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Photobiomodulation Therapy In The Management Of Oral Lichen Planus-A Non-Invasive Alternative For Pain Relief And Mucosal Healing- A Review

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Abstract:
Oral mucosal lesions, including oral lichen planus (OLP), oral mucositis (OM), recurrent aphthous stomatitis (RAS), and erosive oral lesions, often present with pain, inflammation, and delayed wound healing. Conventional treatments, such as corticosteroids, antiseptics, and analgesics, provide symptomatic relief but may be associated with adverse effects or limited efficacy in chronic cases. Photobiomodulation (PBM), formerly referred to as low-level laser therapy (LLLT), offers a promising adjunctive or alternative therapeutic approach by promoting mucosal healing, reducing pain perception, and modulating inflammatory responses without significant side effects.
PBM has gained significant attention in the management of various oral mucosal lesions due to its non-invasive nature. It utilizes non-ionizing light sources, typically in the red or near-infrared spectrum, to modulate biological processes at the cellular level.
This review aims to comprehensively explore the role of PBM in the management of various oral mucosal conditions by evaluating its underlying mechanisms, clinical applications, optimal laser parameters, and therapeutic outcomes based on current evidence. Furthermore, the review highlights recent clinical trials and systematic reviews assessing PBM's efficacy in different oral pathologies, emphasizing its advantages over conventional pharmacological treatments.

Key Word: *Oral Lichen Planus; Photobiomodulation (PBM) Low-Level Laser Therapy (LLLT),.symptomatic relief*

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I. Introduction

Oral lichen planus (OLP) is a chronic inflammatory disease of the oral mucosa characterized by a T-cell-mediated autoimmune response, leading to basal cell apoptosis, inflammation, and epithelial atrophy. The clinical manifestations include reticular, erosive, and ulcerative lesions, often associated with significant pain, discomfort, and potential malignant transformation.[1]

Conventional treatment of OLP involves the use of corticosteroids, immunosuppressants, and topical anesthetics, which provide symptomatic relief but have side effects, such as mucosal thinning, candidiasis, and systemic immunosuppression. [2,3} Most of the studies involving drug treatments report improvement over short periods. However, many patients experience a relapse once the treatment is suspended, with a negativeimpact on quality of life [4]

Non-pharmacological therapy includes Psolaren Ultra-VioletA (PUVA) , photodynamic and laser therapy (5) Photobiomodulation (PBM), previously known as low-level laser therapy (LLLT), has emerged as a promising non-invasive alternative therapy for managing OLP by reducing inflammation, modulating immune responses, and promoting mucosal healing without significant side effects. [1,5])

The effect of PBM in accelerating the healing process was introduced in the 1960s by Endre Mester and National Aeronautics and Space Administration (NASA) researchers used it for enhancing the healing processes in space [6] It has been extensively studied in recent years for its ability to enhance tissue repair, reduce inflammation, and provide analgesic effects. [7] Physiologic effects of low level lasers on tissues are primary or secondary. Primary effects consist of vasodilatation and enhancement of blood flow, lymph drainage, cellular metabolism, neutrophil and fibroblast activation, and pain stimulation threshold.

Secondary effects include aggregation of prostaglandins (such as prostaglandin E2), immunoglobulins and lymphokines, along with beta-endorphin and encephalin in the tissue, resulting in reduction of inflammation, immune response, and pain, respectively [8]

The mechanism of PBM primarily involves the absorption of photons by mitochondrial chromophores, particularly cytochrome c oxidase, leading to increased adenosine triphosphate (ATP) synthesis, modulation of reactive oxygen species (ROS), and activation of transcription factors that facilitate cellular proliferation and tissue regeneration [9]

II. Mechanism Of Action Of Photobiomodulation (PBM) In Healing Of Oral Mucosal Lesions

Photobiomodulation (PBM) therapy involves the application of non-ionizing light in the red (600–700 nm) and near-infrared (780–1100 nm) spectrum to biological tissues. Unlike thermal lasers, PBM does not induce significant heating or tissue damage. Instead, it stimulates cellular and molecular processes, leading to enhanced tissue repair, reduced inflammation, and pain relief.

