



**11<sup>th</sup> BIOPHOTONICS**  
INTERNACIONAL FORUM  
**2025**

# Proceedings of FIB

**Volume XI**



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**10, 11 e 12 de novembro de 2025**

São Paulo, São Paulo Brasil

Realização:

**Programa de Pós-Graduação em**

**Biofotônica-Medicina**

Universidade Nove de Julho

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**EFFECT OF PHOTOBIOMODULATION ON THE SALIVARY GLANDS OF PATIENTS WITH  
HYPOSALIVATION INDUCED BY THE USE OF BENZODIAZEPINES: DOUBLE-BLIND  
RANDOMIZED PLACEBO-CONTROLLED CLINICAL STUDY.**

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**Abstract**

**Introduction:** Depression is one of the most common mental illnesses. Benzodiazepines are the mainstay of treatment for those affected by this condition and this class of drugs is associated with adverse reactions, one of which is hyposalivation. Saliva performs multiple functions and plays a vital role in protecting oral health. Reduced salivary flow is most often manifested by symptoms of dry mouth, a subjective complaint called hyposalivation. Users of antidepressant medication have a number of important systemic and oral complications, including hyposalivation. The infrared laser has been shown to significantly improve salivary flow in patients with hyposalivation due to diabetes, hypertension and chronic renal failure. **Objective:** evaluating the volumetric and biochemical parameters of unstimulated and stimulated saliva samples before and after the application of photobiomodulation in patients with depression taking benzodiazepines. **Material and Method:** Forty-eight participants were included in the protocol, after signing the Informed Consent Form (ICF), they underwent an anamnesis, physical assessment and questionnaires on self-perceived oral health and symptoms related to salivary gland function and were then randomized into two groups: Photobiomodulated (FBM) (n = 24) ; their major salivary glands were irradiated with a diode laser (808nm, 4J per point, 40s) and SHAM (n = 24), which underwent a simulation. We performed pre- and post-treatment sialometry to compare saliva volume and biochemical analysis, where we measured total proteins and calcium. **Results:** 58% of patients believe that hyposalivation related to other oral problems, with hyposalivation being the most prevalent alteration. After the photobiomodulation protocol, the FBM group showed a significant increase in salivary flow, unlike the SHAM group, as well as an increase in biochemical elements. We observed significant differences in both volume and biochemical elements. **Conclusion:** Photobiomodulation caused a significant improvement in sialometric and biochemical parameters in the samples analyzed from these groups of patients.

**Keywords:** photobiomodulation, hyposalivation, depression biochemical, salivary gland

**Study Type:** Ensaio Clínico (Clinical trial)

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## EFFECTS OF AN AEROBIC EXERCISE PROTOCOL ASSOCIATED WITH SYSTEMIC PHOTOBIOMODULATION ON FUNCTIONAL CAPACITY IN WOMEN WITH FIBROMYALGIA: A RANDOMIZED, BLIND CLINICAL TRIAL.

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### Abstract

**Introduction:** Fibromyalgia (FM) is a chronic condition characterized by widespread pain and other symptoms. Physical exercise is strongly recommended to manage these symptoms; however, in some cases, its effects on FM-related pain are limited due to low treatment adherence. Therefore, additional interventions such as photobiomodulation (PBM) have been used to enhance the benefits of exercise. One PBM method is intravascular laser irradiation of blood, which has systemic positive effects on pain reduction and tissue repair. However, there is still a lack of studies investigating the effects of an aerobic exercise protocol (AEP) combined with systemic PBM on functional capacity in FM patients. **Objective:** To investigate the effects of combining an aerobic exercise protocol with systemic PBM (ILIB) on improving functional capacity, assessed by the Six-Minute Walk Test (6MWT), in individuals with FM. **Methods:** This was a blinded, randomized clinical trial. Participants were allocated into two groups: Aerobic Exercise and Active PBM Group (GEFA, n = 17) and Aerobic Exercise and Placebo PBM Group (GEFP, n = 17). The Six-Minute Walk Test (6MWT) was used to assess functional capacity during both the initial and final evaluations. All participants followed an AEP consisting of progressive load training on a stationary cycle ergometer for 20 minutes. After the exercise session, the groups received systemic PBM (active or placebo). The parameters of the active PBM were: red laser with a wavelength of 660 nm; total energy of 144 J; continuous emission mode; optical output power of 80 mW; dose of 286.5 J/cm<sup>2</sup>; applied for 30 minutes, twice a week, for 12 weeks. The study was approved by the Human Research Ethics Committee of UNIFESP (CAAE: 66837323.6.0000.5505). **Results:** Functional capacity, assessed by the 6MWT and expressed in meters walked, showed an intragroup difference ( $p < 0.0146$ ) in the GEFP group ( $410 \pm 39.4$  to  $448 \pm 43.5$ ;  $p = 0.0229$ ). No significant intragroup difference was found in the GEFA group ( $400 \pm 63.1$  to  $426 \pm 59.3$ ;  $p = 0.1691$ ). The between-group analysis at the end of the protocol demonstrated no significant difference between GEFP and GEFA. **Conclusion:** The aerobic exercise protocol associated with ILIB PBM showed improvement in both groups (GEFP and GEFA), but without significant differences between them. This suggests that physical activity is the main determinant of improved functional capacity, regardless of laser use.

**Keywords:** Photobiomodulation, Exercise, Chronic Pain, Fibromyalgia, Functional Capacity.

**Study Type:** Ensaio clínico (Clinical trial)

**EFFECT OF PHOTOBIOMODULATION ON POST-ENDODONTIC PAIN FOLLOWING  
SINGLE-VISIT TREATMENT: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL**

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**Abstract**

The evidence for photobiomodulation in reducing postoperative pain after endodontic instrumentation is classified as low or very low certainty, indicating a need for further research. Longitudinal pain assessments over 24 h are crucial, and studies should explore these pain periods. Background/Objectives: This double-blind, randomized controlled clinical trial evaluated the effect of PBM on pain following single-visit endodontic treatment of maxillary molars at 4, 8, 12, and 24 h. Primary outcomes included pain at 24 h; secondary outcomes included pain at 4, 8, and 12 h, pain during palpation/percussion, OHIP-14 analysis, and frequencies of pain. Methods: Approved by the Research Ethics Committee (5. 598. 290) and registered in Clinical Trials (NCT06253767), the study recruited adults (21–70 years) requiring endodontic treatment in maxillary molars. Fifty-eight molars were randomly assigned to two groups: the PBM Group (n = 29), receiving conventional endodontic treatment with PBM (100 mW, 333 mW/cm<sup>2</sup>, 9 J distributed at 3 points near root apices), and the control group (n = 29), receiving conventional treatment with PBM simulation. Pain was assessed using the Visual Analog Scale. Results: Statistical analyses used chi-square and Mann–Whitney tests, with explained variance ( $\eta^2$ ). Ten participants were excluded, leaving 48 patients for analysis. No significant differences were observed in postoperative pain at 24, 4, 8, or 12 h, or in palpation/percussion or OHIP-14 scores. Pain frequencies ranged from 12. 5% to 25%. Conclusions: PBM does not influence post-treatment pain in maxillary molars under these conditions. These results emphasize the importance of relying on well-designed clinical trials to guide treatment decisions, and future research should focus on personalized dosimetry adapted to the anatomical characteristics of the treated dental region to enhance the accuracy and efficacy of therapeutic protocols.

**Keywords:** endodontics; low-level light therapy; pain management; periapical periodontitis; photobiomodulation

**Study Type:** Ensaio clínico (Clinical trial)

**EVALUATION OF A CLINICAL PROTOCOL FOR PHOTODYNAMIC THERAPY IN THE  
ENDODONTIC TREATMENT OF PRIMARY TEETH – A RANDOMIZED CONTROLLED TRIAL**

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**Abstract**

**Introduction:** Pulp necrosis in primary teeth, commonly caused by trauma or extensive caries, is difficult to manage due to anatomical complexity, thin dentinal walls, and frequent lack of child cooperation. Conventional endodontic treatment may not sufficiently eliminate intracanal microorganisms. Antimicrobial photodynamic therapy (aPDT), which combines a photosensitizing agent and a specific light wavelength, promotes reactive oxygen species formation, leading to effective microbial destruction without resistance, and is especially promising in pediatric dentistry due to its safety and noninvasive nature. **Objective:** To evaluate the efficacy and safety of a clinical aPDT protocol in the endodontic treatment of necrotic anterior primary teeth. **Methodology:** This randomized controlled clinical trial included 20 necrotic anterior primary teeth in children aged 2 to 5 years. Group 1 (G1) underwent conventional endodontic therapy: manual instrumentation, irrigation, and obturation. Group 2 (G2) received the same treatment plus aPDT with 0.005% methylene blue and red laser (660 nm, 100 mW, 90 s, 9 J) via optical fiber. Microbiological samples were collected using sterile absorbent paper points inserted into the canals, then cultured on blood agar under anaerobic conditions (37°C/72 h). CFUs were counted and analyzed using the Mann-Whitney test ( $\alpha = 0.05$ ). **Preliminary Results:** Both groups showed microbial reduction. The mean CFU reduction was higher in the aPDT group, although the difference between groups was not statistically significant ( $p = 0.661$ ). No adverse events were observed, and all children tolerated the protocol well. **Conclusion:** This clinical aPDT protocol proved safe and well-tolerated. While no significant difference was observed in microbial reduction, results suggest potential benefits as an adjunct to conventional endodontic therapy. Continued follow-up and expanded samples are needed to confirm long-term outcomes.

