

Review Article

Various Therapeutic Approaches for Managing Oral Lichen Planus—A Narrative Review

Emma Williams¹, Benjamin Jones^{2*}

¹Department of Oral Medicine, Infection and Immunity, Harvard School of Dental Medicine, Boston, USA.

Division of Oral Medicine and Dentistry, Brigham and Women's Hospital/ Dana Farber Cancer Institute, Boston, USA.

*E-mail ✉ bjones88@outlook.com

Received: 08 November 2022; Revised: 08 February 2023; Accepted: 12 February 2023

ABSTRACT

Oral lichen planus (OLP) is a long-standing inflammatory disorder of uncertain origin that primarily affects the oral mucosa. Clinically, it manifests in several forms, ranging from the usually asymptomatic reticular type to the atrophic–erosive variant, which is often accompanied by pain, a burning sensation, and difficulty eating. Since the underlying cause of OLP remains unclear, management focuses on symptom relief through the use of various topical and systemic medications aimed at reducing inflammation and discomfort. Topical corticosteroids are considered the standard first-line therapy for symptomatic cases, while systemic corticosteroids are reserved for severe or resistant lesions unresponsive to local treatment. Nonetheless, inconsistent therapeutic outcomes and the adverse effects associated with conventional treatments have prompted interest in exploring alternative therapies. Emerging options include tacrolimus, efalizumab, dapsone, interferon, retinoic acid, psoralen combined with ultraviolet A photochemotherapy (PUVA), aloe vera, antimalarial agents, and certain antibiotics. Although these treatments provide varying degrees of benefit, none fully satisfy the criteria of efficacy and safety, underscoring the ongoing need for research into more effective and well-tolerated therapeutic approaches.

Keywords: Oral lichen planus, Adverse effects, Therapeutics, Chronic disease

How to Cite This Article: Williams E, Jones B. Various Therapeutic Approaches for Managing Oral Lichen Planus—A Narrative Review. Int J Dent Res Allied Sci. 2023;3(1):24-36. <https://doi.org/10.51847/fZgaz7WEzu>

Introduction

Lichen planus (LP) is a chronic inflammatory disorder that affects both the skin and mucosal surfaces [1], predominantly appearing in individuals aged 30–60 years, with a higher prevalence among females [2]. The occurrence of oral lesions has been estimated to range from 0.1% to 2.2% [3]. While cutaneous lesions generally resolve spontaneously, oral lichen planus (OLP) tends to persist, exhibiting recurrent cycles of remission and exacerbation. Clinically, OLP manifests in several forms, from the reticular type—usually asymptomatic and marked by the presence of hyperkeratotic Wickham's striae—to the erosive type, which is often painful due to erosions and ulcerations

[4]. The exact etiology of OLP remains uncertain, though existing research highlights its immunopathogenic nature, involving dysregulated cytokine activity [5].

Numerous studies have also suggested a possible link between OLP and psychological conditions such as stress, anxiety, and depression [6]. Di Stasio *et al.* [6], in a comparative study involving 11 OLP patients and 13 controls, reported that 73% of affected individuals displayed mild psychiatric symptoms on the Visual Analogue Scale (VAS), 9% showed depressive traits, and all participants surpassed the threshold for anxiety scores, although these findings did not achieve statistical significance. The authors proposed that larger cohorts might yield more definitive results.

Additionally, the literature identifies a rare variant known as vulvovaginal gingival lichen planus (VVG-LP) [7], affecting about 20% of women with OLP [7]. Lucchese *et al.* [8] documented two VVG-LP cases and emphasized the need for multidisciplinary management, accurate diagnosis, and continuous surveillance of oral and genital lesions owing to the risk of malignant transformation [9].

The World Health Organization (WHO) classifies OLP as a potentially malignant condition [10], with a recent systematic review estimating its malignant transformation rate at 1.37% [11].

Therapeutic management of OLP primarily targets the active inflammatory phase, especially when epithelial disruption is associated with pain or burning sensations. Topical corticosteroids remain the standard and most frequently used treatment modality [12]. In severe or unresponsive cases, systemic corticosteroids or localized corticosteroid injections may be indicated [13, 14], though prolonged systemic use must be approached cautiously due to the risk of adverse effects [13, 15]. Corticosteroids are often combined with retinoids or immunosuppressants, but these agents also pose challenges such as toxicity and recurrence. Recently, newer treatment modalities—including dapsone, antimalarials, interferon, hyaluronic acid, and PUVA therapy—have been explored; however, their clinical use remains limited, and further trials are required to confirm their safety and efficacy [16].

This review aims to summarize contemporary therapeutic strategies for OLP, evaluating their clinical effectiveness and safety profiles. Relevant literature

published between 1970 and 2022 was retrieved from PubMed to provide a comprehensive overview of all available treatment options.

Treatment of OLP

Given the uncertain etiology of OLP, therapeutic management focuses primarily on alleviating symptoms and controlling disease manifestations. Both topical and systemic pharmacologic agents are employed for this purpose.

Although potent topical corticosteroids are widely regarded as the first-line therapy, robust scientific validation for their effectiveness is lacking. A Cochrane systematic review [17] highlighted the insufficient evidence supporting the efficacy of conventional OLP treatments, including corticosteroids, due to limited sample sizes and study numbers. At present, topical or perilesional corticosteroid application remains the mainstay for managing erosive OLP [12]. Nevertheless, there is no consensus regarding second-line therapy; short-term systemic corticosteroid administration is occasionally used to rapidly alleviate symptoms or manage lesions resistant to topical agents [17].

Because the erosive form of OLP is often painful and can significantly diminish patients' quality of life, the therapeutic objective is to select the most potent and tolerable intervention. Besides corticosteroids, various other pharmacological and non-pharmacological therapies have been explored for OLP management [18]. **Table 1** presents a summary of these therapeutic modalities discussed in the study.

Table 1. Therapeutic options in the treatment of OLP.

Corticosteroids	Retinoids	Immunosuppressants	Other Drugs and Preparations
<p>Topical:</p> <p>betamethasone phosphate, clobetasol propionate, flucinolone acetonide, flucinonide, fluticasone propionate, hydrocortisone hemisuccinate, triamcinolone acetonide</p> <p>Systemic: prednisone, methylprednisolone</p>	<p>Topical:</p> <p>fenretinide, isotretinoin, tazaroten, tretinoin</p> <p>Systemic: acitretin, etretinate, isotretinoin, temarotene, tretinoin</p>	<p>azathioprine, cyclosporine, pimecrolimus, tacrolimus</p>	<p>basiliximab, dapsone, doxycycline, glycyrrhizin, hydroxychloroquine sulphate, interferon, levamisole, mesalazine, phenytoin, PUVA, reflexology, surgery, thalidomide, aloe vera, amlexanox, alefacept, efalizumab, sulodexide, hyaluronic acid, curcumin, vitamin D, selenium,</p>

Corticosteroids

Synthetic corticosteroids are chemically modeled after the natural glucocorticoid hydrocortisone (cortisol). Cortisol, the principal glucocorticoid, plays a crucial role in regulating the metabolism of carbohydrates, proteins, and lipids, while also exerting strong anti-inflammatory and immunosuppressive actions [19]. Beyond its use as a hormone replacement in adrenal insufficiency, corticosteroid therapy is widely employed in the management of various inflammatory conditions of uncertain origin—such as rheumatic disorders, lupus, and sarcoidosis—as well as in severe allergic reactions. In the field of dentistry, corticosteroids are prescribed for treating mucosal lesions of differing etiologies, including oral lichen planus (OLP), pemphigus, and traumatic ulcers [20].

