Research, Society and Development, v. 12, n. 3, e9512338070, 2023
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v12i3.38070

Photobiomodulation in the treatment of oral diseases

Fotobiomodulação no tratamento de doenças bucais

Fotobiomodulación en el tratamiento de enfermedades bucodentales

Received: 11/16/2022 | Revised: 12/23/2022 | Accepted: 02/21/2023 | Published: 02/26/2023

Cássia Alves de Lima Luna
ORCID: https://orcid.org/0000-0002-5517-0563
University Center of the State of Pará, Brazil
E-mail: cassiaalves1222@gmail.com
Douglas Magno Guimarães
ORCID: https://orcid.org/0000-0001-7856-1324
University Center of the State of Pará, Brazil
E-mail: douglasmagnoguimaraes@gmail.com
Emily Silva e Silva
ORCID: https://orcid.org/0000-0002-1467-057X
University Center of the State of Pará, Brazil
E-mail: emilly20080031@aluno.cesupa.br
Marina Fadul Neves do Couto
ORCID: https://orcid.org/0000-0002-3076-2159
University Center of the State of Pará, Brazil
E-mail: marina21080005@aluno.cesupa.br
Gerlane Lima Oliveira
ORCID: https://orcid.org/0000-0003-2519-6882
University Center of the State of Pará, Brazil
E-mail:gerlane20080501@aluno.cesupa.br
Mauro Sérgio Almeida Alves
ORCID: https://orcid.org/0000-0003-3306-1072
University Center of the State of Pará, Brazil
E-mail: mauro18080033@aluno.cesupa.br
Marco Tullio Brazão-Silva
ORCID: https://orcid.org/0000-0003-1957-949X
Federal University of Montes Claros, Brazil
E-mail: marcotullio@gmail.com
Caio de Andrade Hage
ORCID: https://orcid.org/0000-0002-0337-1371
University Center of the State of Pará, Brazil
E-mail: caio_hage@hotmail.com

Abstract
The modern conception of dentistry is based on the search for noninvasive clinical applicability methods that improve the prognoses of dental pathologies and, therefore, the interest in light-tissue interaction technology has increased in the last decade. The present study aims to explore the applicability of photobiomodulation (PBM) in dentistry with emphasis on wavelengths provided to target tissues and the underlying mechanisms of action of lasers observed in the treatment of various oral diseases, as well as the affected processes that include, but are not limited to wound healing, tissue biostimulation, tissue and nerve regeneration, inhibition of pain and inflammatory processes. The effects obtained through photobiomodulation are correlated with the parameters involved, such as the equipment used, wavelength, power dosages, irradiation duration, energy density, general patient conditions, target tissue, pathology and etiologies considered. Depending on the conditions reported, the photobiomodulator effect or also known as low intensity laser therapy (LLLT) influences the increase of cellular metabolism through the application of photonic energy that presents monochromaticity and propagates consistently in time and space. Thus, the protocols for the application of the photonic properties of this therapeutic modality should be analyzed in the treatment of oral conditions and pathologies associated with glandular, neural, autoimmune, traumatic, and idiopathic diseases.
Keywords: Laser; Low intensity laser therapy; Photobiomodulation; Oral pathology.

Resumo
A concepção moderna da odontologia é baseada na busca de métodos não invasivos de aplicabilidade clínica que melhorem os prognósticos das patologias dentárias e, por isso, o interesse pela tecnologia de interação luz-tecido aumentou na última década. O presente estudo visa explorar a aplicabilidade da fotobiomodulação (PBM) em odontologia com ênfase nos comprimentos de onda fornecidos aos tecidos-alvo e nos mecanismos subjacentes de ação dos lasers observados no tratamento de várias doenças bucais, bem como nos processos afetados que incluem, mas

não se limitam à cicatrização de feridas, bioestimulação tecidual, regeneração tecidual e nervosa, inibição da dor e processos inflamatórios. Os efeitos obtidos pela fotobiomodulação são correlacionados com os parâmetros envolvidos, como equipamento utilizado, comprimento de onda, dosagens de potência, duração da irradiação, densidade de energia, condições gerais do paciente, tecido-alvo, patologia e etiologias consideradas. Dependendo das condições relatadas, o efeito fotobiomodulador ou também conhecido como laserterapia de baixa intensidade (LLLT) influencia no aumento do metabolismo celular através da aplicação de energia fotônica que apresenta monocromaticidade e se propaga de forma consistente no tempo e no espaço. Assim, os protocolos de aplicação das propriedades fotônicas desta modalidade terapêutica devem ser analisados no tratamento de condições e patologias bucais associadas a doenças glandulares, neurais, autoimunes, traumáticas e idiopáticas.
Palavras-chave: Laser; Laserterapia de baixa intensidade; Fotobiomodulação; Patologia bucal.

Resumen

La concepción moderna de la odontología se basa en la búsqueda de métodos no invasivos de aplicabilidad clínica que mejoren los pronósticos de las patologías dentales y, por ello, el interés por la tecnología de interacción luz-tejido se ha incrementado en la última década. El presente estudio tiene como objetivo explorar la aplicabilidad de la fotobiomodulación (PBM) en odontología con énfasis en las longitudes de onda proporcionadas a los tejidos objetivo y los mecanismos subyacentes de acción de los láseres observados en el tratamiento de diversas enfermedades orales, así como los procesos afectados que incluyen, pero no se limitan a la cicatrización de heridas, bioestimulación tisular, regeneración tisular y nerviosa, inhibición del dolor y procesos inflamatorios. Los efectos obtenidos a través de la fotobiomodulación se correlacionan con los parámetros involucrados, como el equipo utilizado, la longitud de onda, las dosis de potencia, la duración de la irradiación, la densidad de energía, las condiciones generales del paciente, el tejido objetivo, la patología y las etiologías consideradas. Dependiendo de las condiciones reportadas, el efecto fotobiomodulador o también conocido como terapia láser de baja intensidad (LLLT) influye en el aumento del metabolismo celular a través de la aplicación de energía fotónica que presenta monocromaticidad y se propaga consistentemente en el tiempo y el espacio. Así, los protocolos de aplicación de las propiedades fotónicas de esta modalidad terapéutica deben ser analizados en el tratamiento de afecciones y patologías orales asociadas a enfermedades glandulares, neurales, autoinmunes, traumáticas e idiopáticas.
Palabras clave: Láser; Terapia láser de baja intensidad; Fotobiomodulación; Patología bucal.

