*) has recently attracted the attention of the health world because of its effective activity as an antioxidant.¹⁰

Curcumin, which is a substance extracted from the turmeric plant, has long been used as a main compound in medicine.¹¹ Turmeric (*C. longa L.*) contains curcumin, which is the chemical compound of turmeric.¹² Curcumin is commonly used in traditional medicine systems. Turmeric with curcumin as its main compound is being studied as a chemopreventive agent that can inhibit the growth and development of oral cancer. Curcumin and turmeric essential oil can inhibit disease processes through their antioxidant, anti-inflammatory, and anticancer properties.¹³ Based on the explanation above, this study focused on Turmeric (*C. longa L.*) to describe its role as a treatment for OLP. Furthermore, this narrative aims to describe the potential ability of Turmeric (*C. longa L.*) which contains curcumin for OLP treatment.

REVIEW

OLP is a chronic autoimmune mucocutaneous disease that occurs in the oral mucosa. OLP cases occur in approximately 0.5%–2.2% of the adult population. Usually, OLP is treated with systemic or topical corticosteroids. The use of corticosteroid has many side effects, such as telangiectasia, hypothalamic-pituitary-adrenal suppression, and oropharyngeal candidiasis, so it is necessary to look for new active substances to treat OLP.¹⁴ Curcumin is a hydrophobic polyphenolic compound extracted from the rhizome of the herb turmeric (*curcuma longa*). Compared to corticosteroids, curcumin has more advantages.¹⁰ The use of corticosteroids has side effects that can cause mucosal atrophy and candidiasis if used repeatedly.¹⁵

Curcumin, which is the main compound in turmeric, is known to have antioxidant, anti-inflammatory, chemopreventive, and chemotherapeutic effects on several diseases. Curcumin has demonstrated anti-inflammatory effects through the inhibition of various macromolecules involved in inflammation. These macromolecules include cyclooxygenase 2, phospholipase, lipoxygenase, prostaglandins, IL-1 and IL-2, and tumor necrosis factor. Curcumin is also suggested for the treatment of infectious diseases through immunomodulation.¹⁰

High-dose curcumin (6000 mg/day in three divided doses) or placebo is effective in reducing the signs and symptoms of OLP. These results are in line with previous study stated that curcumin applied topically showed a decrease in the signs and symptoms of OLP. In that study, applying curcumin oral gel six times daily was almost as effective as using triamcinolone acetonide. Curcumin contains α - β unsaturated β diketone.^{16,17} The ability of curcumin to inhibit COX2 gene induction has been demonstrated in oral epithelial cells through *in vitro* study.¹¹ Curcumin also plays a role in carcinogenic processes. The role of curcumin as an anticancer is through inhibition of tumor growth and inhibition of angiogenesis.¹⁸ Curcumin affects the inhibition of angiogenesis by producing growth factors, which are part of the formation of blood vessels

in both nonmalignant and malignant cells. Curcumin also has immunomodulatory effects involving activation of natural killer cells and host macrophages and modulation of lymphocyte-mediated functions.¹¹

DISCUSSION

Curcumin is the most active constituent in turmeric preparations containing α - β unsaturated β diketone. Curcumin has been shown to inhibit the induction of Cox2 gene expression, and in the growth and spread of mature malignancies, curcumin influences the process of carcinogenesis. Curcumin is also associated with the inhibition of angiogenesis in malignant and nonmalignant cells through the production of growth factors integral to the formation of blood vessels. Activation of host macrophages and natural killer cells and modulation of lymphocyte-mediated functions are implicated in curcumin's immunomodulatory effects.¹⁶

Oxidative stress is the pathogenesis of OLP, so antioxidants are needed to treat it. Many plants and vegetables can be naturally rich in antioxidants, which are useful in many pathological conditions. Turmeric is a meditative plant native to India that has a main chemical compound in the form of curcumin longa L, which is proven to have antioxidant, anti-inflammatory, antibacterial, anticancer, and antimutagenic properties. For hundreds of years, curcuma has been used as a flavor, color, and preservative.¹² Since ancient times, the extract of curcumin plants has been the main ingredient in medicine. In the traditional medical system, many medicinal properties are attributed to it. Researchers are studying the development of oral cancer, which is inhibited by the curcumin component in turmeric as a chemopreventive agent. In addition, the antioxidant, anti-inflammatory, and anticancer properties of curcumin and essential oils have been shown to inhibit many disease processes.¹⁷

Therefore, it was decided to investigate alternative treatments for OLP patients by using curcumin contained in turmeric.¹¹ Curcumin, as a natural phytochemical in turmeric, does not have a toxic effect. Curcumin has been shown to be able to ward off free radicals due to its antioxidant activity, which is anti-inflammatory, anticancer, immunomodulatory. are two journals that have compared the efficacy of using curcumin with corticosteroids in the standard treatment of OLP patients. 1% curcumin gel and 0.1% triamcinolone acetone was applied six times a day, treatment using 1% curcumin gel was not as effective as 0.1% triamcinolone acetone. In the other hand, administration higher curcumin concentrations makes topical curcumin applications with topical corticosteroids have the same effectiveness.^{16,17}

Curcumin has been shown to have immunomodulatory and inhibitory effects on the growth of cancer cells, for example, prostate, colon, and leukemia cancer cells.¹¹ anticancer effects and chemopreventive effects involved in various biological pathways, such as mutagenesis,

cell cycle regulation, oncogene expression, apoptosis, metastasis, and tumorigenesis.¹⁴ The control group for comparison found a significant decrease in the Reticulation/keratosis, erythema, and ulceration (REU) score in patients treated with curcumin. Patients treated with curcumin had a clinical picture of smaller lesions and a decrease in the severity of the lesions.¹⁹ In addition, as many as 36% of patients experienced a reduction or disappearance of signs of OLP, making it as beneficial as triamcinolone.^{11,12} The contradictory findings found in previous study that there is no consistent benefit in the treatment of OLP with oral curcumin therapy. None of the topical curcumin trials were blinded, so there is a considerable risk of bias in describing and scoring severity. Placebo effects in pain trials can be profound. Some trials used intragroup comparisons versus baseline, which is problematic given the tendency of OLPs to spontaneously remit. Biopsy confirmation of OLP was not mentioned, and there were nine abnormalities manifesting lichenoid lesions and similar symptoms.¹⁴ Complaints about curcumin use are rarely reported by patients; this makes significant side effects of curcumin unknown.¹⁵ Curcumin can cause pharmacokinetic changes in cardiovascular drugs, antibiotics, antidepressant agents, chemotherapy drugs, anticoagulants, and histamine. Therefore, concomitant use of curcumin with conventional medications should be used with caution.¹⁶ This review suggests that OLP treatment using curcumin in Turmeric (*C. longa L.*) is effective because curcumin exhibits antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic activities, as well as immunomodulatory properties.

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