**Keywords:** Antimicrobial photodynamic therapy, Endodontics, Primary teeth

**Study Type:** Ensaio clínico (Clinical trial)

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## CLINICAL PRACTICE FOR THE TREATMENT WITH PHOTOBIOMODIFICATION OF OROFACIAL PAIN CAUSED BY TEMPOROMANDIBULAR DYSFUNCTION: A REVIEW FOCUSING ON QUALITY ASSESSMENT (AGREE II)

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### Abstract

**Background:** The selection of parameters, such as wavelength, energy, application time, and number of sessions, can vary. Despite clinical evidence, there is currently no assessment of clinical protocols for photobiomodulation in the treatment of physical pain due to temporomandibular dysfunction. Standardizing a protocol based on scientific evidence is crucial, making it accessible to clinicians without experience in study analysis. **Objective:** This study aims to evaluate clinical trials in individuals with orofacial muscle pain caused by temporomandibular dysfunction, seeking consensus on the best clinical recommendations. **Methods:** Protocols with high methodological quality were identified through literature research and the Appraisal of Guidelines for Research and Evaluation (AGREE II) tool, a validated instrument for quality assessment. The recommendations from these studies were synthesized and submitted to a group of experts for evaluation and adaptation, and consensus was assessed using the Delphi methodology. The protocol was registered on the Open Science Framework (Identifier: DOI 10.17605/OSF.IO/HFRVX). **Results:** After analyzing the literature on photobiomodulation in temporomandibular dysfunction caused by orofacial pain, studies with the best evidence and clinical recommendations were considered in the development of the clinical recommendation protocol. Judges were invited to evaluate the protocol using the AGREE II method. There was agreement among the evaluators. **Conclusion:** PMB emerged as a positive adjunct to conventional methods for treating TMD-related orofacial pain. The protocol, rooted in literature, received satisfactory evaluation and consensus among evaluators. However, continuous updates are essential as new evidence emerges, reflecting the nature of clinical protocols

**Keywords:** Temporomandibular Joint Disorders, Facial Pain, Orofacial Pain, Low-Level Light Therapy, Photobiomodulation.

**Study Type:** Estudo Delphi (Delphi study)



**ANTIMICROBIAL PHOTODYNAMIC THERAPY AS A TECHNOLOGICAL INNOVATION IN FOOT ULCERS IN PEOPLE WITH DIABETES: A RANDOMIZED CLINICAL STUDY**

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**Abstract**

**Introduction:** Foot ulcers in people with diabetes remain a major challenge, directly affecting quality of life. Antimicrobial Photodynamic Therapy (aPDT) has shown promise as an alternative treatment for these wounds, although scientific gaps regarding its clinical effectiveness still exist. **Objective:** To analyze the effects of aPDT on wound quality and tissue repair using the Bates-Jensen (BJ) scale in people with diabetic foot ulcers. **Method:** A randomized, double-blind controlled clinical trial was conducted with 94 patients: the aPDT group (n = 47) received standard care combined with aPDT, and the control group (n = 47) received the same standard care with simulated aPDT, three times per week, totaling ten consecutive sessions. **Protocol:** red laser cluster (660 nm), power of 100 mW, and energy of 6 J per point, totaling 24 J per session. The photosensitizer used was 1% methylene blue. **Ethics approval:** CAAE 70466823. 9. 0000. 5511 and 70466823. 9. 3001. 5279. **Results:** The aPDT group showed a higher proportion of participants with amputations (70. 2%) compared to the control group (38. 3%). The progression of total BJ scores in both groups (Control and aPDT) was evaluated at five distinct time points: sessions 1, 3, 5, 10, and at 30-day follow-up. Results demonstrated that the group treated with aPDT showed a significant reduction in BJ clinical scores from the fifth session onward ( $p = 0. 002$ ), with improvement maintained up to 30 days after the last application. Other clinical scales also showed significant improvement only in the aPDT group ( $p < 0. 001$ ). Longitudinal analysis using the Friedman test revealed a significant difference over time in the aPDT group ( $p < 0. 0001$ ), whereas in the control group, this difference was not significant ( $p = 0. 2182$ ). In the control group, scores remained relatively stable over time, with no expressive variations in median values or data range, indicating no significant clinical changes in this group during the evaluation period. **Conclusion:** We conclude that aPDT is an effective and safe intervention for the treatment of chronic wounds in patients with diabetes, even in more unfavorable clinical contexts, such as the presence of amputations and larger lesion areas. The application of aPDT resulted in a significant improvement in wound quality, as measured by the Bates-Jensen scale, with a statistically significant reduction in scores.

**Keywords:** diabetic foot, antimicrobial photodynamic therapy, wound, infection, contamination, Bates-Jensen.

**Study Type:** Estudo clínico (Clinical study)

**BETWEEN CLINICAL CARE AND SOCIAL INEQUALITIES: SOCIODEMOGRAPHIC PROFILE OF PEOPLE WITH DIABETIC FOOT ULCERS**

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**Abstract**

**INTRODUCTION:** Foot ulcers in people with Diabetes Mellitus (DM) represent a significant public health issue. In 2021, approximately 537 million adults aged 20 to 79 years were living with DM, corresponding to 10.5% of the global adult population. **OBJECTIVE:** To discuss the sociodemographic characteristics of people with diabetic foot ulcers, considering their relationship with the social determinants of health and their impact on the clinical conditions observed, based on data from a randomized, double-blind controlled clinical trial. **METHOD:** This study is a subset of a randomized, double-blind clinical trial that evaluated the effect of antimicrobial photodynamic therapy (aPDT) on wound quality and tissue repair, using the Bates-Jensen (BJ) scale. A total of 94 participants were included and randomly assigned to two groups: intervention (aPDT) and control. Inclusion criteria: both sexes, diagnosis of diabetic foot ulcer, and BJ score between 13 and 60 points. Exclusion criteria: individuals under 18 years of age, wounds of other etiologies, ankle-brachial index  $<0.7$  or  $>1.3$ , and glycated hemoglobin  $>8\%$ . The study was approved under CAAE 70466823.9.0000.5511 and 70466823.9.3001.5279. **RESULTS:** There was a predominance of males in both groups (89.4% in the aPDT group and 87.2% in the control group;  $p=1.000$ ), consistent with studies indicating that the incidence of diabetic foot ulcers is about 1.5 times higher in men. Although diabetes is more prevalent among women, they tend to show greater adherence to primary care services, which favors prevention. Regarding education, 41.5% had incomplete elementary schooling (42.6% in the aPDT group and 40.4% in the control group;  $p=0.254$ ), reinforcing the association between low educational level and lower adherence to self-care. Retirement predominated (63.8%), reflecting the participants' age profile and the presence of comorbidities. Concerning race/ethnicity, 62.2% identified as Black or Brown and 55.3% as White. Although the sample was homogeneous, 70.2% of individuals in the aPDT group and 38.3% in the control group had previous amputations, reflecting advanced complications. **CONCLUSION:** The results show that sociodemographic factors directly influence the clinical conditions of people with diabetic foot ulcers. Educational, economic, and healthcare access inequalities affect both the onset and recovery processes, highlighting the need for strategies that promote equity and comprehensive care beyond lesion treatment alone.