Topical corticosteroids

Currently, topical corticosteroid formulations represent the primary approach in managing OLP. These preparations are available in multiple forms, including ointments, gels, creams, adhesive pastes, mouth rinses, and sprays. In most patients, OLP manifestations can be effectively controlled with high-potency topical corticosteroids, which demonstrate strong therapeutic efficacy and a reduced risk of systemic side effects compared to oral or injectable formulations. Topical corticosteroids are categorized according to their level of potency, as summarized in **Table 2** [21].

Table 2. Topical steroid preparations according to potency.

Low potency corticosteroids	1% hydrocortisone acetate
	0.05% alclomethasone dipropionate
	0.25% methylprednisolone acetate
Medium potency corticosteroids	0.05% clobetasone butyrate
	0.1% hydrocortisone butyrate
	0.5% flucortolone pivalate
Highly potent corticosteroids	0.025% beclomethasone dipropionate
	0.05% beclomethasone dipropionate
	0.025% betamethasone benzoate
	0.1% betamethasone valerate
	0.1% diflucortolone valerate
	0.025% flucinolone acetonide
Very highly potent corticosteroids	0.05% fluticasone propionate
	0.05% flucinonide
	0.05% clobetasol propionate
	0.3% diflucortolone valerate
	0.01% halcinonide

Triamcinolone acetonide is a commonly used topical corticosteroid available as an adhesive paste, lozenge, or oral suspension for managing OLP lesions [22]. Betamethasone disodium phosphate and clobetasone propionate solutions have also shown good therapeutic outcomes, particularly in treating the diffuse form of OLP; however, their use carries a greater risk of systemic absorption and potential adrenal suppression [23]. Other frequently prescribed topical corticosteroids include betamethasone valerate, clobetasol, fluciclonide acetonide, fluciclonide, and triamcinolone acetonide adhesive paste [22, 24–27]. Fluticasone propionate is sometimes applied for short-term therapy due to its limited tolerability [28]. In more resistant or severe OLP cases, 0.05% fluciclonide or 0.5% fluciclonide acetonide are typically recommended [22, 27], while highly potent agents such as clobetasone are favored for sustaining long-term remission [24, 25].

The most frequent adverse effect of topical corticosteroids is oral candidiasis, which can be minimized with prophylactic antifungal agents or chlorhexidine mouth rinses [22, 24, 27]. Although intralesional corticosteroid injections can rapidly reduce inflammation, discomfort during administration and the potential for local atrophy have limited their widespread use [14]. Topical application remains preferable for localized lesions, given its minimal systemic absorption and reduced risk of adrenal suppression. In addition to local reactions—such as mucosal atrophy and candidiasis [14]—systemic side effects have occasionally been observed, including hirsutism and “moon face” developing between the fourth and sixth week of therapy [23]. Less common reactions include xerostomia, dysgeusia, unpleasant odor, labial swelling, nausea [28], cases of hairy leukoplakia in immunocompetent individuals [24], oral mucosal hypersensitivity [29], hemorrhagic lesions with 0.05% clobetasol propionate solution [30], and iatrogenic Cushing’s syndrome in patients treated with 0.05% clobetasol propionate for OLP or pemphigoid [31].

Systemic corticosteroids

Systemic corticosteroid therapy is reserved for patients with extensive erosive OLP, those unresponsive to topical formulations, or individuals presenting with mucocutaneous disease. Methylprednisolone and prednisone are the most frequently used agents, typically prescribed at 1.5–2 mg/kg/day, with a gradual

taper once clinical improvement occurs. Compared to topical treatments, systemic corticosteroids are associated with a higher risk of serious and frequent adverse effects, necessitating cautious use [13, 15, 32]. Adverse reactions to systemic corticosteroids are dose- and duration-dependent. The most serious complication is adrenal insufficiency leading to an adrenal crisis. Another major consequence is iatrogenic Cushing's syndrome, marked by sodium and water retention, hypokalemia, hyperlipidemia, central obesity, and a characteristic "moon face." Other complications include osteoporosis, hyperglycemia, diabetes mellitus, hypertension, glaucoma, cataract formation, skin thinning with purpura, delayed wound healing, easy bruising, gastritis, peptic ulceration, muscle catabolism with loss of mass, immunosuppression, and neuropsychiatric manifestations [33].

Immunosuppressants

Immunosuppressive agents act by inhibiting T-lymphocyte activation and proliferation, thereby reducing the body's immune response [34]. Drugs such as cyclosporine, azathioprine, tacrolimus, and pimecrolimus are employed in managing OLP. Although numerous studies have confirmed their efficacy, these agents may cause side effects including dysgeusia, burning sensations upon application, nephrotoxicity, hypertension, and high treatment costs [35–37].

Cyclosporine (CSA)

Cyclosporine (CSA) is a macrolide immunosuppressant primarily indicated for preventing graft rejection through immune suppression. It selectively and reversibly inhibits T-lymphocyte activation by binding to cyclophilin, an intracellular protein in lymphocytes. The cyclosporine–cyclophilin complex inhibits calcineurin, a phosphatase that normally stimulates interleukin-2 (IL-2) transcription; as a result, IL-2 synthesis and T-cell activity are reduced. Like tacrolimus and pimecrolimus, CSA functions as a calcineurin inhibitor [34]. Because of its targeted mechanism, CSA is prescribed for resistant OLP cases either as a mouthwash (100 mg/mL, twice daily) or in an adhesive paste formulation. However, its use is limited by disadvantages such as unpleasant taste, high cost, poor solubility, and the potential for cyclosporine-induced gingival hyperplasia [5].

Tacrolimus and pimecrolimus

Tacrolimus (FK-506) is a macrolide immunosuppressant belonging to the calcineurin

inhibitor class and is primarily used to prevent organ transplant rejection. Compared with cyclosporine A (CSA), tacrolimus exhibits superior mucosal permeability and is estimated to be 10–100 times more potent [34]. In OLP management, it is applied topically at a concentration of 0.1%, twice daily, directly to the affected areas. Clinical studies have demonstrated its efficacy in erosive OLP; however, some adverse effects—such as burning sensations on the mucosa and recurrence within 12 months following discontinuation—have been reported. Pimecrolimus shares a similar pharmacological mechanism with tacrolimus and is used as a 1% topical preparation for OLP treatment [5, 38].

Azathioprine

Azathioprine (AZA) is an antimetabolite that interferes with purine biosynthesis, resulting in the suppression of T- and B-lymphocyte proliferation [34]. Besides its immunosuppressive role, AZA possesses anti-inflammatory activity. It is administered systemically in generalized OLP cases, though its use requires careful monitoring due to serious potential complications such as bone marrow suppression, pancytopenia, and hepatic dysfunction [39].