1. Introduction

In dentistry, the most common lasers used in phototherapy and included in photobiomodulation (PBM) are the low-level lasers, thus this therapy was prevous called low intensity laser therapy (LLLT). The procedure can be widely used in dentistry to accelerate cellular processes of post-extraction healing, decrease muscle trismus, edemas, dental analgesia, dental hypersensitivity and osseointegration of implants. This is because of PBM increases cell viability through stimulation of mitochondrial photoreceptors and the cell membrane resulting in increased ATP (Adenosine Triphosphate) synthesis, with better cellular biochemistry and photochemical processes. Low-level laser irradiation is noninvasive, non-carcinogenic, and atraumatic, with no known side effects to date, and, for this reason, has become an adjunct technology to conventional therapies and a therapeutic tool in dentistry (Dompe et al., 2020, Vernon & Hasbun, 2008, Hamblin, et al., 2016).

One of the main characteristics of PBM is its regular, sometimes paradoxical potential (stimulating or inhibiting the same biological effects in different situations) leading the body to homeostasis 3. (Hamblin, et al., 2016). The clinical effects of PBM such as inflammation modulation, decreased neural pain response, increased circulation and lymphatic flow, cell stimulation indicate that it is possible to contain, with biostimulant or bioinhibitors, the advancement of oral pathologies of glandular, neural, autoimmune, traumatic, and idiopathic origins (Dompe et al., 2020, Hamblin, et al., 2016, Ebrahimi et al., 2018, Tanganelli, et al., 2020).

Although many studies have proven the effectiveness of PBM in several fields and is considered a promising low-cost non-pharmacological technique, there are studies that report little or no relevance in association with the treatment of oral pathologies. This is because it is still necessary to understand the ability to manipulate cellular responses allowing the safe and standardized applications of laser therapy in the treatment of these diseases (Dompe et al., 2020, Hamblin, et al., 2016).

Therefore, the present study aims to explore the applicability and efficacy of PBM in the context of dentistry and its possible mechanisms of functioning in target tissues involving local and systemic variables, as well as underlying mechanisms observed in the treatment of various oral diseases, processes that include, but are not limited to tissue repair, biostimulation, inhibition of pain and inflammatory processes.

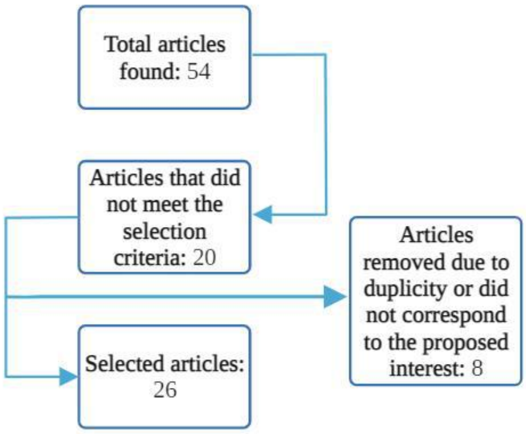
2. Methodology

A integrative literature review was carried out with the aim of compiling the existing scientific knowledge on the subject under study, as well as identifying and describing the results of articles published between 2011 and 2022.

The same inclusion criteria proposed by Dompe et al. (2020) were applied in this study. The publications selected for results analysis were articles, literature reviews, and dissertations published in Portuguese and English. Additionally, only complete publications available in databases such as Google Scholar, Scielo, and PubMed were included. To select the publications, terms related to topics of interest were used, such as the treatment of oral conditions and pathologies associated with glandular, neural, autoimmune, traumatic, and idiopathic diseases.

Articles that did not fit the inclusion criteria were removed, such as articles published in different databases, those that did not address the relevant theme for the literature review, and those that were outside the specified time period. Only the most relevant titles were selected, which were then fully evaluated for inclusion in the review.

Figure 1 - Article selection flowchart.



Source: Authors.

3. Results and Discussion

After performing the searches according to Figure 1, 54 articles were found, however, after applying the criteria, only 34 articles were selected. Out of the 34 selected, 8 were excluded for being duplicates or not corresponding to the proposed theme of interest. Finally, 26 articles were carefully selected that corresponded to the themes, as illustrated in Tables 1, 2, 3, 4, 5, 6, and 7, which contain detailed information on the selected articles, including authors, year of publication, associated pathology, location, as well as wavelength parameters, power, energy, time, and authors' conclusions.

3.1 LLLT Mechanism of Action

For the process of obtaining clinical effects through light, it must be absorbed by the target tissues. The use of red and infrared lights with wavelengths of 630 – 940 nm (nanometers) is known as LLLT. The wavelength determines the absorption capacity of light, and wavelengths of 600 - 1100 nm have greater penetration power due to lower dispersion, while wavelengths ranging between 300 and 400 nm have lower penetration power and greater dispersion (Dompe et al., 2020, Hamblin, et al., 2016, Milward et al., 2014).

Irradiation in the red and infrared spectra results in different stimuli. While mitochondrial biostimulation occurs in the visible electromagnetic spectrum (red spectrum), stimulations of plasma membrane channels occur in the infrared spectrum. In both cases, after photoreaction, a cascade of biochemical effect occurs (Dompe et al., 2020, Hamblin, et al., 2016, Ebrahimi et al., 2018, Ferrandez-Pujante, et al., 2022).

Since the primary effect of LLLT depends on the absorption of chromophore-mediated light, photobioestimulator effect, which improve cellular metabolism, depend on photorereception. The main chromophore that acts on the absorption of light (both visible and infrared) is cytochrome C oxidase or porphyrins, which are components of the cellular respiratory chain. This process results in a cascade of responses such as increased ATP production, oxygen consumption, protein synthesis, oxidative respiration (Figure 2) (Dompe et al., 2020, Vernon & Hasbun, 2008, Hamblin, et al., 2016, Ferrandez-Pujante, et al., 2022, Tanganelli, et al., 2020).

Figure 2 - LLLT Mechanism of Action.