**Keywords:** diabetic foot, antimicrobial photodynamic therapy, wound, Bates-Jensen, social determinants of health.

**Study Type:** Estudo clínico (Clinical study)



## CAN VASCULAR PHOTOBIOMODULATION BE A NON-INVASIVE PATHWAY TO IMPROVE SLEEP QUALITY? A RANDOMIZED PLACEBO-CONTROLLED CLINICAL TRIAL

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### Abstract

**Background:** Sleep quality is a fundamental determinant of human health and well-being. Vascular Photobiomodulation (VPBM), a non-invasive therapeutic modality, has emerged as a potential intervention for sleep-related disturbances. Its proposed mechanisms include the reduction of blood viscosity and platelet aggregation, activation of superoxide dismutase, increased oxygen bioavailability, enhanced microcirculation, elevated serotonin levels, and decreased cortisol concentrations—physiological processes intricately linked to sleep regulation, mood modulation, and stress response. **Objective:** To assess the effects of Vascular Photobiomodulation (VPBM) on sleep quality in individuals with self-reported sleep disturbances. **Methods:** A randomized, placebo-controlled clinical trial was conducted involving participants who reported poor sleep quality. Subjects were allocated into two groups: one received VPBM using a 660 nm red laser, while the control group received a placebo intervention (light emission with sub-therapeutic power, <1 mW). Both groups underwent identical treatment schedules. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) at baseline and after six treatment sessions. **Results:** Participants in the VPBM group demonstrated statistically significant improvements in sleep parameters. PSQI scores decreased from 10.24 at baseline to 6.47 post-treatment, and ESS scores improved from 10.44 to 10.12. These findings indicate enhanced overall sleep quality, reduced sleep latency, and diminished daytime sleepiness, with the most pronounced effects observed in PSQI score reductions. **Conclusion:** Vascular Photobiomodulation appears to be a promising non-invasive strategy to enhance sleep quality. The observed clinical outcomes are comparable to those reported in both pharmacological and behavioral sleep interventions, particularly with regard to improvements in PSQI scores. These preliminary findings demonstrate the safety and efficiency of the application and justify further investigations to elucidate the underlying mechanisms, optimize treatment parameters (e. g. , dosimetry and duration), and expand evaluation protocols to include biomarkers and polysomnographic analysis.

**Keywords:** Photobiomodulation, Vascular photobiomodulation, Sleep quality, Sleep latency, Non-invasive sleep therapy.

**Study Type:** Estudo clínico (Clinical study)

## PHOTOBIMODULATION AND SYNTHETIC BIOMATERIALS IN ALVEOLAR BONE PRESERVATION FOLLOWING MOLAR EXTRACTION: A RANDOMIZED TRIPLE-BLIND PILOT CLINICAL TRIAL

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### Abstract

**Introduction:** Evidence on the effectiveness of photobiomodulation (PBMT) for alveolar bone preservation after permanent molar extraction, either alone or in combination with synthetic biomaterials, remains limited. Preserving the dental alveolus is critical to prevent post-extraction bone atrophy. Photobiomodulation therapy has demonstrated the potential to accelerate bone healing. This is the first clinical study to combine bone graft biomaterials with photobiomodulation therapy. **Methodology:** This randomized, triple-blind clinical trial was approved by the ethics committee (approval number: 6, 045, 673) and registered on ClinicalTrials.gov (NCT06164626). 42 patients (both genders, aged 18 years), of whom 40 completed the protocol, were randomized into four groups (n = 15 per group): Exo (extraction only), Exo+Laser (extraction with PBM therapy), Exo+Biomat (extraction with biomaterial application), and Exo+Biomat+Laser (extraction with biomaterial application and PBM therapy). The biomaterials Plenum® OSShp and Plenum® Guide were applied immediately after tooth extraction. In groups receiving laser therapy ( $\lambda = 808$  nm, power = 100 mW, energy = 3 J per point at three locations: buccal, occlusal, and lingual/palatal), irradiation was performed intraoperatively and repeated after 10 days. Preoperative and three-month postoperative computed tomography (CT) scans were conducted to assess dimensional and fractal changes in the alveolus. The primary outcome was alveolar dimensional preservation, while the secondary outcome was the complexity of the newly formed bone structure. **Results:** Analysis of variance (ANOVA) of fractal dimensions revealed significant differences between groups ( $p = 0.0162$ ). Exo group exhibited significantly lower fractal dimensions compared to the Exo+Biomat and Exo+Biomat+Laser groups ( $p = 0.0056$  and  $p = 0.0176$ , respectively; Tukey's post hoc test). No significant differences were observed between the Exo+Laser group and the groups receiving biomaterial. Significant reductions in both horizontal and vertical alveolar dimensions were detected in the Exo and Exo+Laser groups between pre-and post-treatment assessments ( $p < 0.05$ ). **Conclusion:** Photobiomodulation alone did not significantly impact alveolar bone preservation in terms of dimensional or fractal analyses. Conversely, the biomaterials Plenum® OSShp and Plenum® Guide effectively preserved alveolar bone, promoting trabecular organization and bone formation in the extraction site.

**Keywords:** Photobiomodulation therapy, Laser therapy, Alveolar preservation, Synthetic biomaterial, Bone regeneration.

**Study Type:** Estudo clínico (Clinical study)

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**Photobiomodulation in cows during milking – preliminary study**

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**Abstract**

Bovine mastitis is the most common disease affecting dairy cows, resulting in significant economic losses for dairy farmers. It reduces milk production and compromises the quality of milk suitable for human consumption. Among conventional therapies for prevention and treatment, antibiotics are the predominant, but they have some disadvantages. The objective of this study was to evaluate the photobiomodulation (PBM) in routine cow milking management for future mastitis prevention and to assess its effects on milk quality. Healthy lactating Jersey cows (without mastitis) (n = 4 cows; n = 16 teats) milked twice a day by mechanical milking machines at the farm of State University of Londrina (Animal Ethics Committee - No. 031. 2023) were subjected to PBM for six consecutive weeks at all milkings through an optical device composed of four flanges with infrared LEDs ( $\lambda = 940\text{nm}$ ), each flange consisting of 50 LEDs distributed with an area of  $39\text{cm}^2$ , total optical power of 3.2W (0.8 W/flange), power density of  $20.5\text{mW/cm}^2$ . The innovative device was coupled to the milking equipment, and PBM occurred during the milking only in the anterior teats of each cow, with the posterior teats serving as a control for each animal. To assess milk quality, the pre- (t = 0), during (three consecutive weeks without interruption), and post- (two weeks after removal of the device) PBM data were compared. Two protocols with different Energy Densities (ED) were tested for three consecutive weeks at all milking sessions: a two-minute dose with an ED of  $2.46\text{J/cm}^2$  and an ED of  $4.14\text{J/cm}^2$  (t = 3.4 min. ). Weekly milk samples were collected from all teats (irradiated and control) individually, stored in cold sterile bottles and refrigerated for 24h. These samples were sent to a certified laboratory for analysis of milk composition (fat, protein, lactose, total solids, urea, somatic cell count, and total bacterial count) for quality assessment. The results obtained showed that PBM applied at different ED dosages did not present statistical differences in relation to the milk quality parameters in the teats subjected to PBM compared to the control, maintaining milk quality at all times evaluated and within the criteria of national legislation for human milk consumption. New studies will be conducted using other methods on dairy farms. It is concluded that PBM applied at the specified optical dosages can potentially be safely implemented without altering the quality parameters of bovine milk.

**Keywords:** Bovine, Dairy, LED, Milking machine, Photobiomodulation.

**Study Type:** Estudo clínico em veterinária (Clinical study in veterinary)

## 11

**EFFECTS OF PREVENTIVE AND THERAPEUTIC VASCULAR PHOTOBIOMODULATION ON MUSCLE FIBER DIAMETER AFTER ACUTE INJURY**

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**Abstract**

**Introduction:** The musculoskeletal system is composed of muscles, ligaments, cartilage, nerves, and connective tissues that work synergistically to maintain movement, balance, posture, and body protection. Although it possesses considerable regenerative capacity, injuries often result in scar tissue formation and fibrosis, which can compromise muscle function. Locally applied photobiomodulation (PBM) has demonstrated significant benefits in promoting tissue repair and regeneration. Vascular photobiomodulation (VBM) has shown promise in tissue repair and is therefore being investigated. **Objective:** To evaluate muscle fiber diameter with VBM applied before and after acute muscle injury. **Methods:** Sixty-five animals were randomly distributed into four groups: Control (n=5), Injury (n=20), VPBM pre-injury + injury (n=20), and Injury + VPBM post-injury (n=20). The treated groups were irradiated with an AlGaAs diode laser (780 nm, 40 mW, 0.04 cm<sup>2</sup>, 3.2 J, 80 s) over the artery/vein at the base of the tail. The injury was performed using metal cooled in liquid nitrogen for 30 s and applied twice for 10 s, in the muscle belly of the tibialis anterior (TA) muscle. Euthanasia was performed five and seven days after injury. Muscle samples were fixed and cut transversely at 4 µm and stained with hematoxylin and eosin (H&E). Muscle sections were photographed under an optical microscope at 200× magnification (five fields per slide from five animals per group). Muscle fiber diameter was quantified using ImageJ software by measuring 100 fibers per field, and the mean value was calculated for each slide. **Results:** An increase in muscle fiber diameter was observed in the pre-injury VPBM group compared to the injury group at five days, with no significant difference at seven days. Additionally, only the injury group exhibited a statistically significant reduction in fiber diameter at both five and seven days. **Conclusion:** Pre-injury VPBM promoted an increase in muscle fiber diameter at five days, indicating an early protective effect. By seven days, no significant differences were observed between the groups. Post-injury VPBM treatment did not produce significant effects, suggesting that pre-injury application is more effective in accelerating the initial phase of muscle tissue regeneration.