1. Absorption of Light by Mitochondrial Chromophores:

The primary site of PBM action is the mitochondria, specifically the enzyme cytochrome c oxidase (CCO), which is a key component of the electron transport chain. CCO absorbs photons, particularly in the red and near-infrared wavelengths, leading to increased enzymatic activity. This results in:

• Enhanced ATP Production: Photon absorption accelerates electron transfer, increasing ATP synthesis, which provides energy for cellular repair and regeneration. [10]

• Reduction in Oxidative Stress: PBM modulates the production of reactive oxygen species (ROS), reducing oxidative stress and preventing cell apoptosis in damaged tissues. This modulation of ROS production has been shown to mimic the activity of molecular agents that attenuate tissue damage, such as amifostine, N-acetyl cysteine, and superoxide dismutase [11]

• Release of Nitric Oxide (NO): PBM displaces inhibitory nitric oxide from CCO, improving mitochondrial respiration and increasing local vasodilation, thereby enhancing tissue oxygenation and nutrient delivery. [12] When focused on wound healing, NO could stimulate vasodilatation and indirectly regulate transcription over many mammalian genes [10]

2. Activation of Cellular Signaling Pathways:

Following the absorption of photons by mitochondrial chromophores, a cascade of secondary signaling pathways is activated, including:

• Activation of Transcription Factors: PBM stimulates nuclear factor kappa B (NF-κB), activator protein-1 (AP-1), and nuclear factor erythroid 2-related factor 2 (Nrf2), leading to the upregulation of genes associated with cell survival, growth, and antioxidant defense. [13]

• Stimulation of Growth Factors: PBM induces the release of essential growth factors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and fibroblast growth factor (FGF), which promote angiogenesis and fibroblast proliferation, accelerating wound healing. [10]

• Anti-Inflammatory Effects: PBM reduces levels of pro-inflammatory cytokines like interleukin-1 beta (IL-1β), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6), while increasing anti-inflammatory cytokines such as interleukin-10 (IL-10). This shift in cytokine balance helps in reducing inflammation in conditions like oral lichen planus and oral mucositis. [13]

3. Modulation of Neural Activity and Pain Perception:

PBM has been shown to have significant analgesic effects, which are mediated through:

• Reduction in Nerve Excitability: PBM modulates sodium, potassium, and calcium ion channels in nerve cells, reducing their excitability and decreasing pain perception [14].

• Endorphin Release: Studies suggest that PBM promotes the release of endogenous opioids such as beta-endorphins, leading to natural pain relief. [14]

• Suppression of Pain Mediators: PBM inhibits the release of bradykinin and substance P, which are key mediators of pain and inflammation in oral mucosal lesions. (15)

4. Enhanced Tissue Repair and Regeneration:

Aside from the direct PBM effects on mitochondrial metabolism, red light (635 nm) irradiation has found to significantly upregulate the gene expression of key proteins related to cellular proliferation, such as AKT1, PIK3CA, and CCND1 following in mesenchymal stem cells. [16] AKT1 encodes AKT Serine/Threonine Kinase 1 which once active may increase cell proliferation and suppresses apoptosis. The

activation from the cell survival mechanism and PI3K/AKT/mTOR metabolic activation may lead to a cascade of events related to protein synthesis, lipids, and nucleic acids. [17].
• Stimulation of Fibroblast Activity: Fibroblasts play a crucial role in wound healing by producing collagen and extracellular matrix components. PBM enhances fibroblast proliferation and collagen synthesis, leading to improved tissue regeneration. Growth factors such as bFGF, HGF and SCF contribute to pre-regulate the cytokines responsible for fbroblast proliferation and migration. [10]

Collagen synthesis: TGF-alpha growth factor induces collagen synthesis from fibroblasts to undergo the transformation into myofbloblasts [10]
• Angiogenesis: Increased VEGF levels stimulate the formation of new capillaries, improving blood supply and oxygenation to the affected tissues, which is crucial in healing mucosal lesions. [10]
• Epithelial Cell Proliferation: PBM enhances keratinocyte migration and differentiation, accelerating epithelialization and wound closure in conditions such as recurrent aphthous stomatitis and traumatic ulcers.

III. Role Of Photobiomodulation (PBM) In The Treatment Of Oral Lichen Planus (OLP)

•Reduction of Inflammatory Response:

PBM modulates the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), which are implicated in OLP pathogenesis. It enhances the expression of anti-inflammatory cytokines (IL-10 and transforming growth factor-beta [TGF-β]), reducing chronic inflammation in affected mucosa.[13]

•Immunomodulation:

OLP is driven by an aberrant T-cell-mediated response against basal keratinocytes. PBM reduces T-helper 1 (Th1) and Th17 cell activity, thereby limiting immune-mediated damage.