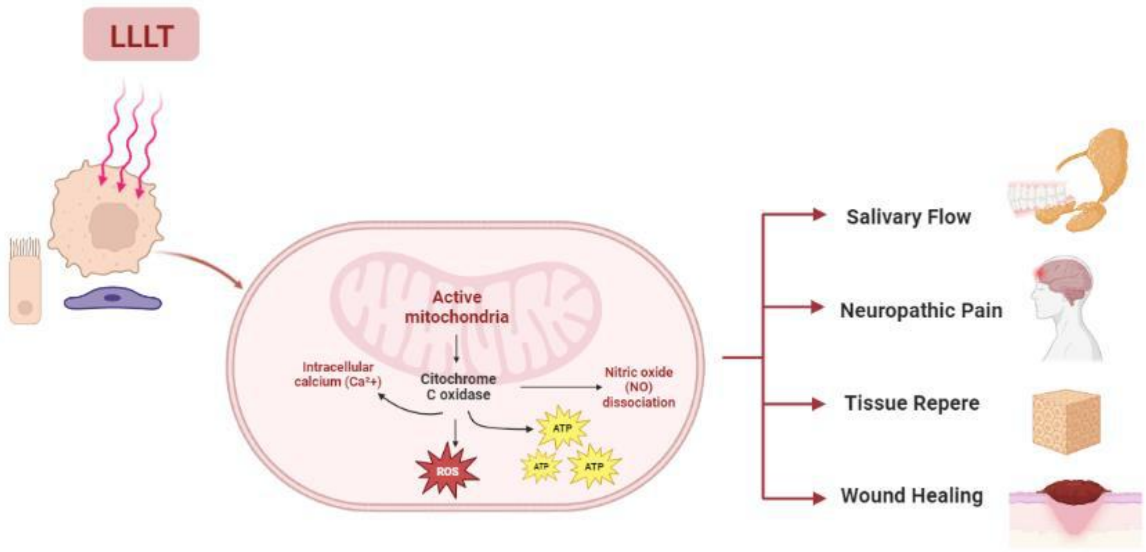


Figure 2 – As light penetrates the tissues, mitochondrial activation occurs. The red and infrared light photons are absorbed by cytochrome C oxidase leading to nitric oxide (NO) dissociation and this leads to a cascade of events. There is an increase in adenosine triphosphate (ATP), reactive oxygen species (ROS) and increased intracellular calcium (Ca^{2+}). With this, it is possible to verify the increase in observable effects, such as decreased pain of neuropathic origin, increased healing, and tissue repair, decreased burning sensation, increased salivary flow, among others. Source: Authors.

Dosimetry is one of the main devices for successful treatment with laser use, therefore, irradiation parameters are used to describe LLLT as energy (J), dose, fluency, or energy density (J/cm²), wavelength (nm), power (W) or power density (W/cm²), exposure time (Dompe et al., 2020).

The effects caused by tissue-light interaction in biological tissues are angiogenesis stimulation, collagen production, muscle regeneration, decreased inflammation and edema, nerve regeneration, cartilage production, bone formation (Dompe et al., 2020, Milward et al., 2014).

Growth, cytoprotection, migration and differentiation occur in different ways for each cell type. Many studies reveal these effects on immune, blood cells derived from soft and hard tissues. In association, this information promotes the advancement of applications in the treatment of diseases in various clinical situations (Dompe et al., 2020, Hamblin, et al., 2016, Milward et al., 2014).

3.2 LLLT in the treatment of oral diseases

3.2.1 Glands diseases

Recent studies tried to clarify the effectiveness of the use of PBM to increase salivary production by reducing the symptoms caused by xerostomia, known as a dry mouth sensation. These studies demonstrated that xerostomia must be associated with the use of medications for various treatments or also associated with the deleterious effect of diseases (Lončar et al., 2011, Terlević Dabić et al., 2016).

In a recent study, Ferrandez-Pujante et. al. (2022) evaluated the efficacy of PBM in patients with xerostomia and hyposalivation. This study found that laser irradiation treatment with wavelength of 810 nm, 1W power and 6J/cm² energy in the parotid gland and submandibular gland, in 6 sessions (one session per week) was effective in patients with xerostomia, in view of increased salivary production, reduction of dry mouth symptoms and improvement in the patient's quality of life (Ferrandez-Pujante, et al., 2022).

Another study, by Oliveira et. al. (2020) analyzes the effects of PBM in a case of a patient who presents xerostomia due to systemic scleroderma (a disease characterized by excessive collagen production). The aspects presented by the patient were dry skin, trismus, xerostomia, malocclusion, and difficulty swallowing. In this specific case, the irradiated spots were the sublingual, parotid glands, and submandibular glands. It was possible to verify salivary increase and total remission of xerostomia, in addition to the improvement in chewing and swallowing (Oliveira et al., 2020).

Lončar B. et. al. (2011) concludes in evaluations of patients who present xerostomia that the effect of PBM not only stimulates salivary production in the glands, but also showed regenerating effect since there was a gradual and linear increase in the amount of salivation. Another argued mechanism is the PBM effect on the salivary glands favoring the nerve stimuli increasing the salivary flow (Louzeiro et al., 2020).

Table 1 – Summary of the studies included in the literature review that evaluated LLLT in the treatment of Xerostomia.

Study	Disease	Region (area)	Wavelength	Power	Energy	Time and reputation	Conclusion
Ferrandez -Pujante, A. et. al. (2022)	Xerostomia	Parotid gland	810 nm	1W	6 J/cm²	144s (total) - 6 sessions/1 month and a half/1 session per week	Positive
		Submandibular gland	810 nm	1W	6 J/cm²	72s (total) - 6 sessions/1 month and a half/1 session per week	
Louzeiro, G. C. et al. (2020)	Xerostomia	Parotid gland (6 points), submandibular gland extraorally (3 points) and intraorally (2 points).	810 nm	40 mW	25 J/cm²	17.5s	Negative
		Commissure (1 point), Labial mucosa (8 points), oral mucosa (12 points), palate (12 points), soft palate (4 points), edge of tongue (6 points), ventral surface of the tongue (6 points), oral floor (4 points).	660 nm	40 mW	10 J/cm²	7s	
Oliveira A. B., et al. (2020)	Xerostomia	Intraoral sublingual glands (4 points).	660 nm	100mW	0.8 J/cm²	8s per point/ 6 sessions with 72h interval between sessions.	Positive
		Parotid glands (8 points) and submandibular glands (6 points).	808 nm	100mW	0.8 J/cm²		
Terlević Dabić, D. Et Al. (2016)	Xerostomia	Parotid glands, Submandibular glands, and Intraoral Sublingual Gland.	830 nm	35mW	1.6 J/cm²	Every day/ 14 days/ 10 sessions 120s per session	Negative
Saleh, Jamil et al. (2014)	Xerostomia	Parotid gland (3 points), Submandibular gland (2 points) and Sublingual gland (2 points).	830 nm	100mW	71 J/cm²	14 points per session/ 6 weeks/ 12 sessions/20s per point	Negative
Lončar, B., et al. (2011)	Xerostomia	Extraoral parotid gland and intraoral sublingual gland.	904 nm	6mW	29.5 J/cm²	120s per daily travel/ 10 consecutive days	Positive

Source: Authors.

Unfortunately, as shown in Table 1, there are constant variations in the protocols in the literature, which may result in controversial conclusions about the effectiveness of PBM. Inadequate wavelength, underdosages, or exposure time may interfere with expected responses. However, it is not yet possible to establish an adequate dosage because we also found variations in studies that have proven the efficacy of laser therapy (Lončar et al., 2011, Terlević Dabić et al., 2016, Saleh et al., 2014).