**Keywords:** Vascular photobiomodulation (FBMV), acute muscle injury, muscle regeneration, muscle fiber diameter, low-level laser, and tibialis anterior.

**Study Type:** Estudo experimental em animais (Experimental study in animals)

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**Fluorescence-Based Detection of Breast Cancer Metastasis Using Indocyanine Green:  
Development of a Sensitive In Vivo Imaging Model**

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**Abstract**

Background: Breast cancer is one of the most frequent and lethal malignancies worldwide, representing a persistent challenge to global health systems. Although therapeutic advances have improved survival, metastasis—the dissemination of cancer cells to distant organs—remains the principal cause of mortality. Early and accurate detection of metastatic spread is critical for improving prognosis and guiding therapeutic interventions. Preclinical models are essential to reproduce the biological complexity of tumor progression and validate innovative diagnostic tools. In this scenario, optical methods based on fluorescence imaging have emerged as promising noninvasive strategies, offering high sensitivity, real-time visualization, and submillimetric spatial resolution for mapping tumor dissemination. Aim: To develop and validate a preclinical model capable of detecting breast cancer metastases through fluorescence imaging using Indocyanine Green (ICG), a clinically approved dye that selectively accumulates in tumor tissues. Methodology: Murine 4T1 breast carcinoma cells were cultured under optimized conditions and subcutaneously inoculated into the lower left mammary fat pad of BALB/c nude mice. Tumor progression was monitored daily, and metastatic foci were evaluated by in vivo fluorescence imaging after intraperitoneal injection of ICG. The ideal dose and incubation time were determined to optimize the signal-to-noise ratio. Imaging was performed using a customized optical prototype with 780 nm excitation and 810 nm emission detection, allowing high-contrast, quantitative analysis of fluorescence distribution. Results: Metastatic dissemination was consistently detected between 21 and 28 days after tumor induction. Fluorescence imaging revealed intense ICG accumulation in tumor-bearing tissues, enabling detection of metastatic lesions as small as 1 mm<sup>3</sup>. Quantitative pixel intensity mapping demonstrated a clear contrast between metastatic and surrounding normal regions, confirming the method's high sensitivity, reproducibility, and spatial precision. Conclusion: Fluorescence imaging with Indocyanine Green proved to be a highly sensitive and noninvasive approach for detecting micro-metastases in the 4T1 murine model. The technique provides a reliable and translational platform for studying metastatic progression and supports future clinical applications in early cancer diagnosis, image-guided surgery, and optical monitoring of therapeutic response.

**Keywords:** Fluorescence Imaging, Tumor Metastasis, Optical Diagnosis

**Study Type:** Estudo experimental em animais (Experimental study in animals)



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**Influence of Vascular Photobiomodulation on Trophic Factors and Regeneration in Acute Muscle Injury**

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**Abstract**

Background: Photobiomodulation therapy (PBM) has gained prominence due to its benefits in muscle repair and regeneration, particularly when applied directly to the injury site (LPBM). However, vascular photobiomodulation (VPBM) exerts systemic effects and shows promise in both preventive and therapeutic contexts. Despite its potential, there is a lack of studies investigating its effects on skeletal muscle. Aim: This study aimed to evaluate the effects of preventive and therapeutic VPBM on the expression of myostatin and MuRF-1 in acute muscle injury. Methods: Wistar rats ( $n = 65$ ), aged twelve weeks, were randomly divided into four groups: Control ( $n = 5$ ), Injury ( $n = 20$ ), VPBMpre + Injury ( $n = 20$ ), and VPBM post + Injury ( $n = 20$ ). Treated groups were irradiated over the caudal artery using an AlGaAs diode laser (780 nm, 40 mW, 0.04 cm<sup>2</sup>, 3.2 J, 80 s), either as a single application 24 h before surgery for preventive treatment or 2 h after injury for therapeutic treatment, followed by daily irradiation. A cryolesion was performed on the tibialis anterior (TA) muscle using a metal bar cooled in liquid nitrogen for 30 seconds and applied twice for 10 seconds. The animals were euthanized at 1-, 2-, 5-, and 7-days post-injury. TA muscle samples were collected, processed for total RNA extraction, and reverse-transcribed into cDNA to analyze the gene expression of atrophy-related markers, myostatin and MuRF-1. Quantification was performed by qPCR using specific primers for the target genes, with GAPDH as the endogenous control. Results: VPBM reduced Myostatin expression until day 2 in both preventive and post-injury applications. On day 7, the pre-injury group showed increased myostatin compared to control and Injury groups, whereas the post-injury group maintained lower levels, similar to the Injury group. Regarding MuRF-1, both VPBM pre- and post-injury groups maintained reduced levels up to day 5. By day 7, both treated groups exhibited decreased expression compared to the Injury group, reaching levels similar to the Control. Conclusion: Vascular photobiomodulation modulated Myostatin and MuRF-1 expression, promoting a favorable environment for muscle regeneration. The post-injury application showed more sustained effects, while the preventive approach indicated adaptive responses, suggesting that VPBM outcomes depend on the timing of application.

**Keywords:** Vascular photobiomodulation, modified ILIB, muscle repair, muscle injury, muscle atrophy.

**Study Type:** Estudo experimental em animais (Experimental study in animals)

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**PHOTOBIOMODULATION EFFECTS ON IMMOBILIZATION-INDUCED MUSCLE ATROPHY:  
MORPHOLOGICAL IMPLICATIONS FOR POST-SURGICAL REHABILITATION**

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(1); Instituto Neo Mama, Santos, São Paulo, Brasil (2)**Abstract**

**INTRODUCTION:** Skeletal muscle atrophy (MA), characterized by loss of mass and function, often occurs due to disuse, such as after post-surgical immobilization. This condition results from an imbalance between protein synthesis and degradation, associated with inflammation and fibrosis, which compromise functional and aesthetic recovery. Photobiomodulation (PBM) is a non-invasive therapy with modulatory effects on inflammation and regenerative potential already demonstrated in experimental models, although it remains little explored in immobilization-induced atrophy. **OBJECTIVE:** To evaluate the effects of PBM on morphological and histochemical changes in an experimental model of muscular atrophy induced by joint immobilization. **METHODS:** Sixteen male Wistar rats were randomly divided into two groups (n=8): Control Atrophy and Atrophy + PBM. Muscle atrophy was induced by joint immobilization for five days. The treated group received PBM (808 nm, 30 mW, 1.4 J/point, continuous mode, contact technique, two points on the gastrocnemius muscle, nine daily sessions). After treatment, muscles were analyzed histologically using hematoxylin and eosin staining. All evaluations were performed blindly by two trained observers. Data were analyzed using the Mann-Whitney test ( $p \leq 0.05$ ). **RESULTS AND DISCUSSION:** Animals subjected to immobilization presented classic features of MA such as inflammatory infiltration, thickening of intramuscular connective tissue, and variation in fiber size. In the PBM-treated group, a significant reduction in inflammatory infiltration and connective tissue thickening was observed, along with an increase in the number of fibers with central nuclei and a higher proportion of oxidative fibers, indicating enhanced regeneration and metabolic recovery. These findings are consistent with previous studies demonstrating the ability of PBM to modulate TGF- $\beta$  expression, reduce fibrosis, and stimulate mitochondrial activity and myogenesis. These morphological findings suggest that PBM helps prevent or mitigate disuse-induced muscle atrophy and has translational potential for clinical application in postsurgical rehabilitation. **CONCLUSION:** PBM reduced inflammation and connective tissue thickening, increased the proportion of oxidative fibers, and promoted muscle regeneration in the proposed experimental model, suggesting it is a promising complementary approach for early rehabilitation and prevention of functional loss after surgical immobilization.