PBM promotes the activation of regulatory T-cells (Tregs), which suppress excessive immune responses and help restore mucosal homeostasis. [16]

•Stimulation of Fibroblast and Keratinocyte Proliferation:

PBM enhances fibroblast activity and collagen synthesis, leading to improved extracellular matrix remodeling and mucosal repair. It promotes the migration and proliferation of keratinocytes, accelerating epithelialization and restoring the mucosal barrier function. [10]

• Enhanced Angiogenesis and Wound Healing:

By increasing vascular endothelial growth factor (VEGF) expression, PBM stimulates the formation of new blood vessels, improving tissue oxygenation and nutrient supply. [10]
This process enhances tissue repair and reduces ulceration in erosive-atrophic OLP.

• Pain Reduction and Nerve Modulation:

PBM inhibits pain mediators such as substance P and bradykinin, reducing burning sensations associated with erosive OLP. It modulates peripheral nerve activity, leading to decreased nociceptive signaling and improved patient comfort. [14]

IV. Clinical Evidence Supporting Role Of PBM In OLP:

Several clinical studies have evaluated the efficacy of PBM in managing OLP, demonstrating positive outcomes:

• LLLT as a stand-alone treatment for OLP:

Mahdavii et al and Derikvand et al. report cases of OLP not responding to conventional therapy given LLLT. Both found improvement in symptoms and no recurrence on followup. [18]

Kollner K et al.[19], Cafaro A et al, [20] Jajarm H et al[21] and Saleh et al [22] all found reduction in OLP lesional size and burning sensation. Cafaro A et al., [20] and Al-Maweri et al. [23] significantly reduced pain scores in OLP patients. Dillenburg CS et al.,[24] Pedro LA et al.,[25] Rezaei F et al [26] found reduction in recurrence Many patients experience prolonged symptom-free periods following PBM treatment.

• Use of LLLT in combination therapy:

Panchal et al. compared the efficacy of LLLT therapy with concurrent topical steroid application, with therapy based on topical steroid application alone and found better outcome with combination therapy than steroid alone.[27]

• Comparison of the efficacy of LLLT with the traditional OLP treatment regimen:

Reem Kamal Mohamed et al [28] and Dillenburg CS et al[24] found improvement in symptoms in both groups . However found better results and persistence of positive treatment effects in patients treated with the laser (Table 1)

Table no 1: Advantages of PBM Over Conventional OLP Treatments

Feature	Photobiomodulation (PBM)	Corticosteroids and Immunosuppressants
Pain Relief	Effective	Effective
Inflammation Reduction	Yes	Yes
Mucosal Healing	Accelerated	Delayed
Side effects	Minimal	Mucosal Thinning Candidiasis Systemic immune suppression
Patient Compliance	High	Low to Moderate

V. Parameters For PBM Therapy In OLP

There has been a varied opinion on the ideal parameters. wavelength 630 to 970 nm, power output from 10 mW to 3 W, laser energy from 0.3 up to 6 J/cm2, power density between 10 and 1000 mW/cm. The most used type of laser was the diode laser. Reported exposure time was comprised between 5s and 8 min, and also the number of sessions varied a lot from 4 to 12 sessions [5]

VI. Limitations And Future Directions

Despite the promising results, PBM therapy for OLP has some limitations. Lack of standardization: There is variability in laser parameters across studies, making it challenging to establish optimal treatment protocols. Cost and Accessibility: PBM devices may not be widely available in all dental clinics, limiting patient access to therapy. Need for larger clinical trials: Further randomized controlled trials with larger sample sizes are needed to confirm PBM's long-term effectiveness in managing OLP**.**

Future research should focus on:
• Comparative studies between PBM and pharmacological treatments.
• Combination therapies (PBM + corticosteroids) to enhance treatment outcomes.
•Investigating PBM's potential in preventing malignant transformation of OLP**.**

VII. Conclusion

PBM is a promising non-invasive, drug-free alternative for managing oral lichen planus. By reducing inflammation, modulating immune responses, enhancing mucosal healing, and providing effective pain relief, PBM offers distinct advantages over conventional pharmacological treatments. Although further research is needed to standardize treatment protocols, PBM has the potential to become a mainstream therapy in the management of OLP, improving patient outcomes and quality of life. The mechanism of PBM is multifaceted, involving mitochondrial activation, modulation of inflammatory pathways, and enhanced tissue repair. Its ability to reduce pain, promote wound healing, and restore oral mucosal integrity makes it a promising therapeutic tool in managing various oral mucosal lesions. However, further clinical studies are needed to optimize treatment parameters, including wavelength, energy density, and treatment duration, to maximize its therapeutic benefits.