3.2.2 Neural Diseases

3.2.2.1 Trigeminal neuralgia

The trigeminal nerve is the main nerve of orofacial motor and sensory innervation, with its branches V2 (maxillary branch) and V3 (mandibular branch) as the main targets of studies in the dental field. Trigeminal neuralgia is associated with small changes in the axons and myelin sheath of neurons in situations of trigeminal nerve compression and blood pressure on the superior cerebral artery (Ebrahimi et al., 2018, Ribeiro et al., 2021).

PBM as an alternative or adjuvant treatment for trigeminal neuralgia is shown to be viable because the use of laser to reduce the release of substances that stimulate nocipceptors has positive results, as shown in isolated applications or in association with drugs (Hamblin, et al., 2016, Ribeiro et al., 2021). The effects of low-intensity laser on pain reduction and analgesic effects occur due to a number of mechanisms, of which reduction of histamine, prostaglandins, bradykinin and the neurotransmitter acetylcholine can be highlighted (Ebrahimi et al., 2018, Ribeiro et al., 2021).

There are several cases reported in the literature that offer a treatment guide for trigeminal neuralgia. Studies reveal that infrared wavelengths (808 nm and 810 nm) used in scan or pain trigger points show decreased pain and improved patient quality of life.

A recent study by Tanganeli, J. P. C et al. (2020) demonstrates that infrared laser photobiomodulation presents excellent results when associated with drugs suitable for pain control. The use of PBM corroborated with reduction of doses of treatment drugs improving the patient's quality of life. This therapeutic benefice of PMB reinforces this approach as viable, noninvasive and without adverse effects, since the increase in the dose of the drugs to control pain could sometimes be associated with higher side effects, drastically decreasing the quality of life.

In another publication, PBM inclusion on the treatment regimen for a patient whose pain due to trigeminal neuralgia did not respond to pharmacological treatment leaded to a drastic reduction of pain. The protocol used was also with a wavelength of 808 nm, power of 200mW and enegia of 6J/cm² once a day for 5 consecutive days (following 2-day intervals). The protocol used was also with a wavelength of 808 nm. And with this it was observed that the modality of pain treatment was highly effective (Vernon & Hasbun, 2008).

In a controlled clinical trial, 15 patients diagnosed with trigeminal neuralgia or who had already undergone other pharmacological treatments, but without effects, were treated with PBM with wavelength of 810 nm and compared to a control group of 15 patients. The results showed that both groups improved, reinforcing the idea that PBM associated with the treatment drugs represents the better choice (Ebrahimi et al., 2018).

Figure 3 - Representative scheme of the irradiation points of LLLT in case of Trigeminal neuralgia.

Source: Authors.

Studding 32 patients with trigeminal neuralgia submitted to PBM, some authors showed improvement of both trigeminal neuralgia and pain in the temporomandibular joint, muscle pain, attributing the success of trigeminal neuralgia treatment to the recovery of neural function and neuronal activities (Pinheiro et al., 1997).

This topic of PBM has shown the literature current position of research favoring this approach as helpful and reproducible solution for neural diseases in maxillofacial region, even with diversity of protocols.

Table 2 - Summary of the studies included in the literature review that evaluated LLLT in the treatment of Trigeminal Neuralgia.

Study	Disease	Region (area)	Wavelength	Power	Energy	Time and reputation	Conclusion
Terlević Tanganeli, J. P. C. et al. (2020)	Trigeminal Neuralgia	Along the path of the maxillary branch of the lower region of the zygomatic arch to the emergence of the infraorbital nerve, and along the lower alveolar nerve part of the mandibular branch of the trigeminal, extraoral path and intraoral region tongue and mint foramen.	808 nm	100 mW	133.2 J/cm²	10 sessions and 72h interval between applications	Positive
Ebrahimi, H. et al. (2018)	Trigeminal Neuralgia	Trigger point or 2 to 3 points in the pain path indicated by the patient.	810 nm	200mW	6.36 J/cm²	25s / 9 sessions (3 sessions per week)	Positive
Vernon, L. F. and Hasbun, R. L. (2008)	Trigeminal Neuralgia	Point where an incision would be made if decompression surgery was being performed on the trigeminal nerve (about two inches deep).	808 nm	200 mW	6 J/cm²	1 time a day for 5 consecutive days, followed by an interval of 2 days	Positive

Source: Authors.

3.2.2.2 Burning Mouth Syndrome (BMS)

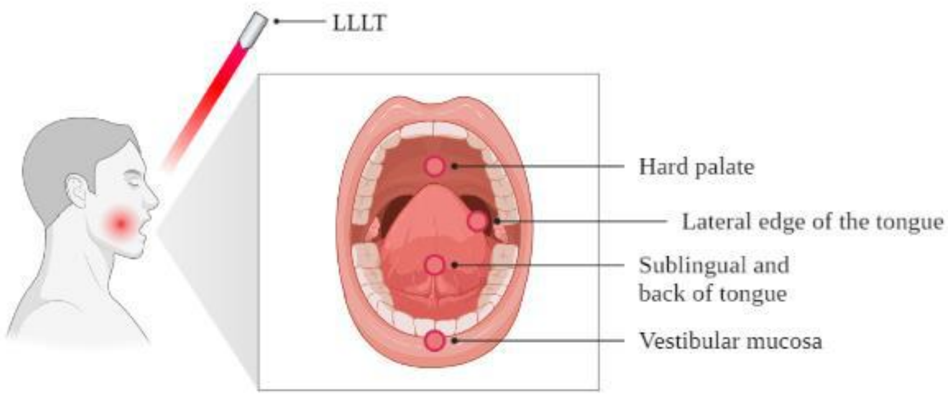
The definitions of Burning Mouth Syndrome are not consensual in the literature but are characterized by the burning sensation around the oral cavity. Because it is a pathology of uncertain etiology, its treatments are ineffective. Patients with this disorder usually present with anxiety, depression, altered pain perception, decreased quality of life due to frustration caused by the absence of adequate treatment and satisfactory results. In order to mitigate the problems raised by inefficient pharmacological treatment options, PBM has presented itself with an effective possibility of treatment in reducing unpleasant symptoms of oral burning and improving the quality of life of patients (Škrinjar et al., n.d., De Pedro et al., 2020)

In a recent study conducted in 14 patients of both sexes, 12 completed the protocol using infrared laser light with a wavelength of 904 nm and red laser light with a combined wavelength of 658 nm. Interestingly, results showed that young male patients were more adept at treatments using technological tools. Women in this study preferred to resort to treatment with drugs. All patients reported a significant reduction in symptoms or reduction of the points affected by the burning sensation (Balcheva et al., 2021).