Retinoids

Retinoids, derivatives of vitamin A (retinol), are employed both topically and systemically in managing OLP. They are essential for normal epithelial growth and differentiation, and a deficiency can lead to keratinization of oral mucosal cells [40]. The most frequently used topical retinoids—tretinoin, isotretinoin, and fenretinide in 0.1% gel form—help reduce reticular and plaque-type lesions, although relapse is common once therapy ceases [41]. Systemic retinoids, including etretinate, isotretinoin, and tretinoin, have also been explored but are limited by adverse effects such as cheilitis, hepatotoxicity, and teratogenicity. Tazarotene has shown therapeutic potential in OLP management with fewer associated side effects [5, 41].

Other drugs and preparations

Dapsone

Dapsone has shown limited success in managing erosive OLP [42, 43]. Given its potential adverse effects, including hemolysis and headaches [44], it is not considered a preferred therapeutic option for OLP.

Amlexanox

Amlexanox (C₁₆H₁₄N₂O₄) is a topical anti-inflammatory medication approved for treating

recurrent aphthous ulcers [45]. Its mechanism of action involves inhibiting the synthesis and release of histamine, TNF- α , and leukotrienes from mast cells, neutrophils, and mononuclear cells [46]. To date, only one pilot study has investigated the use of topical amlexanox paste for erosive OLP, revealing no statistically significant difference compared with dexamethasone in improving clinical symptoms. The authors proposed that amlexanox might serve as an alternative to corticosteroids. Reported adverse effects include mucosal burning, xerostomia, and localized bleeding at the application site [47].

PUVA therapy

PUVA (psoralen + UVA) therapy, a form of photochemotherapy that involves the use of psoralen either topically or systemically, has been successfully applied in the treatment of cutaneous lichen planus [48, 49] and was first reported in OLP for refractory cases [50]. Clinical improvements were observed in 87% of patients treated with UVA alone, without any added photosensitizer [51]. A controlled trial further confirmed the efficacy of PUVA therapy with systemic psoralen administration in severe OLP [52]. Common adverse effects include nausea, dizziness, headaches, paresthesia, and visual disturbances [53]. Additionally, PUVA therapy carries an oncogenic risk [53], and thus it is recommended only for severe, treatment-resistant OLP cases [54].

Antibiotics

Tetracyclines have occasionally been used for OLP management, particularly in gingival lesions, though their overall therapeutic benefit is limited [55, 56]. Consequently, antibiotics are no longer advised for routine OLP treatment [56].

Antimalarial drugs

Hydroxychloroquine sulfate has demonstrated improvement in 9 out of 10 OLP cases [57], and chloroquine phosphate therapy for three months showed clinical benefit in patients with lip lesions of lichen planus [58]. However, due to the risk of drug-induced lichenoid reactions, antimalarials are not recommended as standard therapy for OLP [59].

Glycyrrhizin

Licorice, a medicinal plant used for centuries, contains glycyrrhizin within its root structure. This compound has demonstrated therapeutic benefits in managing oral lichen planus (OLP), particularly among patients suffering from chronic hepatitis C [60, 61]. Owing to its hepatoprotective properties, further clinical

evaluation is necessary to fully determine the potential of glycyrrhizin in treating OLP lesions.

Interferon

Topical administration of alpha- and beta-interferons has been proposed as a therapeutic option for erosive OLP [62]. Nevertheless, several reports have described the onset or worsening of OLP during or following alpha-interferon therapy in patients infected with hepatitis C virus (HCV) [63–65]. Despite these observations, systemic alpha-interferon has shown therapeutic success in treating OLP among individuals both with and without HCV infection [66–68].

Levamisole

Levamisole functions as an immunomodulatory agent and has been applied in the treatment of OLP [69]. Evidence from a prospective study indicates that combining low-dose systemic corticosteroids with levamisole can effectively manage severe erosive variants of OLP [70]. However, cases of lichenoid eruptions affecting the skin and oral cavity have been documented in patients receiving levamisole for rheumatoid arthritis, with these lesions resolving after discontinuation of the drug [71].

Mesalazine

Mesalazine, also known as 5-aminosalicylic acid, is primarily used in treating inflammatory bowel diseases. Its topical form has demonstrated comparable efficacy to clobetasol in alleviating symptoms of OLP [72]. Similar to other therapeutic agents for OLP, mesalazine has been associated with the emergence of drug-induced lichenoid reactions [73].

Phenytoin

Clinical reports have explored phenytoin use in OLP management, showing complete remission in two of four treated patients [74]. However, subsequent studies failed to confirm its therapeutic efficacy or notable adverse effects, although phenytoin is known to occasionally trigger lichenoid lesions [75].

Aloe vera

Aloe vera has been investigated as both a topical and systemic treatment for OLP in several clinical studies [76]. In a randomized, double-blind, placebo-controlled trial, topical aloe vera gel significantly improved clinical symptoms and patient-reported discomfort compared with placebo [77]. Another study using aloe vera solution over a four-week period demonstrated marked improvement in OLP signs and symptoms [78]. Additionally, a double-blind

randomized study found that aloe vera gel enhanced the quality of life of OLP patients relative to placebo [79].

Monoclonal antibodies

Preliminary evidence from an open-label pilot trial suggests that efalizumab, a monoclonal antibody, may serve as a therapeutic alternative for erosive and ulcerative forms of OLP. Nevertheless, serious adverse events occurred in two out of four participants—one developing urticaria and a staphylococcal hip infection, and another presenting with subacute cutaneous lupus. Consequently, the authors advise careful consideration when prescribing this biologic agent [80].

Sulodexide

Sulodexide is a low-molecular-weight compound composed of 80% heparin and 20% dermatan sulfate, possessing minimal anticoagulant activity. Its therapeutic benefits are linked to the modulation of plasmin activity, cell proliferation, and cytokine regulation [81, 82]. Due to its endothelial-protective properties [83] and ability to facilitate cellular repair [82, 84], sulodexide may hold promise in treating erosive forms of OLP. An open, non-randomized clinical comparison of systemic sulodexide versus topical cyclosporine in twenty patients with chronic erosive OLP resistant to corticosteroids showed significant symptom relief and clinical improvement in both groups, with slightly faster recovery observed in those treated with sulodexide. One patient, however, experienced dizziness and vomiting and was withdrawn from the study [85].

Reflexo-Therapy

Reflexology has also been explored as an adjunctive therapy for symptomatic OLP. Published reports highlight several treatment protocols designed to accelerate epithelial regeneration of erosive and ulcerative buccal lesions, emphasizing the pronounced analgesic effects associated with this therapeutic approach [86].

Surgery

Both surgical excision [87, 88] and cryosurgical procedures [89] have been employed effectively in managing erosive oral lichen planus (OLP) cases that fail to respond to conventional therapies [90]. Nevertheless, lesion recurrence following cryosurgery is frequent [91], often accompanied by the emergence of new lesions in the healing areas and scar tissue, typically associated with more pronounced symptoms. Additionally, free soft tissue grafts [92] and free

gingival grafts [93] have been successfully applied for treating localized erosive OLP lesions.

Hyaluronic acid

Topical hyaluronic acid (HA) has been investigated for its therapeutic potential in OLP management. In a randomized, double-blind, placebo-controlled trial, the efficacy of a 0.2% HA gel formulation was tested in patients with erosive OLP. Results revealed a significant decrease in pain intensity within 4 hours post-application compared to placebo. After 28 days of therapy, lesion size was significantly reduced from baseline, although the difference between treatment and placebo groups was not statistically significant. The researchers recommended HA gel as a supportive topical therapy for OLP when applied frequently [94]. Another comparative study between 0.1% triamcinolone acetonide (TA) and 0.2% HA in 40 patients demonstrated reductions in both pain and lesion size in each group, without any significant differences in outcomes [95].