References

[1]. Mahdavi O.A, Boostani N.B, Jajarm HH.C, Falaki F.C, Tabesh A Use Of Low Level Laser Therapy For Oral Lichen Planus: Report Of Two Cases. J Dent Shiraz Univ Med Sci., Dec. 2013; 14(4): 201-204
[2]. García-Pola, M.J.; González-Álvarez, L.; Garcia-Martin, J.M. Treatment Of Oral Lichen Planus. Systematic Review And Therapeutic Guide. Med. Clin. (Barc.) 2017, 149, 351–362.
[3]. Lodi, G.; Manfredi, M.; Mercadante, V.; Murphy, R.; Carrozzo, M. Interventions For Treating Oral Lichen Planus: Corticosteroid Therapies. Cochrane Database Syst Rev. 2020, 2, CD001168
[4]. Salinas-Gilabert, C, Gómez, García, F, Galera Molero, F, Pons-Fuster, E.; Vander Beken, S, Lopez Jornet, P. Photodynamic Therapy, Photobiomodulation And Acetonide Triamcinolone 0.1% In The Treatment Of Oral Lichen Planus: A Randomized Clinical Trial. Pharmaceutics 2023, 15, 30. Https://Doi.Org/10.3390/ Pharmaceutics 15010030
[5]. Mameli A, Murgia MS, Orrù G, Casu. Extended Erosive Oral Lichen Planus Treated With A Very Low-Level Laser Therapy: A Case Report. The Open Dentistry Journal. DOI: 10.2174/1874210602014010687, 2020, 14, 687-691
[6]. Whelan, H.T. The NASA Light-Emitting Diode Medical Program—Progress In Space Flight And Terrestrial Applications. In Proceedings Of The AIP Conference Proceedings; AIP Publishing: College Park, MD, USA,2003; Volume 504, Pp. 37–43.
[7]. El Shenawy HM, Eldin AM. A Comparative Evaluation Of Low-Level Laser And Topical Steroid Therapies For The Treatment Of Erosive-Atrophic Lichen Planus. OA Maced J Med Sci. 2015 Sep 15; 3(3):462-466. Http://Dx.Doi.Org/10.3889/Oamjms.2015.072
[8]. Shirani AM, Gutknecht N, Taghizadeh M, Mir M. Lowlevel Laser Therapy And Myofacial Pain Dysfunction Syndrome: A Randomized Controlled Clinical Trial. Lasers Med Sci 2009; 24: 715-720.

[9]. Dompe C, Moncrie L, Matys J, Grzech-Le´Sniak K, Kocherova I, Bryja A Et Al. Photobiomodulation—Underlying Mechanism And Clinical Applications. J. Clin. Med. 2020, 9, 1724; Doi:10.3390/Jcm9061724

[10]. Courtois Et Al. Mechanisms Of Photobiomodulation (PBM) Focused On Oral Mucositis Prevention And Treatment: A Scoping Reviewbmc Oral Health (2021) 21:220.

[11]. Nammour, S.; El Mobadder, M.; Brugnera, A.J.; Namour, M.; Houeis, S.; Heysselaer, D.;Et Al. Photobiomodulation Therapy Vs. Corticosteroid For The Management Of Erosive/Ulcerative And Painful Oral Lichen Planus. Assessment Of Success Rate During One-Year Follow-Up: A Retrospective Study. Healthcare 2021, 9, 1137. Https://Doi.Org/10.3390/ Healthcare9091137

[12]. 12 Huang Y-Y, Sharma SK, Carroll J, Hamblin MR. Biphasic Dose Response In Low Level Light Therapy—An Update. Dose Response. 2011;9:602–18.

[13]. Silva GBL, Sacono NT, Othon-Leite AF, Mendonca EF, Arantes AM, Bariani C, Et Al. Effect Of Low-Level Laser Therapy On Inflammatory Mediator Release During Chemotherapy-Induced Oral Mucositis: A Randomized Preliminary Study. Lasers Med Sci. 2015;30:117–26.