In a randomized clinical study, also using wavelengths combined between 660-970 nm, in addition to the scope of pain, the functional limitations, physical pain, psychological discomfort, physical activity, psychological and social disability were also evaluated. The analysis showed improvement in quality of life related to oral health after the 7th week of treatment (Bardellini et al., 2019).

In a randomized clinical trial, the parameters used were 810 nm wavelength, power of 0.6W and application time of 10 s at 56 points. The placebo group participated in the clinical steps without knowing that the device was “off” for them. All patients had improvement in pain. After 4 months of treatment, 90% of patients undergoing PBM was better against only 20% of the placebo group. It is important to highlight that there was a significant decrease in anxiety in the study group and no adverse effects (De Pedro et al., 2020).

Figure 4 - Representative scheme of the irradiation points of LLLT in case of Burnt Mouth Syndrome.



Source: Authors.

In another randomized clinical study, in addition to pain analysis, salivary cortisol level was analyzed. All 23 participants had no side effects and pain scores were significantly lower after LLLT, as well as decreased salivary cortisol level, reducing stress (Škrinjar et al., n.d.). This result leads to the belief that condition improvement also generates stress reduction.

Finally, in a study by Spanemberg, J. C. et al. (2015), with 78 participants over 40 years of age with symptoms of burning in the oral mucosa, three different parameters with red and infrared light were used as detailed in Table 3 and compared to the control group that received placebo therapy. In addition to the pain, the quality of life regarding the oral health of these patients was evaluated, both aspects showing the positive influence of this therapy on the patient’s health.

It is important to mention that the study sought the analgesic effects of PBM considering that the suggested cause of Burning Mouth Syndrome of these patients were neuropathic factors. Although it is difficult to compare the protocols used in the studies due to the wide variety of parameters, types of devices, wavelength, number of applications and sessions, all studies demonstrated improvement in symptoms reported by patients.

Table 3 - Summary of the studies included in the literature review that evaluated LLLT in the treatment of BMS.

Study	**Disease**	**Region (area)**	**Wavelength**	**Power**	**Energy**	**Time and reputation**	**Conclusion**
Balcheva, M. Et.Al., 2021	BMS	-	904 nm and 658 nm	2 and 4mW	1-4 J/cm²	82 s and 76 s	Positive
De Pedro et al. (2020)	BMS	Vestibular mucosa (3 points), mucosa (4 points), hard palate (6 points), lateral edge of the tongue (4 points), back of tongue (6 points), sublingual region (4 points).	810 nm	0.6 mW	12 J/cm²	10 seconds at each point/10 sessions	Positive
Škrinjar et al., (2020)	BMS	-	685 nm	30 mW	2 J/cm²	Daily for 10 consecutive days, excluding weekends.	Positive
Bardellini, E. et al., (2019)	BMS	In the most painful areas of the oral cavity.	660 - 970 nm	3.2 W	-	3 min and 51 s	Positive
Spanemberg, J. C., (2015)	BMS	Apex of the tongue (3 points), side of the tongue (4 points), dorsum of the tongue (10 points), buccal mucosa (8 points), labial mucosa (5 points), hard palate (8 points), soft palate (3 points), and gums or alveolar ridge mucosa (3 points per sextant).	830 nm	100 mW	5th J	50 s per point/ Weekly for 10 weeks/ 10 Sessions	Positive
			830 nm	100 mW	5th J		
			685 nm	35 mW	2nd J	58 s per point	
Kazemikhoo, N., et. al. (2022)	Pemphigus vulgaris	-	650 nm	150 mW	2 J/cm²	Every day/ 10 sessions and 2 times a week for 6 more sessions.	Positive
Pontes, R. R. L. D. A., et. al. (2020)	Pemphigus vulgaris	Lip and intraoral mucosa.	660 nm and 780 nm	-	8 J/cm²	-	Positive
Minicucci, E. M., et. al. (2012)	Pemphigus vulgaris	Above and around each blister (4 points), and erosion approximately 6 mm from the oral mucosa.	660 nm	100 mW	35 J/cm²	20s	Positive

Source: Authors.

3.2.3 Immune disorders

3.2.3.1 Liquen Planus

Oral Lichen Planus (OLP) is a chronic an immune-related disorder of unknown etiology. Typically, this disease presents as multiple lesions with bilateral involvement. The lesions varies between white plaques mainly forming stretch-like marks (Wickham’s Striae) and erosions or desquamative areas in the oral cavity and gingival region. Corticosteroids are the main allies in this treatment, but present numerous chronic side effects such as thinning of the oral mucosa and candidiasis (Mutafchieva et al., 2018, Mahdavi et al., 2013).

PBM as non-pharmacological therapeutics for the treatment of this disease with no know side effects currently represents a therapeutic tool in substitution or combination with corticosteroids.

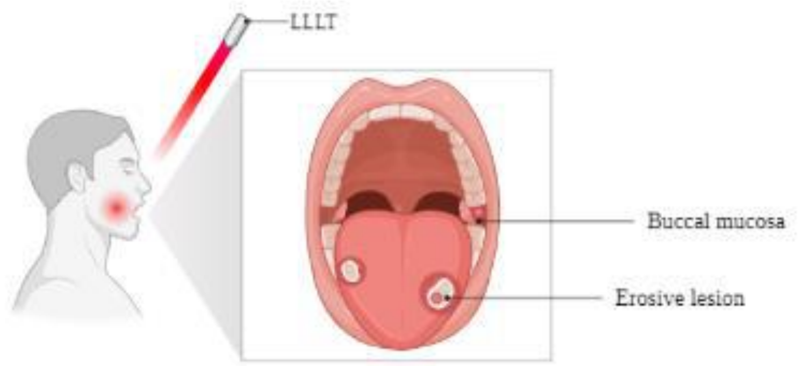
Some authors conduced an experimental group of 30 patients diagnosed with Lichen Planus treated with PBM compared to the control group treated with local corticosteroids followed by rinsing with nystatin. The results showed that the levels of improvement of symptoms were similar in both groups. Thus, PBM has been shown to be as effective as topical corticosteroid therapy in the treatment of Lichen Planus, including with better results, without undesirable side effects (Jajarm et al., 2011).