**Keywords:** Lasers, Muscle atrophy, Phototherapy, Rehabilitation.**Study Type:** Estudo experimental em animais (Experimental study in animals)



**PHOTODYNAMIC THERAPY METHYLENE BLUE-BASED IN BREAST TUMOR CELLS****Authors:** Souza AC (1), dos Anjos LMJ (1), Mencalha AL (2), Fonseca AS (2,3,4), Paoli F (1)

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**Abstract**

Photodynamic therapy (PDT) has emerged as a promising alternative for treating several types of cancer, owing to its selectivity and cytotoxicity toward malignant tissues. There is growing consensus that PDT can activate multiple cell death pathways including apoptosis, necrosis, autophagy, and necroptosis. Therefore, understanding the interplay among these mechanisms is crucial for elucidating the cellular responses triggered by PDT and for identifying potential resistance processes that may arise. The objective of this study is to investigate the activation of distinct cell death pathways induced by methylene blue-based PDT in a murine model of breast cancer. A total of  $1.5 \times 10^6$  4T1 murine breast cancer cells were injected into the mammary gland of BALB/c mice. When the tumor mass reached a diameter of  $\sim 5$  mm, mice received two photodynamic therapy (PDT) sessions with intratumoral injections of methylene blue (MB) at 25  $\mu\text{M}$  or 50  $\mu\text{M}$ , followed by red laser irradiation (660 nm, 100 mW, 100 J/cm<sup>2</sup>, 28 s, energy per point of 2.8 J and continuous emission mode). Five groups were studied: control, MB25, MB50, PDT25, and PDT50. Twenty-four hours after the second PDT session, animals were euthanized and tumor tissues were collected for histological processing. Tissue sections were immunostained using antibodies (Invitrogen, Thermo Fisher) against MLKL, CASP3, and LC3, markers associated with necroptosis, apoptosis, and autophagy pathways, respectively. MLKL and LC3 immunostaining showed a significant increase in animals treated with MB50  $\mu\text{M}$  and PDT50 ( $p < 0.05$ ), while Caspase-3 expression showed no statistical difference compared with control group ( $p > 0.05$ ). Necroptosis, regulated by MLKL, is an immunogenic form of cell death that promotes the release of DAMPs, stimulating the immune system and potentially contributing to a long-lasting antitumor response. In contrast, autophagy is a dual-faceted mechanism that can either lead to programmed cell death or support cellular survival and adaptation following PDT. PDT effectively activated necroptosis and autophagy pathways, both of which may contribute to cell death or, alternatively, autophagy contributes as mechanisms of cellular adaptation and therapeutic escape. In contrast, Caspase-3 remained unchanged, indicating a limited role for apoptosis under these conditions. Notably, higher concentrations of MB (50  $\mu\text{M}$ ) exhibited dark toxicity, suggesting intrinsic cytotoxic effects independent of light.

**Keywords:** Photodynamic therapy, low-level laser, breast tumor, methylene blue**Study Type:** Estudo experimental em animais (Experimental study in animals)

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### **Photobiomodulation Therapy Attenuates Lung Inflammation: Insights From An Experimental Asthma-Copd Overlap Model**

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#### **Abstract**

**Introduction:** Asthma and Chronic Obstructive Pulmonary Disease (COPD) are pathologies triggered by different mechanisms, with distinct characteristics and symptoms of airway inflammation and obstruction. It has been demonstrated that patients can exhibit features of both asthma and COPD, which is termed Asthma-COPD Overlap (ACO). Photobiomodulation (PBM) has been used in the treatment of various pathologies, where the interaction of light with tissues leads to the modulation of biological functions and anti-inflammatory effects. Previous studies evaluating the effect of low-intensity LASER on COPD demonstrated a reduction in the levels of pro-inflammatory cytokines with a Th2 profile (IL-4, IL-5, and IL-13) and an increase in IL-10. Furthermore, a reduction in inflammation was observed in an experimental model of asthma with PBM. **Objective:** Based on these findings, we aim to evaluate the effect of laser therapy in an experimental model of ACO with PBM (660 nm). **Methodology:** BALB/c mice were subjected to the ACO induction protocol with the administration of House Dust Mite extract (asthma induction) and cigarette smoke extract (COPD induction), irradiated with 660 nm LASER to evaluate: 1) pulmonary inflammation in bronchoalveolar lavage fluid (BALF) through total and differential cell counts; 2) the levels of cytokines with Th1, Th2, Th17 profiles; 3) airway remodeling by histology. **Results:** Local FBM 6J reduced the number of inflammatory cells in BALF compared to the ACO group ( $17.7 \pm 1.4$  vs  $37.5 \pm 3.3$ , respectively). In contrast, the ACO group did not show a significant difference compared to the ACO + vascular FBM 20J ( $37.5 \pm 3.3$  vs  $28.0 \pm 4.6$ ). **Conclusion:** Local FBM at 6J attenuated pulmonary inflammation, in contrast, vascular PBM at 20J was not able to promote a significant anti-inflammatory response. Therefore, additional energy doses will be tested to determine the optimal vascular PBM parameters capable of inducing a therapeutic effect in this model. Overall, These findings support our hypothesis that PBM can reduce pulmonary inflammation in ACO, representing a promising therapeutic strategy without the adverse effects associated with conventional treatments.

**Keywords:** Asthma-COPD Overlap; Pulmonary Inflammation; Photobiomodulation.

**Study Type:** Estudo experimental em animais (Experimental study in animals)

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**THERAPEUTIC POTENTIAL OF PHOTOBIOMODULATION AND CORTICOSTEROIDS IN CHRONIC LUNG INFLAMMATION IN AN EXPERIMENTAL MODEL OF ASTHMA**

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**Abstract**

**INTRODUCTION:** Asthma is a heterogeneous disease characterized by chronic inflammation of the airways. The current treatment uses corticosteroids, which have side effects. Photobiomodulation therapy (BMT) can reduce inflammatory parameters, and is suggested in several lung diseases with no harmful effects. **OBJECTIVES:** To evaluate the effects of BMT-mixed or non-corticosteroid (CORT) in an experimental model of ovalbumin-induced chronic pulmonary allergic inflammation (OVA). **METHODS:** Balb/C mice were divided into 7 groups: Basal, CORT, FBM, OVA, OVA+CORT, OVA+FBM, OVA+CORT+FBM. Chronic pulmonary allergic inflammation was induced by subcutaneous immunization (SC) with 4 µg of ovalbumin (OVA), mixed with alum (days 0 and 14), and orotracheal challenge with 10 µg of OVA (three days a week for five weeks). The groups treated with TFBM were irradiated with a diode laser of 660 nm wavelength, 30mW of average radiant power and 3 J of radiant energy. In the groups treated with CORT, intranasal fluticasone furoate (0.0275 mg/dose) was used. Twenty-four hours after the last treatment, the inflammation, remodeling, and pulmonary function were analyzed. **RESULTS:** In relation to the OVA group, both treatments reduced the total number of cells ( $p < 0.05$ ), macrophages, neutrophils, lymphocytes and eosinophils, with the exception of macrophages in the OVA+CET group. With the use of TFBM, there was a reduction in the production of IL-4, IL-5, IL-1 $\beta$ , TNF- $\alpha$  and IL-13, in addition to an increase in IL-10 in BAL ( $p < 0.05$ ) in all treated groups. In the OVA + CORT, OVA + FBM and OVA + CORT + FBM groups, there was a reduction in collagen deposition ( $p < 0.05$ ) and mucus production ( $p < 0.05$ ) compared to the OVA group. Also in the groups in which BMT-MTT was applied, there was an improvement in pulmonary function in relation to the AVO and OVA + CORT groups ( $p < 0.05$ ). **CONCLUSION:** We demonstrated that both therapies are efficient, although BMT, alone or in combination with conventional treatment, seems to have a promising role in the treatment of asthma.