Curcumin

Curcuma longa, long utilized in traditional Indian medicine, possesses well-established anti-inflammatory, antioxidant, and anticarcinogenic properties, along with proven wound-healing and safety profiles [96, 97]. In a 2015 study by Kia *et al.*, the efficacy of 5% curcumin oral paste was compared with 0.1% triamcinolone paste, each applied thrice daily over four weeks [98]. Complete pain relief was reported in 36% of patients using curcumin and 32% of those using triamcinolone, while complete lesion remission occurred in 4% of each group, showing no significant difference between treatments. Some participants using curcumin experienced transient burning sensations, swelling, and dry mouth, which resolved within one week; yellow discoloration of the gingiva was also commonly observed. In the triamcinolone group, isolated cases of burning sensation and mucosal desquamation were recorded. The authors proposed topical curcumin as a natural alternative to synthetic corticosteroids for OLP therapy due to its anti-inflammatory efficacy and minimal side effects [98]. Furthermore, other researchers have suggested curcumin as a maintenance therapy following corticosteroid treatment [99]. However, a study by Amirchaghmaghi *et al.* found no therapeutic benefit of curcumin for OLP management [100].

Vitamin D

Since vitamin D receptors (VDRs) are expressed on immune cells such as T and B lymphocytes, vitamin D

is considered integral to immune regulation [101]. A pilot clinical study assessing vitamin D supplementation in OLP patients demonstrated significant improvements in both subjective symptoms and clinical findings among those receiving vitamin D, either alone or combined with psychological counseling, alongside short-term topical corticosteroid therapy. Despite the limited sample size and uneven participant distribution, the researchers suggested a potential role of vitamin D in OLP pathogenesis and its therapeutic management [102]. In a separate study by Nazeer *et al.* [103], involving 450 OLP patients categorized based on serum vitamin D levels, the greatest clinical improvement occurred in participants who received vitamin D supplementation.

Selenium

Selenium (Se), an essential micronutrient with potent antioxidant activity, naturally occurs in the human body and contributes to oxidative stress protection, immune modulation, antiviral defense, chemoprevention, and metabolic regulation [104]. A randomized controlled clinical study evaluated the efficacy of selenium—administered as a topical hydrogel or oral capsule—in patients with erosive OLP. Participants were divided into three groups: topical corticosteroids (Group I), topical Se (Group II), and systemic Se (Group III), with all treatments lasting six weeks. Each group demonstrated significant improvement in symptoms and lesion severity, though no statistically significant differences were observed among them by week six. Compared to corticosteroids, selenium exhibited certain advantages, including longer-lasting effects, greater pain relief, and a lower risk of secondary infection [105]. Nonetheless, further large-scale clinical investigations are needed to validate these preliminary findings.

NAVS naphthalan

Non-aromatic very rich in steranes (NAVS) naphthalan is a natural mineral oil characterized by a high sterane content and a molecular structure resembling that of vitamin D₃ and steroid hormones [106, 107]. Its therapeutic potential in treating oral lichen planus (OLP) has been examined in two clinical investigations. In an initial pilot study, improvements in both clinical symptoms and lesion appearance were observed among 11 patients with OLP [108]. Subsequently, a double-blind, randomized controlled trial involving 39 patients compared the efficacy of NAVS with 0.05% betamethasone dipropionate oral paste over a 28-day treatment period. Both groups demonstrated clinical improvement, but no statistically

significant difference was found regarding pain intensity or overall disease activity between treatments [109]. Importantly, NAVS produced no adverse effects, whereas three patients in the betamethasone group developed *Candida* infections. Although these findings are encouraging, the small sample size underscores the need for additional, larger-scale clinical studies to confirm its therapeutic role.

Photodynamic therapy (PDT)

Photodynamic therapy (PDT) has emerged as a promising alternative approach for OLP management. This method relies on the interaction of a photosensitizing agent (PS) with a specific light wavelength, generating reactive oxygen species that induce selective cellular damage [110]. Commonly used photosensitizers include methylene blue (MB), 5-aminolevulinic acid (5-ALA), and chlorin e₆ derivatives. According to a systematic review assessing PDT's effectiveness in OLP, topical application of 5-ALA achieved superior clinical responses compared to MB [111]. The review analyzed 16 studies qualitatively and 13 quantitatively, concluding that PDT offers comparable efficacy to topical corticosteroids and may serve as a viable option for patients who are unresponsive to, or unable to tolerate, corticosteroid therapy. However, variability in study design, outcome parameters, wavelength ranges, and energy density limited the strength of these conclusions. Consequently, further standardized, high-quality trials are essential to substantiate the therapeutic benefits of PDT in OLP treatment [111].

Low-level laser therapy (LLLT)

Low-level laser therapy (LLLT) has been explored as another potential therapeutic modality for OLP management. Various types of lasers—including helium–neon, ultraviolet, and diode lasers—are used with differing power outputs, doses, exposure durations, and session frequencies [112, 113]. Photobiomodulation (PBM), operating at wavelengths between 400 and 1100 nm, enhances cellular activity and tissue repair without thermal damage or harm to surrounding structures [114]. Despite its clinical promise, no universally accepted treatment protocol was available as of 2021. Del Vecchio *et al.* [114] suggested energy doses between 2 and 3 J/cm² as potentially effective for OLP lesions. A reported case involving a 42-year-old male demonstrated complete healing of erosive OLP following two sessions of diode laser irradiation at 660 nm for 5 minutes each, conducted weekly, with no recurrence over four months [115].

A systematic review by Akram *et al.* [116] compared LLLT and corticosteroid therapy in OLP across five clinical studies using wavelengths from 630–970 nm, power outputs between 10 and 3000 mW, and exposure times from 6–480 seconds. Three studies favored corticosteroids as more effective, one supported LLLT superiority, and another showed comparable results between the two. However, the review highlighted a high risk of bias in most included studies, leading to the conclusion that current evidence is insufficient to confirm whether LLLT is more effective than corticosteroids [116].

A more recent systematic review evaluated PBM's efficacy in treating atrophic–erosive OLP relative to other modalities [117]. Of 297 identified studies, seven met inclusion criteria. Most compared PBM with topical corticosteroids, while others compared it with laser therapy combined with corticosteroids [117] or surgical excision using a cold knife [118]. Findings revealed that PBM effectively alleviated clinical symptoms and improved lesion appearance. Mutafchieva *et al.* [119] reported improvement in 59.3% of cases, while Khater *et al.* [120] documented complete lesion remission in 37.3% of patients. Nevertheless, limitations—such as small sample sizes, inconsistent follow-up, and methodological heterogeneity—restricted the reliability of these results [121]. The authors concluded that developing a standardized, universally accepted clinical protocol is crucial to enhance comparability across studies and generate stronger scientific evidence regarding PBM efficacy in OLP therapy.