Other clinical study has conducted with 20 patients to evaluate the effects of PBM on symptomatic atrophic OLP. Authors compared clinical scores of the lesions size and pain before and after PBM. After therapy, all patients experienced relief of pain symptoms, improvement of clinical signs of lesions and in most of them, there was moderate recovery, and one patient presented total remission, with normal mucosa and without pain (Jajarm et al., 2011)

In an interesting case report, in addition to OLP, the patient presented xerostomia, gingivitis and other erythema lesions. The therapeutic regimen initially included Nystatin, chlorhexidine, and triamcinolone ointment, but symptoms persisted. After discontinuation of medications, she underwent laser therapy with a wavelength of 980 nm. As a result, the patient did not present pain, besides presenting significant salivary increase in the first week of treatment (Derikvand et al., 2017).

Other authors obtained successfully therapeutic response with PMG at wavelengths ranging 980 nm. The treatment resulted in total resolution of lesions with symptoms remission perceiving two months of follow-up, with no side effects. There was also no recurrence of the lesions within the seven-month analysis period (Misra et al., 2013). Other paper reported two cases of OLP one of them suffering severe pain. Using PBM they observed a decrease in pain at session three and disappearance of pain at session seven. After one month, there was total remission of the OLP. The other case referred to a patient with well-controlled diabetes mellitus in which OLP changed from atrophic to keratotic type after one month of PBM, becoming asymptomatic (Mahdavi et al., 2013).

Figure 5 - Representative scheme of the irradiation points of LLLT in Oral Liquen Planus cases.



Source: Authors.

Although this review admits the need for more controlled studies to ratify the efficacy of PBM in the treatment of OLP, there is currently some evidence showing also the possibility to fully resolve the OLP disease. The main advantage observed in all cases is the increase in the quality of life of patients due to decreased pain.

Table 4 – Summary of the studies included in the literature review that evaluated LLLT in the treatment of Lichen Plan.

Study	**Disease**	**Region (area)**	**Wavelength**	**Power**	**Energy**	**Time and reputation**	**Conclusion**
Mutafchieva, M. Z. et. al. (2018)	Lichen Plan	The longest distance in mm from end to end of the atrophic and erosive areas of the lichen planus.	810 nm	0.5 W	1.2 J/cm²	30s / 3 times per week at intervals of a day for a month.	Positive
Derikvand, N., et. al. (2017)	Lichen Planus	On the corner of the left buccal mucosa and anterior maxillary gingiva.	980 nm	0.3 W	6 J/cm²	20s / 4 sessions	Positive
				0.2 W (after slight decrease of pain)	4 J/cm² (after slight decrease of pain)	20s / 10 sessions / 3 sessions in a week (after slight decrease of pain)	
Mahdavi, O., et. al. (2013)	Lichen Planus	Case 1 - Left tongue border. Case 2 - 1.5 cm erosive lesion on left buccal mucosa	630 nm	10 mW	1.5 J/cm²	150 seconds during each Session / Every 3 days for 1 month.	Positive
Misra, N., et. al. (2013)	Lichen Planus	The right and left buccal mucosa	940 nm	-	-	2 times weekly for 2 months	Positive
Jajarm, H. H., et. al. (2011)	Lichen Planus	Tongue or buccal mucosa, sized 3 cm.	630 nm	10mW	1.5 J/cm²	2.5 min / 2 times a week for a maximum of 10 sessions.	Positive

Source: Authors.

3.2.3.2 Pemphigus Vulgar

Pemphigus Vulgaris is an autoimmune disease with antibodies that react against Pemphigus Vulgaris (PV) is an autoimmune disease with antibodies that react against keratinocytes and the most common affected areas are the buccal mucosa and gums. The main therapeutic modality of treatment of this disease is based on topic and systemic corticosteroids, thus raising those well-known therapeutic-related adverse effects (Mansouri et al., 2020, Minicucci et al., 2012).

Most studies documented in the literature use wavelengths in the 660 nm range to prove the efficacy of PBM in the treatment of PV. A recent study by Kazemikhoo, N. et al. (2022), brought up a case report of an elderly woman suffering with desquamative gingivitis. She underwent laser therapy with a wavelength of 650 nm. After four sessions, his pain score decreased to zero and after three months, there was no symptom of pain or inflammation (Kazemikhoo et al., 2022).

In two other case reports, PBM was the therapeutic modality used to reduce oral pain and stimulate oral healing of lesions, together with systemic therapy with prednisone and dapsone diamino-diphenyl sulfone. The wavelength used was 660 nm and applied by scanning. After the first session, the pain reduction was 70% and patients with greater comfort in the mucosa to eat properly (Pontes et al., 2020).

Table 5 – Summary of the studies included in the literature review that evaluated LLLT in the treatment of Pemphigus vulgaris.

Study	**Disease**	**Region (area)**	**Wavelength**	**Power**	**Energy**	**Time and reputation**	**Conclusion**
Kazemikhoo, N., et. al. (2022)	Pemphigus vulgaris	-	650 nm	150 mW	2 J/cm²	Every day/ 10 sessions and 2 times a week for 6 more sessions.	Positive
Pontes, R. R. L. D. A., et. al. (2020)	Pemphigus vulgaris	Lip and intraoral mucosa.	660 nm and 780 nm	-	8 J/cm²	-	Positive
Minicucci, E. M., et. al. (2012)	Pemphigus vulgaris	Above and around each blister (4 points), and erosion approximately 6 mm from the oral mucosa.	660 nm	100 mW	35 J/cm²	20s	Positive

Source: Authors.

3.2.4 Traumatic and idiopathic ulcerations

3.2.4.1 *Aphthous stomatitis*

Aphthous stomatitis is one of the most common pathologies of the oral cavity, being multifactorial and manifesting as painful necrotizing ulcers that can last for up to two weeks, affecting the patient's eating, hygienic and communicative habits. Due to the analgesic, anti-inflammatory and regenerative efficacy effects, PBM has been an ally in the treatment of aphthous stomatitis (Marangoni et al., 2022, Ślebioda & Dorocka-Bobkowska, 2020).

In a recently published case report authors showed a patient submitted to PBM with a wavelength of 808 nm at the site of the lesion, as well as on the submandibular and cervical lymph nodes for lymphatic drainage on the side of the lesion. The patient report the end of recurrences for about two years, and the results showed the effectiveness of PBM in tissue repair, analgesia and recurrence of lesions quickly, painlessly and reliably (Marangoni et al., 2022).

Table 6 – Summary of the studies included in the literature review that evaluated LLLT in the treatment of Aphthous Stomatitis.

Study	**Disease**	**Region (area)**	**Wavelength**	**Power**	**Energy**	**Time and reputation**	**Conclusion**
Marangoni, A.F., et. al. (2022)	Aphthous Stomatitis	Extraoral (lymphatic drainage), puntual irradiation and on the submandibular and cervical lymph nodes, on the side referring to the location of the lesion.	808 nm	120 mW	105.0 J/cm²	2 sessions / Intervals of 24h/48h and 60 days.	Positive

Source: Authors.