**Keywords:** asthma, photobiomodulation, pulmonary inflammation, corticosteroid.

**Study Type:** Estudo experimental em animais (Experimental study in animals)

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**THERAPEUTIC POTENTIAL OF PHOTOBIOMODULATION THERAPY ON THE  
INFLAMMATORY RESPONSE IN AN EXPERIMENTAL MODEL OF SILICA-INDUCED  
PULMONARY FIBROSIS**

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**Abstract**

Pulmonary fibrosis is a chronic and progressive disease characterized by the replacement of normal lung parenchyma with dense fibrotic connective tissue, resulting from an abnormal tissue repair response to recurrent alveolar epithelial injury. This process leads to structural disorganization of the lung, thickening of the alveolar septa, and irreversible loss of elasticity and gas exchange efficiency. Conventional treatment involves the use of anti-inflammatory corticosteroids, antibiotics, and respiratory physiotherapy, and may include oxygen therapy or lung transplantation in advanced stages. Previous studies have demonstrated the beneficial effects of photobiomodulation therapy (PBMT) in experimental models of asthma and chronic obstructive pulmonary disease (COPD). However, few studies have investigated its therapeutic potential in pulmonary fibrosis, particularly in silica-induced experimental models. Therefore, the present study aimed to evaluate the effects of PBMT in an experimental model of pulmonary fibrosis induced by silicon dioxide (SiO<sub>2</sub>). **Materials and Methods:** Male C57BL/6 mice (~7 weeks old; 25 g) were randomly divided into six experimental groups: Basal, Control + PBMT (3 J, local), Control + PBMT (10 J, vascular), Fibrosis, Fibrosis + PBMT (3 J, local), and Fibrosis + PBMT (10 J, vascular). Fibrosis was induced by orotracheal instillation of SiO<sub>2</sub> particles (0.5–10 µm; ~80% between 1–5 µm; Sigma) in 50 µL of sterile saline solution (0.9%). After 40 days, PBMT was administered for seven consecutive days using a diode laser (660 nm, 100 mW). Local irradiation was performed with 3 J for 30 s at three points (trachea, right and left lung lobes), while vascular irradiation was performed with 10 J for 100 s in the caudal region. On day 48, animals were euthanized for total and differential cell counts in bronchoalveolar lavage fluid (BAL) and peripheral blood. **Results:** Induction of pulmonary fibrosis promoted a significant increase in total cells in the BAL compared with the basal group ( $p < 0.001$ ). Photobiomodulation therapy, both local (3 J) and systemic (10 J), significantly reduced total cell counts, macrophages, neutrophils, and lymphocytes recovered from the BAL ( $p < 0.01$ ). Conversely, total circulating leukocytes increased after local PBMT (3 J) in the fibrosis group compared with untreated fibrotic animals ( $p < 0.01$ ). These findings demonstrate that photobiomodulation therapy exerts a modulatory and anti-inflammatory effect, attenuating pulmonary inflammation and possibly stimulating tissue repair mechanisms within the lung parenchyma.

**Keywords:** Pulmonary inflammation, pulmonary fibrosis, photobiomodulation therapy.

**Study Type:** Estudo experimental em animais (Experimental study in animals)

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**ANALYSIS OF THE ABRASIVE EFFECT OF STANNOUS FLUORIDE TOOTHPASTES ON COMPOSITE RESINS: IN VITRO STUDY USING SPECKLE TECHNIQUE**

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**Abstract**

**Introduction:** Composite resins are among the most used restorative materials in modern dentistry due to their esthetic qualities, adhesion, and minimally invasive approach. However, daily brushing with abrasive toothpastes may lead to surface degradation, loss of gloss, and increased roughness of restorations. Stannous fluoride ( $\text{SnF}_2$ ) provides anticariogenic and antierosive protection by forming a tin-rich protective layer, but little is known about its influence on composite surfaces with different abrasivity levels. **Objective:** This in vitro study will evaluate the abrasive effect of  $\text{SnF}_2$ -containing toothpastes with different abrasivity levels on nanofilled composite resin samples using optical profilometry and laser speckle imaging. **Material and Methods:** Forty specimens of Filtek Z350 XT (3M ESPE) will be fabricated and divided into four groups ( $n = 10$ ): Sensodyne Sensibilidade e Gengivas (RDA  $52.89 \pm 1.66$ ), Oral-B Gengiva Detox (RDA  $148.49 \pm 7.92$ ), Colgate Total Prevenção Ativa Fresh Mint (RDA  $172.58 \pm 2.73$ ), and a negative-control group (water only). Specimens will undergo 20,000 brushing cycles (two-year simulation) in an automated brushing machine according to ISO 11609. Surface changes will be measured by optical profilometry and analyzed through laser speckle imaging.

**Keywords:** Composite resin; stannous fluoride; toothpaste abrasivity; laser speckle imaging; surface roughness.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)



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**COMPARATIVE EVALUATION OF CELL VIABILITY AND PHOTODYNAMIC EFFECTS OF BUTYL TOLUIDINE BLUE O, TOLUIDINE BLUE O, AND METHYLENE BLUE IN MURINE L929 FIBROBLASTS**

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**Abstract**

**Background:** Antimicrobial photodynamic therapy is a promising strategy against infections under rising antimicrobial resistance. Photosensitizers generate reactive oxygen species upon light activation, providing broad antimicrobial effects with minimal systemic impact. They should be chemically pure, stable, and efficient in producing singlet oxygen within the 550–700 nm range. Butyl toluidine blue O, a TBO derivative, absorbs maximally at 637 nm, shows enhanced singlet oxygen generation, broad antimicrobial activity, and reduced dimerization, surpassing conventional antiseptics such as chlorhexidine. **Aim:** This study compared the effects of butyl toluidine blue O (BuTBO), toluidine blue O (TBO), and methylene blue (MB) on L929 fibroblast viability. Concentration–response assays were conducted in the dark to assess cytocompatibility, followed by evaluation of phototoxic effects under irradiation. **Methods:** Fibroblasts were seeded in 96-well plates ( $2 \times 10^4$  cells/well) and, after 24 h, exposed to butyl toluidine blue O, toluidine blue O, or methylene blue (0.39–100  $\mu\text{M}$ ). Cell viability was assessed by MTT immediately and on parallel plates after 24 h, while crystal violet staining was performed on separate plates immediately to quantify adherent cells. For photodynamic therapy, cells were treated with 25  $\mu\text{M}$  for 5 min, irradiated with red LED light, and analyzed by MTT. Parallel plates were stained with crystal violet for adherent biomass. Kolmogorov–Smirnov test assessed normality; ANOVA with Bonferroni post hoc assessed group differences. **Results:** Without irradiation, all photosensitizers showed no cytotoxicity by MTT ( $\text{OD} \approx 1.0$ ,  $p > 0.05$ ) and maintained adherent cell density by crystal violet ( $\text{OD} 1.2$ – $1.4$ ,  $p > 0.05$ ), indicating preserved viability across all concentrations. PDT reduced mitochondrial activity, most for BuTBO ( $\text{OD} \approx 0.6$ ), then TBO ( $\approx 0.75$ ) and MB ( $\approx 0.8$ ), with BuTBO significantly lower ( $p < 0.001$ ). Crystal violet showed no loss of adherent cells ( $p > 0.05$ ). **Conclusion:** Despite causing acute metabolic reduction under PDT, butyl toluidine blue O maintained cytocompatibility, demonstrating its effectiveness and potential for clinical applications.

**Keywords:** photochemotherapy, cell survival, photosensitizing agents, fibroblasts, coloring agents, cells cultured.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

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**DOSIMETRIC EVALUATION OF ANTIMICROBIAL PHOTODYNAMIC THERAPY (aPDT) IN CANDIDA ALBICANS BIOFILMS USING METHYLENE BLUE IN A POLYMERIC FORMULATION**

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**Abstract**

**Introduction:** *Candida albicans* infections remain a major clinical concern due to rising resistance to conventional antifungals such as fluconazole and nystatin. The biofilm architecture further enhances this resistance by restricting drug diffusion and protecting fungal cells. Antimicrobial Photodynamic Therapy (aPDT) has emerged as a promising alternative, combining a photosensitizer and light to generate reactive oxygen species capable of microbial destruction without inducing resistance. Methylene blue (MB), particularly when combined with sodium dodecyl sulfate (SDS), enhances singlet oxygen production and photodynamic efficiency. Polymeric formulations improve bioadhesion and photosensitizer retention, favoring greater interaction with fungal biofilms. However, optimal irradiation parameters for this combination remain undefined. **Objective:** To perform a preliminary dosimetry evaluation of aPDT using MB in a polymeric formulation against *C. albicans* biofilms, comparing 3- and 5-minute laser irradiation under stationary and scanning conditions. **Methodology:** *C. albicans* (ATCC 90028) biofilms were developed in 48-well plates and treated with MB (0.01% in aqueous or polymeric formulation) for 5 min in the dark, followed by irradiation with a 660 nm diode laser (100 mW, irradiance 35,714 mW/cm<sup>2</sup>, spot area 0.0028 cm<sup>2</sup>). Irradiation was done for 3 or 5 min, either stationary (fixed point) or scanning. Control groups included dark and laser-only conditions. After treatment, biofilms were dispersed, serially diluted, and plated on Sabouraud agar for CFU counting. **Results:** aPDT led to greater reduction in viable fungal cells compared to dark controls. For 3 min irradiation, the mean log reduction was 1.0 log for both formulations, whereas 5 min resulted in ~1.6 log reduction for the polymeric formulation, with no additional effect for the aqueous one. Scanning irradiation yielded comparable results for aqueous and polymeric MB formulations but slightly superior outcomes to stationary exposure at 3 min (1.7 vs 1.1 log reduction). At 5 min, no further improvement was detected. **Conclusion:** The optimized aPDT protocol using MB in polymeric formulation showed effective antifungal activity against *C. albicans* biofilms, particularly under 3 min scanning irradiation. The lack of further improvement at 5 min suggests photobleaching. These findings highlight the relevance of dosimetry optimization to achieve homogeneous light distribution and maximize antifungal efficacy.