Results and Discussion

Lichen planus (LP) is a prevalent chronic immune-mediated inflammatory disorder affecting the skin and mucous membranes [122]. Given its unclear etiology, treatment is primarily symptomatic, aimed at alleviating clinical signs and patient discomfort. A Cochrane systematic review highlighted the limited and inconclusive evidence regarding the efficacy of many treatments, including topical corticosteroids [17]. A literature search identified 220 articles discussing current therapeutic approaches for OLP, of which 15 randomized trials involving 667 participants were included, with 473 subjects presenting with the erosive form of the disease. Most studies had small sample sizes ranging from 12 to 39 participants and exhibited substantial heterogeneity in outcome measures and disease scoring systems. Consequently, the Cochrane review recommended the adoption of standardized methods for evaluating treatment

outcomes and assessing clinical severity. While six studies included patients with non-erosive OLP, this review focused exclusively on the erosive form. Due to the methodological variability, pooling results across studies was not feasible [17]. A 2020 update of this review concentrated solely on corticosteroid therapy [123], incorporating 35 randomized trials: 7 at low risk of bias, 11 unclear, and 17 at high risk. Findings indicated that topical corticosteroids in adhesive paste form are effective in reducing pain in OLP, although the overall quality of evidence remains low. Moreover, no corticosteroid formulation demonstrated clear superiority over another, nor was there strong evidence that calcineurin inhibitors, such as tacrolimus, offer greater pain relief than corticosteroids [123]. Among all therapeutic strategies explored, topical corticosteroids remain the most extensively studied, frequently serving as either the intervention or control in clinical trials. Their widespread use as first-line therapy is justified by their ability to reduce inflammation and pain with minimal adverse effects, as well as their favorable cost–benefit profile.

Conclusion

Although the immunopathogenic mechanisms of OLP are increasingly understood, the initial trigger for lesion development remains unknown. This uncertainty contributes to the absence of an ideal therapeutic agent for OLP, as reflected by the wide variety of currently available treatments. Existing interventions provide only partial efficacy and safety, underscoring the ongoing need for the development and evaluation of new therapeutic strategies.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Omal P, Jacob V, Prathap A, Thomas NG. Prevalence of oral, skin, and oral and skin lesions of lichen planus in patients visiting a dental school in southern India. *Indian J Dermatol.* 2012;57(2):107-9.
2. Le Cleach L, Chosidow O. Clinical practice. Lichen planus. *N Engl J Med.* 2012;366(8):723-32.

3. Gonzalez-Moles MÁ, Warnakulasuriya S, Gonzalez-Ruiz I, Gonzalez-Ruiz L, Ayen Á, Lenouvel D, et al. Worldwide prevalence of oral lichen planus: a systematic review and meta-analysis. *Oral Dis.* 2021;27(4):813-28.
4. Mattson U, Jontell M, Holmstrup P. Oral lichen planus and malignant transformation: is a recall of patients justified? *Crit Rev Oral Biol Med.* 2002;13(5):390-6.
5. Lavanya N, Jayanthi P, Rao UK, Ranganathan K. Oral lichen planus: an update on pathogenesis and treatment. *J Oral Maxillofac Pathol.* 2011;15(2):127-32.
6. Di Stasio D, Lauritano D, Gritti P, Migliozi R, Maio C, Minervini G, et al. Psychiatric disorders in oral lichen planus: a preliminary case control study. *J Biol Regul Homeost Agents.* 2018;32(2 Suppl 1):97-100.
7. Pelisse M, Leibowitch M, Sedel D, Hewitt J. A new vulvovagino-gingival syndrome. Plurimucous erosive lichen planus. *Ann Dermatol Venereol.* 1982;109(9):797-8.
8. Lucchese A, Dolci A, Salerno C, Di Stasio D, Minervini G, Laino L, et al. Vulvovaginal gingival lichen planus: report of two cases and review of literature. *Oral Implantol (Rome).* 2016;9(1):54-60.
9. Kennedy CM, Peterson LB, Galask RP. Erosive vulvar lichen planus: a cohort at risk for cancer? *J Reprod Med.* 2008;53(10):781-4.
10. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, González-Moles MÁ, Kerr AR, et al. Oral potentially malignant disorders: a consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. *Oral Dis.* 2021;27(8):1862-80.
11. Giuliani M, Troiano G, Cordaro M, Corsalini M, Gioico G, Lo Muzio L, et al. Rate of malignant transformation of oral lichen planus: a systematic review. *Oral Dis.* 2019;25(3):693-709.
12. Carbone M, Arduino PG, Carrozzo M, Caiazzo G, Broccoletti R, Conrotto D, et al. Topical clobetasol in the treatment of atrophic-erosive oral lichen planus: a randomized controlled trial to compare two preparations with different concentrations. *J Oral Pathol Med.* 2009;38(2):227-33.
13. Lodi G, Scully C, Carrozzo M, Griffiths M, Sugarman PB, Thongprasert K. Current controversies in oral lichen planus: report of an international consensus meeting. Part 2. Clinical management and malignant transformation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2005;100(2):164-78.
14. Lo Muzio L, della Valle A, Mignogna MD, Pannone G, Bucci P, Bucci E, et al. The treatment of oral aphthous ulceration or erosive lichen planus with topical clobetasol propionate in three preparations: a clinical and pilot study on 54 patients. *J Oral Pathol Med.* 2001;30(10):611-7.
15. Carbone M, Goss E, Carozzo M, Castellano S, Conrotto D, Broccoletti R, et al. Systemic and topical corticosteroid treatment of oral lichen planus: a comparative study with long-term follow-up. *J Oral Pathol Med.* 2003;32(6):323-9.
16. Sridharan K, Sivaramakrishnan G. Interventions for oral lichen planus: a systematic review and network meta-analysis of randomized clinical trials. *Aust Dent J.* 2021;66(3):295-303.
17. Cheng S, Kirtschig G, Cooper S, Thornhill M, Leonardi-Bee J, Murphy R. Interventions for erosive lichen planus affecting mucosal sites. *Cochrane Database Syst Rev.* 2012;2012(2):CD008092.
18. Vindiš E. Therapeutic options for the treatment of oral lichen planus [master's thesis]. Zagreb: University of Zagreb, School of Dental Medicine; 2018. Available from: <https://urn.nsk.hr/urn:nbn:hr:127:212213>. Accessed September 29, 2022.
19. Scherholz ML, Schlesinger N, Androulakis IP. Chronopharmacology of glucocorticoids. *Adv Drug Deliv Rev.* 2019;151-152:245-61.
20. Kiran MS, Vidya S, Aswal GS, Kumar V, Rai V. Systemic and topical steroids in the management of oral mucosal lesions. *J Pharm Bioallied Sci.* 2017;9(Suppl 1):S1-S3.
21. Pels R, Sterry W, Ledermann J. Clobetasol propionate--where, when, why? *Drugs Today (Barc).* 2008;44(7):547-57.
22. Thongprasom K, Luangjarmekorn L, Sererat T, Taweasap W. Relative efficacy of fluocinonone acetone compared with triamcinolone acetone in treatment of oral lichen planus. *J Oral Pathol Med.* 1992;21(10):456-8.
23. Gonzalez-Moles MA, Morales P, Rodriguez-Archilla A, Isabel IR, Gonzalez-Moles S. Treatment of severe chronic oral erosive lesions with clobetasol propionate in aqueous solution. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;93(3):264-70.
24. Lozada-Nur F, Huang MZ, Zhou GA. Open preliminary clinical trial of clobetasol propionate ointment in adhesive paste for treatment of