3.2.4.2 Mucositis

Mucositis is a type of shallow ulcer caused by a complex inflammation causing severe pain in regions of the mouth and throat. It is associated with the use of chemotherapy, radiotherapy or both. According to the American Academy of Pediatric Dentistry, mucositis is the main documented oral pathology of sepsis in patients undergoing antineoplastic treatment in the head and neck regions (Sonis et al., 2016, Melo, 2020)

A significant number of studies demonstrates the positive effects of PBM on pain inhibition, inflammatory reaction, as well as improvement of the healing process of oral mucositis.

In a recent case report, the patient diagnosed with diffuse large B-cell lymphoma underwent different types of chemotherapy without being able to contain the progression of the disease. Due to the medication, he presented ulcers in the labial commissure and oral mucosa. The diagnosis was grade 3 oral mucositis. The treatment with a 635 nm laser diode was advised. The treatment provided total remission of mucositis on the 21st day of treatment, in which the lesion was healed, obtaining pink mucosa pain relief (Jabłoński et al., 2022).

This is observed in the studies by Melo, M. C. F. (2020) and El Mobadder, M. et al. (2018), in which all these effects were evaluated. The first is the evaluation of the efficacy of PBM in the treatment of mucositis in children and adolescents undergoing chemotherapy. In this pilot study, the only intervention before treatment was guidance on the importance of oral hygiene of patients during cancer treatment. This study proposed a comparison with the wavelength of 660 nm and 808 nm, as well as the combined use in their respective parameters as specified in Table 7. The study reveals that the two spectra, red and infrared, are effective in the treatment of oral mucositis. However, infrared laser performs better in reducing the severity of mucositis (Melo, 2020).

In the second study, the patient, after undergoing radiotherapy, complained of pain, dysgeusia and dry mouth. After the PBM applied according to the parameters of Table 7, analyses were performed both patient's hyposalivation, dysgeusia and mucositis throughout the treatment. The results showed that only five PBM sessions were sufficient to solve the three conditions of the patient (El Mobadder et al., 2018).

It is suggested that the analgesic effects of PBM are achieved with wavelengths of 630-650 nm and 780-900 nm, the inflammatory effect is at the same wavelengths and the healing effect between 780-805 nm (Hamblin, Agrawal, & De Sousa, 2016, Jabłoński et al., 2022).

Although there is no consensus in the literature about the parameters used in the resolution of oral mucositis, there seems to be an agreement that wavelengths in the 660 nm range have better results in the treatment of the disease (Hamblin, Agrawal, & De Sousa, 2016, Jabłoński et al., 2022).

Table 7 – Summary of the studies included in the literature review that evaluated LLLT in the treatment of Mucositis.

Study	**Disease**	**Region (area)**	**Wavelength**	**Power**	**Energy**	**Time and reputation**	**Conclusion**
Jabłonski, P. et. al. (2022)	Mucositis	The lateral surface of the tongue, descending to its abdominal surface on the left side, also on the right palatal arch, descending into the retromolar triangle region and on the side surface of the pharynx.	635 nm	100 mW	4 J/cm²	20 s of irradiation / Seven treatment procedures perfomed 2 times a week (21 days total).	Positive
Melo, M. C. F. D. (2020)	Mucositis	Lower lip, jugal mucosa, oral floor, and oropharynx	Control Group: 660 nm	100 mW	70 J/cm²	20s per point.	Positive
			Experimental Group A: 808 nm				
			Experimental Group B: 660 nm + 808 nm		35 J/cm²		
El Mobadder, M., et. al. (2018)	Mucositis	The tongue (4 points), the oropharynx (2 points).	980 nm	-	3 J/cm²	12s on each point / 3 times for one week within 48h between each session.	Positive

Source: Authors.

4. Conclusion

This review presented studies regarding the use of Photobiomodulation (PBM) in the most frequent clinical situations in dentistry. There is evidence of the use of PBM as an adjuvant or alternative approach in the treatment of glandular, neural, autoimmune, traumatic, and idiopathic diseases, which have great potential for success through inhibitory or stimulatory effects that can be controlled by specific parameters.

The various areas of PBM use presented in the literature point to an understanding of the therapeutic margin of these parameters, as recorded in the tables of this review. Perhaps understanding the effects of low-power lasers and known therapeutic doses is sufficient for a professional to understand how to adapt the resource to each case. In addition, the evolution of the literature will show more parameters of therapeutic success and failure, which can increase the possibilities of PBM use. Other pathologies that still lack investigation and the establishment of therapeutic parameters will be discovered with the advancement of research.

Several authors have evaluated the use of PBM as a safe and efficient tool in the treatment of various oral diseases, encouraging the incorporation of this tool into current dental practice, as there are diseases that can have an impact on people's lives and whose therapeutic resources were, until then, insufficient for some situations.

In this sense, despite promising evidence regarding the use of PBM in dentistry, there are still gaps regarding the knowledge of the ideal parameters for its application in different clinical conditions. Therefore, new research can focus on identifying optimal parameters of dose, wavelength, and irradiation time to maximize the therapeutic effects of PBM in different oral pathologies. In addition, it may be interesting to investigate the underlying molecular mechanisms of the effects of PBM, in order to better understand how it acts in the modulation of inflammatory and reparative processes in oral tissues.

Additional studies can also explore the feasibility of PBM in combination with other conventional therapies, such as surgery and medications, to enhance the efficacy of treatment in different clinical situations.

References

Balcheva, M., et al. (2021). Low-level laser therapy in cases of burning mouth syndrome. *In: Journal of Physics: Conference Series. IOP Publishing*, p. 012036.

Bardellini, E., et al. (2019). Efficacy of the photobiomodulation therapy in the treatment of the burning mouth syndrome. *Medicina Oral, Patología Oral y Cirugía Bucal*, 24(6), e787.

De Pedro, M., et al. (2020). Effects of photobiomodulation with low-level laser therapy in burning mouth syndrome: A randomized clinical trial. *Oral Diseases*, 26(8), 1764-1776.

Derikvand, N., et al. (2017). Management of oral lichen planus by 980 nm diode laser. *Journal of Lasers in Medical Sciences*, 8(3), 150.

Dompe, C., De Marchi, T., Lualdi, M., Dallari, S., Tschon, M., & Pulsatelli, L. (2020). Photobiomodulation—Underlying Mechanism and Clinical Applications. *Journal of Clinical Medicine*, 9(6), 1724.