[14]. Sil S,Ghosh S. Low Level Laser As A Therapeutic Alternative In Treatment Of Oral Lichen Planus- Review Of Literature. Journal Of Clinical And Diagnostic Research. 2019 Jul, Vol-13(7): ZE06-ZE09.

[15]. Kalakonda B, Farista S, Koppolu P, Baroudi K, Uppada U, Mishra A, Savarimath A, Lingam AS (2016) Evaluation Of Patient Perceptions After Vestibuloplasty Procedure: A Comparison Of Diode Laser And Scalpel Techniques. J Clin Diagn Res 10(5):Zc96–Zc100. Doi: 10.7860/Jcdr/2016/17623.7820

[16]. Al-Mawer SA, Kalakonda B, Al-Soneidar WA, Al-Shamiri HM, Alakhali MS, Alaizari N. Efficacy Of Low-Level Laser Therapy In Management Of Symptomatic Oral Lichen Planus: A Systematic Review. Lasers Med Sci. DOI 10.1007/S10103-017-2233-7

[17]. M.C.P. Felician Et Al. Photobiomodulation: Cellular, Molecular, And Clinical Aspects. Journal Of Photochemistry And Photobiology 17 (2023) 100197

[18]. Derikvand N, Ghasemi SS, Moharami M, Shafi Ei E, Chiniforush N. Management Of Oral Lichen Planus By 980 Nm Diode Laser. J Lasers Med Sci. 2017;8:150-4.

[19]. Köllner K, Wimmershoff M, Landthaler M, Hohenleutner U. Treatment Of Oral Lichen Planus With The 308-Nm UVB Excimer Laser--Early Preliminary Results In Eight Patients. Lasers In Surg And Med. 2003;33:158-60.

[20]. Cafaro A, Albanese G, Arduino G, Mario C, Massolini G, Mozzati M, Et Al. Effect Of Low-Level Laser Irradiation On Unresponsive Oral Lichen Planus: Early Preliminary Results In 13 Patients. Photomedicine And Laser Surgery. 2010;28(2):99-103.

[21]. Jajarm H, Falaki F, Mahdavi O. A Comparative Pilot Study Of Low Intensity Laser Versus Topical Corticosteroids In The Treatment Of Erosive-Atrophic Oral Lichen Planus. Photomedicine And Laser Surgery. 2011;29(6):421-25.

[22]. Saleh HA, Tayel MY, El-Baz RA. Evaluation Of Low-Level Laser Therapy As An Alternative Treatment For Oral Lichen Planus: A Randomized Controlled Trial. BMC Oral Health. 2020;20(1):266. Doi:10.1186/S12903-020-01240-X.

[23]. Al-Maweri SA, Kalakonda B, Al-Soneidar WA, Al-Shamiri HM, Alahmary AW, Halboub ES. Efficacy Of Photobiomodulation In The Treatment Of Symptomatic Oral Lichen Planus: A Systematic Review. Lasers Med Sci. 2017;32(6):1429-1437. Doi:10.1007/S10103-017-2269-1

[24]. Dillenberg CS, Martins MA, Munerato MC, Marques M, Carrad VC, Filho MA, Et Al. Efficacy Of Laser Phototherapy In Comparison To Topical Clobetasol For The Treatment Of Oral Lichen Planus: A Randomized Controlled Trial. Journal Of Biomedical Optics. 2014;19(6):68-102.

[25]. Pedro LA, Fernandes D, Ferrisse T, Almeida Ld, León Je, Bufalino A. Use Of Low-Level Laser Therapy As A Treatment Proposal For Oral Lichen Planus In Children. J Oral Maxillofac Surg, Med, Pathol. 2018;126(3):53-55.

[26]. Rezaei F, Dehghani N. Efficiency Of CO2 Laser Therapy On Resistant Oral Lichen Planus. Journal Of Lasers In Medical Sciences. 2018;9:23-28

[27]. Panchal KG, Gupta E, Kumar A, Samir PV, Devika GS, Awasthi V, Et Al. Comparing The Effectiveness Of Low-Level Laser Therapy And Topical Steroid Therapy Combination Regimen With Routine Topical Steroid Therapy In The Management Of Oral Lichen Planus Symptomatic Patients. Cureus. 2023;15:E44100.

[28]. Mohamed RK, Elsayed NM, Mahmoud SA, Gaweesh YY. Photobiomodulation Versus Corticosteroid In The Management Of Erosive Oral Lichen Planus: A Randomized Controlled Clinical Trial. BMC Oral Health. 2024;24:246.