**Keywords:** antimicrobial photodynamic therapy, *Candida albicans*, methylene blue, dosimetry, sodium dodecyl sulfate.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

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**EFFECT OF MONOWAVE LED AND POLIWAVE LED ON THE POLYMERIZATION AND PROPERTIES OF BIOACTIVE DENTAL RESINS: AN IN-VITRO STUDY**

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**Abstract**

**Introduction:** Photopolymerization is crucial for the durability of dental restorations, and bioactive resins have gained attention for their ability to release ions that aid in enamel remineralization. However, the efficiency of polymerization can vary depending on the light source used. A comparison between Monowave LED (single wavelength) and Polywave LED (multiple wavelengths) may influence the degree of conversion and the mechanical properties of the resins. **Objective:** This study aims to evaluate the impact of Monowave LED and Polywave LED light sources on the photopolymerization of bioactive resins, analyzing the degree of monomer conversion, microhardness, abrasion resistance, and spectrophotometry of the resins. **Methodology:** Test specimens will be prepared using a bioactive resin from Shofu. The specimens will be photopolymerized using Monowave LED (wavelength around 470 nm) and Polywave LED (wavelengths ranging from 385 to 515 nm), divided into two groups according to the light source used. The degree of conversion will be assessed by Fourier Transform Infrared Spectroscopy (FT-IR), microhardness will be measured using the Knoop test, abrasion resistance will be tested through simulated brushing, and the spectrophotometry and speckle of the resins will also be evaluated. **Expected Results:** It is expected that the specimens photopolymerized with Polywave LED will show a higher degree of conversion, superior microhardness, and better abrasion resistance compared to those polymerized with Monowave LED, which may present lower curing depth. Based on the results, clinical recommendations will be provided for the optimal choice of light source to enhance the effectiveness and durability of bioactive resins in dental restorations.

**Keywords:** Bioactive resin, Monowave LED, Polywave LED, Photopolymerization, Speckle.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)



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**EFFECTS OF LOW-POWER RED AND NEAR-INFRARED LASER ON THE NON-CANCEROUS MAMMARY EPITHELIUM CELL LINE MCF10A**

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**Abstract**

**Background:** Low-power lasers emit non-ionizing radiation at specific wavelengths whose therapeutic utility lies in the specificity of their monochromatic radiation for endogenous photoacceptors, which confers the ability to induce photobiomodulation (PBM). Although some studies have reported the use of PBM in the treatment of breast lymphedema and radiodermatitis, there is a lack of evidence regarding the safety of applying low-level laser therapy (LLLT) to mammary epithelial cells, particularly in terms of its potential to induce adverse effects, including proliferation, cell death, or even malignant transformation of mammary epithelia. **AIM:** We aimed to examine the biological effects of red and infrared LLLT on the cellular viability, proliferation, and oxidative stress levels of mammary epithelial cells. **METHODS:** MCF10A cells were subjected to irradiation with red (660 nm) and near-infrared (808 nm) lasers at fluences of 0.9 and 1.9 J/cm<sup>2</sup>, followed by assays to examine the colony formation potential, WST-1-based proliferation rate, and reactive oxygen species (ROS) levels' detection using DCFH2-DA probe combined with flow cytometry analysis. Data were acquired from at least three independent experiments and analyzed using ANOVA test with  $p < 0.05$  (two-sided) considered statistically significant. **RESULTS:** No significant changes were observed in cell viability compared to the control group ( $p = 0.961$ ). Accordingly, no significant changes were observed in cell proliferation compared to the control counterpart ( $p = 0.318$ ). Regarding ROS production, absolute levels showed a non-statistically significant decrease ( $p = 0.0753$ ) in irradiated conditions compared to the control group, while relative ROS levels reported a significant reduction in cells exposed to 808 nm at 1.9 J/cm<sup>2</sup>, suggesting a potential antioxidant effect of this condition. **CONCLUSION:** Our findings suggest that there are no changes in either the viability or proliferation of mammary epithelial cells exposed to LLLT. Also, we demonstrated that these parameters did not induce oxidative stress in this model. Therefore, we demonstrated that the used laser protocol neither contributes to the malignant transformation nor induces cell death of mammary epithelial cells. In perspective, our findings support the safety of PBM application in breast diseases.

**Keywords:** Breast, epithelia, photobiomodulation, proliferation, laser.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

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**EVALUATION OF INFLAMMATORY INFILTRATE IN ORAL SQUAMOUS CELL CARCINOMA FOLLOWING PHOTODYNAMIC THERAPY WITH 5-ALA: AN IN VIVO STUDY.**

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**Abstract**

Photodynamic therapy (PDT) combines light, oxygen, and a photosensitizer (PS) to generate reactive oxygen species (ROS), which can destroy tumor cells and modulate the tumor microenvironment. Oral squamous cell carcinoma (OSCC) is an aggressive cancer with a high recurrence rate. Although PDT has shown promise, its immunological effects in vivo remain incompletely understood. This study aims to investigate the immune response induced by PDT in an in vivo experimental model of OSCC. Forty male C57BL/6 mice will be randomly assigned to four groups: control (n=10), 5-ALA (n=10), laser (n=10), and PDT (n=10). Tumors will be induced using the MOC2 cell line, derived from chemically induced OSCC in C57BL/6 mice. MOC2 is characterized by aggressive growth, low immunogenicity, and histopathological similarity to human OSCC, making it a widely used model in PDT research. A total of  $5 \times 10^5$  MOC2 cells will be resuspended in 100  $\mu$ L of PBS and subcutaneously inoculated into the right dorsal region of each animal. Tumor growth will be monitored three times per week using a digital caliper. Once tumors reach a volume between 70 and 100 mm<sup>3</sup>, treatment will be administered according to group allocation. The 5-ALA and PDT groups will receive 100 mg/kg of 5-ALA diluted in water via intraperitoneal injection and kept in the dark for 4 hours. The laser and PDT groups will undergo a single irradiation using the Photon Laser device (DMC, Brazil) with the following parameters:  $660 \pm 20$  nm, 100 mW, 18 J, 90 J/cm<sup>2</sup>, 180 s. Euthanasia will be performed at 7 and 15 days post-treatment, and tumors will be collected for immunohistochemical analysis. Cellular infiltrates—lymphocytes, macrophages, NK cells, and neutrophils—will be characterized to assess the role of the immune response in PDT efficacy. Tissue sections will be analyzed in five fields (200x magnification) using ImageJ software, and data will be subjected to statistical analysis. The findings are expected to enhance understanding of the immunological mechanisms associated with PDT, highlighting its potential as an immunomodulatory antitumor therapy.