Ebrahimi, H., Amini, A., Beigi, B., & Hosseini, S. M. (2018). Therapeutic and analgesic efficacy of laser in conjunction with pharmaceutical therapy for trigeminal neuralgia. *Journal of Lasers in Medical Sciences*, 9(1), 63.

El Mobbadder, M., et al. (2018). Photobiomodulation therapy in the treatment of oral mucositis, dysgeusia and oral dryness as side-effects of head and neck radiotherapy in a cancer patient: a case report. *Dentistry Journal*, 6(4), 64.

Ferrandez-Pujante, A., Pons-Fuster, E., & López-Jornet, P. (2022). Efficacy of photobiomodulation in reducing symptomatology and improving the quality of life in patients with xerostomia and hyposalivation: A randomized controlled trial. *Journal of Clinical Medicine*, 11(12), 3414.

Hamblin, M. R., Agrawal, T., & De Sousa, M. (Eds.). (2016). Handbook of low-level laser therapy. *CRC Press.*

Jabłoński, P., et al. (2022). Photobiomodulation Therapy in the Treatment of Oral Mucositis—A Case *Report. Medicina*, 58(5), 618.

Jajarm, H. H., Falaki, F., & Mahdavi, O. (2011). A comparative pilot study of low intensity laser versus topical corticosteroids in the treatment of erosive-atrophic oral lichen planus. *Photomedicine and laser surgery*, 29(6), 421-425.

Kazemikhoo, N., et al. (2022). Treatment-resistant gingivitis responding to photobiomodulation in pemphigus vulgaris. *Journal of Oral Research and Review*, 14(2), 142.

Lončar, B., Nikolić, M., Jovanović, M., & Stošić, L. (2011). The effect of low-level laser therapy on salivary glands in patients with xerostomia. *Photomedicine and Laser Surgery*, 29(3), 171-175.

Louzeiro, G. C., Antequera, R., Galvão, M. S. R., Marques, M. M., & Bussadori, S. K. (2020). Effect of photobiomodulation on salivary flow and composition, xerostomia and quality of life of patients during head and neck radiotherapy in short term follow-up: A randomized controlled clinical trial. *Journal of Photochemistry and Photobiology B: Biology*, 209, 111933.

Mahdavi, O., et al. (2013). Use of low level laser therapy for oral lichen planus: report of two cases. *Journal of Dentistry*, 14(4), 201.

Mansouri, V., et al. (2020). Evaluation of efficacy of low-level laser therapy. *Journal of Lasers in Medical Sciences*, 11(4), 369.

Marangoni, A. F., Et Al. (2022). Fotobiomodulação por Laser em Baixa Intensidade no tratamento da estomatite aftosa maior–acompanhamento de dois anos. *Research, Society and Development*, 11(6).

Melo, M. C. F. (2020). Eficácia da fotobiomodulação no tratamento da mucosite oral em crianças e adolescentes submetidos à quimioterapia: um estudo piloto [Efficacy of photobiomodulation in the treatment of oral mucositis in children and adolescents undergoing chemotherapy: a pilot study] (*Master's thesis, Universidade Federal de Pernambuco*).

Milward, M. R., Chapple, I. L., & Wilson, N. H. (2014). Low Level Light Therapy (LLLT) for the treatment and management of dental and oral diseases. *Dental Update*, 41(9), 763-772.

Minicucci, E. M., et al. (2012). Low-level laser therapy on the treatment of oral and cutaneous pemphigus vulgaris: case report. *Lasers in medical science*, 27(5), 1103-1106.

Misra, N., et al. (2013). Efficacy of diode laser in the management of oral lichen planus. *Case Reports*, 2013, bcr2012007609.

Mutafchieva, M. Z., et al. (2018). Effects of low level laser therapy on erosive-atrophic oral lichen planus. *Folia Medica*, 60(3), 417-424.

Oliveira, A. B., Fernandes, M. B., Ferreira, E. F., Bariani, C., Gonçalves, C., & Bussadori, S. K. (2020). Photobiomodulation in the treatment of xerostomia associated with hyposalivation in a pediatric patient with systemic scleroderma. *Autopsy and Case Reports*, 11, e2020227.

Pinheiro, A. L. B., Gerbi, M. E. M., Marzola, C., & Ramalho, L. M. P. (1997). Low-level laser therapy in the management of disorders of the maxillofacial region. *Journal of Clinical Laser Medicine & Surgery*, 15(4), 181-183.

Pontes, R. R. L. A., Et Al. (2020). Low-Level Laser Therapy In The Treatment Of Oral Pemphigus Vulgaris: 2 Case Reports. Oral Surgery, Oral Medicine, *Oral Pathology and Oral Radiology*, 129(1), e108-e109.

Ribeiro, R. F., Silva, C. S. S., Santos, R. L. S., Santos, R. C. S., Freitas, R. L. S., De Paula, L. C. B., & Castro, J. F. L. (2021). Efeitos da terapia a laser de baixa potência em pacientes com neuralgia trigeminal [Effects of low power laser therapy in patients with trigeminal neuralgia]. *Brazilian Journal of Health Review*, 4(3), 14340-14351.

Škrinjar, I., Boras, V. V., Filipi, J., Čohadžić, T., & Ivanović, A. (2020). Salivary cortisol levels and burning symptoms in patients with burning mouth syndrome before and after low level laser therapy: A double blind controlled randomized clinical trial. *Acta stomatologica Croatica: International journal of oral sciences and dental medicine*, 54(1), 44-50.

Ślebioda, Z., & Dorocka-Bobkowska, B. (2020). Low-level laser therapy in the treatment of recurrent aphthous stomatitis and oral lichen planus: a literature review. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*, 37(4), 475-481.

Sonis, S. T., et al. (2016). Could the biological robustness of low level laser therapy (Photobiomodulation) impact its use in the management of mucositis in head and neck cancer patients. *Oral Oncology*, 54, 7-14.

Spanemberg, J. C., et al. (2015). Efficacy of low-level laser therapy for the treatment of burning mouth syndrome: a randomized, controlled trial. *Journal of biomedical optics*, 20(9), 098001.

Tanganeli, J., Haddad, D., Bussadori, S. Fotobiomodulação como adjuvante no tratamento farmacológico da neuralgia trigeminal. Relato de caso. *Brazilian Journal of Pain*, v. 3, p. 285-287, 2020.

Terlević Dabić, D., Špalj, S., Gamulin, O., Gamulin, S., & Perović, I. (2016). The effectiveness of low-level laser therapy in patients with drug-induced hyposalivation: A pilot study. *Photomedicine and Laser Surgery*, 34(9), 389-393.

Vernon, L. F., & Hasbun, R. L. (2008). Low-level laser therapy for trigeminal neuralgia. *Practical Pain Management*, 8(1).