- chronic oral vesiculoerosive diseases. *Oral Surg Oral Med Oral Pathol*. 1991;71(3):283-7.
25. Carbone M, Conrotto D, Carrozzo M, Broccoletti R, Gandolfo S, Scully C. Topical corticosteroids in association with miconazole and chlorhexidine in the long-term management of atrophic-erosive oral lichen planus: a placebo-controlled and comparative study between clobetasol and fluocinonide. *Oral Dis*. 1999;5(1):44-9.
 26. Lozada F, Silverman S Jr. Topically applied fluocinonide in an adhesive base in the treatment of oral vesiculoerosive diseases. *Arch Dermatol*. 1980;116(8):898-901.
 27. Voute AB, Schulten EA, Langendijk PN, Kostense PJ, van der Waal I. Fluocinonide in an adhesive base for treatment of oral lichen planus. A double-blind, placebo-controlled clinical study. *Oral Surg Oral Med Oral Pathol*. 1993;75(2):181-5.
 28. Hegarty AM, Hodgson TA, Lewsey JD, Porter SR. Fluticasone propionate spray and betamethasone sodium phosphate mouthrinse: a randomized crossover study for the treatment of symptomatic oral lichen planus. *J Am Acad Dermatol*. 2002;47(2):271-9.
 29. González-Moles MA, Scully C. Vesiculo-erosive oral mucosal disease--management with topical corticosteroids: (1) Fundamental principles and specific agents available. *J Dent Res*. 2005;84(4):294-301.
 30. González-Moles MA, Scully C. Vesiculo-erosive oral mucosal disease--management with topical corticosteroids: (2) Protocols, monitoring of effects and adverse reactions, and the future. *J Dent Res*. 2005;84(4):302-8.
 31. Decani S, Federighi V, Baruzzi E, Sardella A, Lodi G. Iatrogenic Cushing's syndrome and topical steroid therapy: case series and review of the literature. *J Dermatolog Treat*. 2014;25(6):495-500.
 32. Chainani-Wu N, Silverman S Jr, Lozada-Nur F, Mayer P, Watson JJ. Oral lichen planus: patient profile, disease progression and treatment responses. *J Am Dent Assoc*. 2001;132(7):901-9.
 33. Sharma ST, Nieman LK. Cushing's syndrome: all variants, detection, and treatment. *Endocrinol Metab Clin North Am*. 2011;40(2):379-91.
 34. Frey BM. Mechanism of action of immunosuppressive agents. *Ther Umsch*. 1993;50(2):71-6.
 35. Epstein JB, Truelove EL. Topical cyclosporine in a bioadhesive for treatment of oral lichenoid mucosal reactions: an open label clinical trial. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1996;82(5):532-6.
 36. Porter SR, Scully C, Eveson JW. The efficacy of topical cyclosporin in the management of desquamative gingivitis due to lichen planus. *Br J Dermatol*. 1993;129(6):753-5.
 37. Eisen D, Ellis CN, Duell EA, Griffiths CE, Voorhees JJ. Effect of topical cyclosporine rinse on oral lichen planus. A double blind analysis. *N Engl J Med*. 1990;323(5):290-4.
 38. Radwan-Oczko M. Topical application of drugs used in treatment of oral lichen planus lesions. *Adv Clin Exp Med*. 2013;22(6):893-8.
 39. Al-Hashimi I, Schifter M, Lockhart PB, Wray D, Brennan M, Migliorati CA, et al. Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103 Suppl:S25.e1-S25.e12.
 40. Germain P, Chambon P, Eichele G, Evans RM, Lazar MA, Leid M, et al. International Union of Pharmacology. LXIII. Retinoid X receptors. *Pharmacol Rev*. 2006;58(4):760-72.
 41. Petruzzi M, Lucchese A, Lajolo C, Campus G, Lauritano D, Serpico R. Topical retinoids in oral lichen planus treatment: an overview. *Dermatology*. 2013;226(1):61-7.
 42. Falk DK, Latour DL, King LE Jr. Dapsone in the treatment of erosive lichen planus. *J Am Acad Dermatol*. 1985;12(3):567-70.
 43. Beck HI, Brandrup F. Treatment of erosive lichen planus with dapsone. *Acta Derm Venereol*. 1986;66(4):366-7.
 44. Matthews RW, Pinkney RC, Scully C. The management of intransigent desquamative gingivitis with dapsone. *Ann Dent*. 1989;48(1):41-3.
 45. Eisen D, Lynch DP. Selecting topical and systemic agents for recurrent aphthous stomatitis. *Cutis*. 2001;68(3):201-6.
 46. Saijo T, Kuriki H, Ashida Y, Makino H, Maki Y. Mechanism of the action of amoxanox (AA-673), an orally active antiallergic agent. *Int Arch Allergy Appl Immunol*. 1985;78(1):43-50.
 47. Fu J, Zhu X, Dan H, Zhou Y, Liu C, Wang F, et al. Amlexanox is as effective as dexamethasone in topical treatment of erosive oral lichen planus: a short-term pilot study. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;113(5):638-43.
 48. Gonzalez E, Momtaz T, Freedman S. Bilateral comparison of generalized lichen planus treated with psoralens and ultraviolet A. *J Am Acad Dermatol*. 1984;10(6):958-61.

49. Helander I, Jansen CT, Meurman L. Long-term efficacy of PUVA treatment in lichen planus: comparison of oral and external methoxsalen regimens. *Photodermatology*. 1987;4(5):265-8.
50. Jansen CT, Lehtinen R, Happonen RP, Lehtinen A, Soderlund K. Mouth PUVA: new treatment for recalcitrant oral lichen planus. *Photodermatology*. 1987;4(3):165-6.
51. Chen HR. A newly developed method for treatment of oral lichen planus with ultraviolet irradiation. *Taiwan Yi Xue Hui Za Zhi*. 1989;88(3):248-52.
52. Lundquist G, Forsgren H, Gajecki M, Emtestam L. Photochemotherapy of oral lichen planus. A controlled study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1995;79(5):554-8.
53. Lindelof B, Sigurgeirsson B, Tegner E, Larko O, Johannesson A, Berne B, et al. PUVA and cancer: a large-scale epidemiological study. *Lancet*. 1991;338(8759):91-3.
54. Seoane J, Vazquez J, Romero MA, Aguado A, Pomareda M. Photochemotherapy in the treatment of oral erosive lichen planus. *Letter. Acta Otorrinolaringol Esp*. 1997;48(3):251-3.
55. Ronbeck BA, Lind PO, Thrane PS. Desquamative gingivitis: preliminary observations with tetracycline treatment. *Oral Surg Oral Med Oral Pathol*. 1990;69(6):694-7.
56. Walchner M, Messer G, Salomon N, Plewig G, Rocken M. Topical tetracycline treatment of erosive oral lichen planus. *Arch Dermatol*. 1999;135(1):92-3.
57. Eisen D. Hydroxychloroquine sulfate (Plaquenil) improves oral lichen planus: an open trial. *J Am Acad Dermatol*. 1993;28(4):609-12.
58. De Argila D, Gonzalo A, Pimentel J, Rovira I. Isolated lichen planus of the lip successfully treated with chloroquine phosphate. *Dermatology*. 1997;195(3):284-5.
59. Magro CM, Crowson AN. Lichenoid and granulomatous dermatitis. *Int J Dermatol*. 2000;39(2):126-33.
60. Nagao Y, Sata M, Tanikawa K, Kameyama T. A case of oral lichen planus with chronic hepatitis C successfully treated by glycyrrhizin. *Kansenshogaku Zasshi*. 1995;69(8):940-4.
61. Nagao Y, Sata M, Suzuki H, Tanikawa K, Itoh K, Kameyama T. Effectiveness of glycyrrhizin for oral lichen planus in patients with chronic HCV infection. *J Gastroenterol*. 1996;31(5):691-5.
62. Sato M, Yoshida H, Yanagawa T, Yura Y, Urata M, Nitta T, et al. Therapeutic effect of human fibroblast interferon on premalignant lesions arising in oral mucosa. A pilot study. *Int J Oral Surg*. 1985;14(2):184-94.
63. Areias J, Velho GC, Cerqueira R, Barbedo C, Amaral B, Sanches M, et al. Lichen planus and chronic hepatitis C: exacerbation of the lichen under interferon-alpha-2a therapy. *Eur J Gastroenterol Hepatol*. 1996;8(8):825-8.
64. Sugiyama T, Shimizu M, Ohnishi H, Noguchi N, Iwata K, Kojima Y, et al. Clinical evaluation in oral lichen planus with chronic hepatitis C: the role of interferon treatment. *Nippon Shokakibyo Gakkai Zasshi*. 2000;97(5):568-74.
65. Guijarro GB, Lopez Sanchez AF, Hernandez Vallejo G. Presence of lichen planus during a course of interferon alpha-2a therapy for a viral chronic C hepatitis. *Med Oral*. 2001;6(5):358-63.
66. Doutre MS, Beylot C, Couzigou P, Long P, Royer P, Beylot J. Lichen planus and virus C hepatitis: disappearance of the lichen under interferon alfa therapy. *Dermatology*. 1992;184(3):229.
67. Hildebrand A, Kolde G, Luger TA, Schwarz T. Successful treatment of generalized lichen planus with recombinant interferon alfa-2b. *J Am Acad Dermatol*. 1995;33(5 Pt 1):880-3.
68. Nagao Y, Sata M, Suzuki H, Kameyama T, Ueno T. Histological improvement of oral lichen planus in patients with chronic hepatitis C treated with interferon. *Gastroenterology*. 1999;117(1):283-4.
69. Sun A, Chiang CP, Chiou PS, Wang JT, Liu BY, Wu YC. Immunomodulation by levamisole in patients with recurrent aphthous ulcers or oral lichen planus. *J Oral Pathol Med*. 1994;23(4):172-7.
70. Lu SY, Chen WJ, Eng HL. Dramatic response to levamisole and low-dose prednisolone in 23 patients with oral lichen planus: a 6-year prospective follow-up study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1995;80(6):705-9.
71. Kirby JD, Black MM, McGibbon D. Levamisole-induced lichenoid eruptions. *J R Soc Med*. 1980;73(3):208-11.
72. Sardella A, Demarosi F, Oltolina A, Rimondini L, Carrassi A. Efficacy of topical mesalazine compared with clobetasol propionate in treatment of symptomatic oral lichen planus. *Oral Dis*. 1998;4(4):255-9.
73. Alstead EM, Wilson AG, Farthing MJ. Lichen planus and mesalazine. *J Clin Gastroenterol*. 1991;13(3):335-7.
74. Bogaert H, Sanchez E. Lichen planus: treatment of thirty cases with systemic and topical phenytoin. *Int J Dermatol*. 1990;29(2):157-8.

75. Tone T, Nishioka K, Kameyama K, Asai T, Takezaki S, Nishiyama S. Common histopathological processes of phenytoin drug eruption. *J Dermatol.* 1992;19(1):27-34.
76. Hayes SM. Lichen planus--report of successful treatment with aloe vera. *Gen Dent.* 1999;47(3):268-72.
77. Choonhakarn C, Busaracome P, Sripanidkulchai B, Sarakarn P. The efficacy of aloe vera gel in the treatment of oral lichen planus: a randomized controlled trial. *Br J Dermatol.* 2008;158(3):573-7.
78. Mansourian A, Momen-Heravi F, Saheb-Jamee M, Esfehiani M, Khalilzadeh O, Momen-Beitollahi J. Comparison of aloe vera mouthwash with triamcinolone acetonide 0.1% on oral lichen planus: a randomized double-blinded clinical trial. *Am J Med Sci.* 2011;342(6):447-51.
79. Salazar-Sánchez N, López-Jornet P, Camacho-Alonso F, Sánchez-Siles M. Efficacy of topical Aloe vera in patients with oral lichen planus: a randomized double-blind study. *J Oral Pathol Med.* 2010;39(10):735-40.
80. Heffernan MP, Smith DI, Bentley D, Tabacchi M, Graves JE. A single-center, open-label, prospective pilot study of subcutaneous efalizumab for oral erosive lichen planus. *J Drugs Dermatol.* 2007;6(3):310-4.
81. Tardieu M, Bourin MC, Desgranges P, Barbier P, Barritault D, Caruelle JP. Mesoglycan and sulodexide act as stabilizers and protectors of fibroblast growth factors (FGFs). *Growth Factors.* 1994;11(4):291-300.
82. Rajtar G, Marchi E, de Gaetano G, Cerletti C. Effects of glycosaminoglycans on platelet and leucocyte function: role of N-sulfation. *Biochem Pharmacol.* 1993;46(5):958-60.
83. Kristova V, Kriska M, Babal P, Djibril MN, Slámová J, Kurtansky A. Evaluation of endothelium-protective effects of drugs in experimental models of endothelial damage. *Physiol Res.* 2000;49(1):123-8.
84. Jensen PJ, Rodeck U. Autocrine/paracrine regulation of keratinocyte urokinase plasminogen activator through the TGF-alpha/EGF receptor. *J Cell Physiol.* 1993;155(2):333-9.
85. Femiano F, Gombos F, Scully C. Oral erosive/ulcerative lichen planus: preliminary findings in an open trial of sulodexide compared with cyclosporine (ciclosporin) therapy. *Int J Dermatol.* 2003;42(4):308-11.
86. Maksimovskaia LN, Barashkov GN, Trestsov NG. The methods of modern reflexotherapy in the combined treatment of patients with erosive-ulcerative processes of the oral mucosa. *Stomatologiya (Mosk).* 1991;(4):36-7.
87. Emslie ES, Hardman FG. The surgical treatment of oral lichen planus. *Trans St Johns Hosp Dermatol Soc.* 1970;56(1):43-4.
88. Vedtofte P, Holmstrup P, Hjorting-Hansen E, Pindborg JJ. Surgical treatment of premalignant lesions of the oral mucosa. *Int J Oral Maxillofac Surg.* 1987;16(6):656-64.
89. Malmstrom M, Leikomaa H. Experiences with cryotherapy in the treatment of oral lesions. *Proc Finn Dent Soc.* 1980;76(3):117-23.
90. Loitz GA, O'Leary JP. Erosive lichen planus of the tongue treated by cryosurgery. *J Oral Maxillofac Surg.* 1986;44(7):580-2.
91. Bekke JP, Baart JA. Six years' experience with cryosurgery in the oral cavity. *Int J Oral Surg.* 1979;8(4):251-70.
92. Hovick CJ, Kalkwarf KL. Treatment of localized oral erosive lichen planus lesions with free soft tissue grafts. *Periodontal Case Rep.* 1987;9(1):21-4.
93. Tamizi M, Moayedi M. Treatment of gingival lichen planus with a free gingival graft: a case report. *Quintessence Int.* 1992;23(4):249-51.
94. Nolan A, Badminton J, Maguire J, Seymour RA. The efficacy of topical hyaluronic acid in the management of oral lichen planus. *J Oral Pathol Med.* 2009;38(3):299-303.
95. Hashem AS, Issrani R, Elsayed TEE, Prabhu N. Topical hyaluronic acid in the management of oral lichen planus: a comparative study. *J Investig Clin Dent.* 2019;10(2):e12385.
96. Chainani-Wu N, Silverman S, Reingold A, Bostrom A, McCulloch C, Lozada-Nur F, et al. A randomized, placebo-controlled, double-blind clinical trial of curcuminoids in oral lichen planus. *Phytomedicine.* 2007;14(7-8):437-46.
97. Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of tumeric (*Curcuma longa*). *J Altern Complement Med.* 2003;9(1):161-8.
98. Kia SJ, Shirazian S, Mansourian A, Khodadadi Fard L, Ashnagar S. Comparative efficacy of topical curcumin and triamcinolone for oral lichen planus: a randomized, controlled clinical trial. *J Dent (Tehran).* 2015;12(11):789-96.
99. Thomas AE, Varma B, Kurup S, Jose R, Chandy ML, Kumar SP, et al. Evaluation of efficacy of 1% curcuminoids as local application in management of oral lichen planus--interventional study. *J Clin Diagn Res.* 2017;11(5):ZC89-ZC93.

100. Amirchaghmaghi M, Pakfetrat A, Delavarian Z, Ghalavani H, Ghazi A. Evaluation of the efficacy of curcumin in the treatment of oral lichen planus: a randomized controlled trial. *J Clin Diagn Res.* 2016;10(5):ZC13-ZC15.
101. Aranow C. Vitamin D and the immune system. *J Investig Med.* 2011;59(6):881-6.
102. Gupta J, Aggarwal A, Asadullah Md Khan MH, Agrawal N, Khwaja KJ. Vitamin D in the treatment of oral lichen planus: a pilot clinical study. *J Indian Acad Oral Med Radiol.* 2019;31(3):222-7.
103. Nazeer J, Singh S, Jayam C, Singh R, Iqbal MA, Singh R. Assessment of the role of vitamin D in the treatment of oral lichen planus. *J Contemp Dent Pract.* 2020;21(4):390-5.
104. Savitha P. Role of selenium. *J Pharm Sci Res.* 2014;6(1):56.
105. Qataya PO, Elsayed NM, Elguindy NM, Ahmed Hafiz M, Samy WM. Selenium: a sole treatment for erosive oral lichen planus (randomized controlled clinical trial). *Oral Dis.* 2020;26(4):789-804.
106. Alajbeg I, Ivankovic S, Jurin M, Alajbeg IZ, Grget-Rosin K, Cekic-Arambasin A. Non-aromatic naphthalene as a potential healing medium. *Period Biol.* 2002;104(1):81-7.
107. Alajbeg I, Dinter G, Alajbeg A, Telen S, Proštenik M. Study of Croatian non-aromatic naphthalene constituents with skeletons analogous to bioactive compounds. *J Pharm Biomed Anal.* 2001;25(5-6):918.
108. Andabak Rogulj A, Brkić D, Alajbeg I, Džanić E, Alajbeg I. NAVS naphthalan for the treatment of oral mucosal diseases—a pilot study. *Acta Dermatovenerol Croat.* 2014;22(4):250-8.
109. Rogulj AA, Alajbeg I, Brailo V, Škrinjar I, Žužul I, Vučićević-Boras V, et al. Topical NAVS naphthalan for the treatment of oral lichen planus and recurrent aphthous stomatitis: a double blind, randomized, parallel group study. *PLoS One.* 2021;16(4):e0249862.
110. Di Stasio D, Romano A, Gentile C, Maio C, Lucchese A, Serpico R, et al. Systemic and topical photodynamic therapy (PDT) on oral mucosa lesions: an overview. *J Biol Regul Homeost Agents.* 2018;32(2 Suppl 1):123-6.
111. He Y, Deng J, Zhao Y, Tao H, Dan H, Xu H, et al. Efficacy evaluation of photodynamic therapy for oral lichen planus: a systematic review and meta-analysis. *BMC Oral Health.* 2020;20(1):302.
112. Cafaro A, Arduino PG, Massolin G, Romagnoli E, Broccoletti R. Clinical evaluation of the efficiency of low-level laser therapy for oral lichen planus: a prospective case series. *Lasers Med Sci.* 2014;29(1):185-90.
113. Cronshaw M, Parker S, Anagnostaki E, Mylona V, Lynch E, Grootveld M. Photobiomodulation dose parameters in dentistry: a systematic review and meta-analysis. *Dent J (Basel).* 2020;8(4):114.
114. Del Vecchio A, Palaia G, Grassotti B, Tenore G, Ciolfi C, Podda G, et al. Effects of laser photobiomodulation in the management of oral lichen planus: a literature review. *Clin Ter.* 2021;172(5):464-7.
115. Mamelì A, Murgia MS, Orrù G, Casu C. Extended erosive oral lichen planus treated with a very low-level laser therapy: a case report. *Open Dent J.* 2020;14(1):687-91.
116. Akram Z, Abduljabbar T, Vohra F, Javed F. Efficacy of low-level laser therapy compared to steroid therapy in the treatment of oral lichen planus: a systematic review. *J Oral Pathol Med.* 2018;47(1):11-7.
117. Lavaee F, Shadmanpour M. Comparison of the effect of photodynamic therapy and topical corticosteroid on oral lichen planus lesions. *Oral Dis.* 2019;25(8):1954-63.
118. Tarasenko S, Stepanov M, Morozo E, Unkovskiy A. High-level laser therapy versus scalpel surgery in the treatment of oral lichen planus: a randomized control trial. *Clin Oral Investig.* 2021;25(10):5649-60.
119. Mutafchieva MZ, Draganova-Filipova MN, Zagorchev PI, Tomov GT. Effects of low level laser therapy on erosive-atrophic oral lichen planus. *Folia Med (Plovdiv).* 2018;60(3):417-24.
120. Khater MM, Khattab FM. Efficacy of 1064 Q switched Nd: YAG laser in the treatment of oral lichen planus. *J Dermatolog Treat.* 2020;31(6):655-9.
121. Ruiz Roca JA, López Jornet P, Gómez García FJ, Marcos Aroca P. Effect of photobiomodulation on atrophic-erosive clinical forms of oral lichen planus: a systematic review. *Dent J (Basel).* 2022;10(12):221.
122. Eversole LR. Immunopathogenesis of oral lichen planus and recurrent aphthous stomatitis. *Semin Cutan Med Surg.* 1997;16(4):284-94.
123. Lodi G, Manfredi M, Mercadante V, Murphy R, Carozzo M. Interventions for treating oral lichen planus: corticosteroid therapies. *Cochrane Database Syst Rev.* 2020;2(2):CD001168.