**Keywords:** oral squamous cell carcinoma, photodynamic therapy, inflammatory infiltrate, in vivo study.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

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**IMPACT OF VASCULAR PHOTOBIOMODULATION ON BONE MARROW AND BLOOD RECRUITMENT OF CLASSICAL MONOCYTES AND MCP-1 IN THE ACUTE PHASE AFTER IN VIVO MUSCLE INJURY**

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**Abstract**

BACKGROUND: SKELETAL MUSCLE IS FREQUENTLY INJURED BUT DEMONSTRATES A REMARKABLE CAPACITY FOR REGENERATION. AFTER INJURY, AN INTENSE INFLAMMATORY RESPONSE OCCURS WITH RECRUITMENT OF NEUTROPHILS AND MACROPHAGES, MEDIATED BY CHEMOKINES SUCH AS MCP-1. VASCULAR PHOTOBIOMODULATION (VPBM) HAS SHOWN POTENTIAL TO MODULATE INFLAMMATORY PROCESSES AND PROMOTE MUSCLE REPAIR. AIM: THIS STUDY AIMS TO EVALUATE THE EFFECT OF VPBM WITH LOW-LEVEL LASER THERAPY (LLLT) ON THE RECRUITMENT OF BONE MARROW AND BLOOD MONOCYTES, AS WELL AS MCP-1 SYNTHESIS, AT DIFFERENT APPLICATION TIMES AFTER ACUTE MUSCLE INJURY IN RATS. METHODS:/ RESULTS: MALE WISTAR RATS WERE RANDOMLY DIVIDED INTO: INJURY, PREVIOUS VPBM+INJURY, AND INJURY+ POST-VPBM. ANIMALS RECEIVED VPBM USING AN ALGAAS DIODE LASER (780 NM, 40 MW, 0.04 CM<sup>2</sup>, 3.2 J, 80 S) ON THE TAIL ARTERY/VEIN. SUBSEQUENTLY, THE RATS WERE SUBMITTED TO A CRYOINJURY ON THE TIBIALIS ANTERIOR MUSCLES (TA) AND WERE EUTHANIZED AT 1- AND 2-DAYS POST-INJURY. TA MUSCLE SAMPLES WERE COLLECTED, AND ELISA DETERMINE THE PROTEIN EXPRESSION OF MCP-1. BONE MARROW SAMPLES WERE USED TO ASSESS CLASSICAL MONOCYTES (CD43LOWHIS48HIGH) AND QUANTIFICATION BY FLOW CYTOMETRY. THE DATA WERE SUBMITTED TO STATISTICAL ANALYSIS. RESULTS: REGARDING THE PREDOMINANCE OF CLASSICAL BONE MARROW MONOCYTES (CD43LOW/HIS48HIGH), ON DAY 1, THE INJURY + POST-VPBM GROUP SHOWED A DECREASE IN PERCENTAGE IN COMPARISON TO THE INJURY AND PREVIOUS VPBM+INJURY GROUPS. AFTER 2 DAYS, BOTH TREATED GROUPS SHOWED AN INCREASE COMPARED TO THE INJURY GROUP. MCP-1 PROTEIN LEVELS WERE HIGHER IN THE INJURY + POST-VPBM GROUP WHEN COMPARED TO THE OTHER EXPERIMENTAL GROUPS ON DAY 1. ON DAY 2, AN INVERSION WAS SHOWN IN THE RESPONSES OF TREATED GROUPS, EXHIBITING HIGHER MCP-1 SYNTHESIS AND RECRUITMENT OF THE CIRCULATING MONOCYTES IN THE PREVIOUS VPBM+INJURY GROUP. CONCLUSION: VPBM INFLUENCES THE RECRUITMENT OF CLASSICAL MONOCYTES IN BONE MARROW, BLOOD MONOCYTES, AND MCP-1 LEVELS AFTER MUSCLE INJURY, WITH DISTINCT TEMPORAL EFFECTS DEPENDING ON THE TIMING OF THE IRRADIATION.

**Keywords:** Vascular photobiomodulation, modified ILIB, muscle injury, protein expression, MCP-1, monocytes.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

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**PHOTOBIOMODULATION AS A THERAPEUTIC APPROACH IN ASTHMA AND COPD OVERLAP SYNDROME: AN IN VITRO STUDY**

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**Abstract**

Asthma and COPD (Chronic Obstructive Pulmonary Disease) are chronic inflammatory conditions with high prevalence worldwide, significantly impacting patients' quality of life. Asthma-COPD Overlap Syndrome (ACOS) can be diagnosed in patients who exhibit characteristics of both conditions. However, the clinical manifestations are not yet fully recognized or clearly defined. The treatment is based on behavioral interventions, along with pharmacological approaches, primarily involving the use of inhaled glucocorticoids. Photobiomodulation (PBM) therapy uses low-intensity light to modulate cellular pathways, exhibiting anti-inflammatory activity and potential beneficial effects in pulmonary diseases and other pathologies. This study aimed to evaluate the effects of PBM on the inflammatory process in an in vitro experimental model of ACOS. Human bronchial epithelial cells (BEAS-2B) were cultured and plated ( $5 \times 10^4$  cells/well) in 24-well plates and distributed into six experimental groups (n=4). After 24 hours of culture, the cells were incubated or not with cigarette smoke extract (CSE, 2.5%; 100  $\mu$ l) and house dust mite (HDM, 1g/ml). After 1 hour, the plates were irradiated with a diode laser (660nm, 30mW, 5, 4J, 180s) or dexamethasone (DEXA) diluted in DMSO ( $10^{-7}$  M). The groups were divided into: Baseline group; CSE + HDM - positive control (ACOS group); DEXA-treated cells; Laser-irradiated cells; CSE + HDM + DEXA group; CSE + HDM + LASER group. After 24 hours, cytokine levels were quantified by ELISA. A significant reduction ( $p < 0,05$ ) was observed in IL-1 $\beta$ , IL-6, TNF- $\alpha$ , IL-4, IL-5, IL-13, IL-17, IL-21 and IL-23 levels, along with a significant increase ( $p < 0,05$ ) in IL-10 and IFN- $\gamma$  levels in laser-irradiated ACOS group cells compared to the positive control group. These results suggest that photobiomodulation may beneficially modulate the inflammation in ACOS in vitro. However, additional studies are needed to confirm its clinical applicability and, in the future, consider photobiomodulation as a complementary therapeutic alternative for this condition.

**Keywords:** Asthma-COPD Overlap Syndrome, ACOS, Photobiomodulation Therapy.**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

**PHOTOBIMODULATION AS AN ADJUVANT TO DEXAMETHASONE THERAPY FOR  
MODULATING PRO-INFLAMMATORY M1 MACROPHAGES.**

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**Abstract**

**Introduction:** Inflammation is a fundamental homeostatic process, the dysregulation of which is implicated in the pathophysiology of numerous chronic diseases. The functional plasticity of macrophages, particularly their polarization towards pro-inflammatory (M1) or anti-inflammatory (M2) phenotypes, is pivotal in this process. Dexamethasone (DEXA), a potent glucocorticoid, is standard therapy for suppressing inflammation but exhibits notable cytotoxicity, limiting its therapeutic window. Photobiomodulation (PBM) emerges as a non-invasive therapeutic modality with the potential to modulate inflammatory cascades and mitigate oxidative stress with a favorable safety profile. **OBJECTIVE:** This study aimed to investigate the immunomodulatory and cytoprotective effects of PBM, alone and in combination with DEXA, on murine J774 macrophages polarized towards an M1 pro-inflammatory phenotype. Specifically, we assessed cell viability and the secretion of hallmark pro-inflammatory cytokines. **METHODOLOGY:** The murine macrophage cell line J774 was stratified into seven experimental groups. M1 polarization was induced by co-stimulation with LPS (1 µg/mL) and IFN-γ (0.2 µg/mL). PBM was administered using a 780 nm diode laser (70 mW, 17.5 J/cm<sup>2</sup>). Cellular viability was quantified via MTT assay, and supernatant concentrations of TNF-α and IL-6 were determined by ELISA at 24 and 48-hour time points. **RESULTS:** After 24 hours, the combined PBM and DEXA (2 µM) treatment exhibited significantly enhanced cellular viability compared to DEXA monotherapy. While DEXA effectively suppressed cytokine secretion, PBM co-administration partially restored cellular metabolic activity. Notably, the cytoprotective effect of PBM persisted at the 48-hour time point, indicating a sustained modulatory effect. **CONCLUSION:** Our findings elucidate a synergistic interaction between PBM and low-concentration DEXA, characterized by enhanced macrophage viability without compromising the potent anti-inflammatory action of the glucocorticoid. Consequently, PBM presents as a promising adjuvant strategy to broaden the therapeutic index of glucocorticoid treatments. These results underscore the therapeutic potential of PBM in immunomodulation. Further investigation into the underlying molecular pathways via quantitative PCR is warranted.

**Keywords:** Photobiomodulation, Dexamethasone , M1 Macrophages, Inflammation, Cytokine Modulation.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)



**RED AND INFRA-RED LASER EXPOSURE UPREGULATES NRF2 AND REDUCES PROLIFERATION IN TRIPLE-NEGATIVE HCC-1937 BREAST CANCER CELLS**

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**Abstract**

Background: Breast cancer is the leading cause of cancer-related death among women. Among the primary risk factors are mutations in the BRCA1. Recent studies have shown that Photobiomodulation (PBM) could potentially induce mitotic recombination events and sensitize cancer cells. AIM: We aimed to examine the effects of low-intensity therapeutic lasers on inducing programmed cell death and oxidative stress in triple-negative BRCA1-mutated BC cells. METHODS: Human BRCA1-mutant BC HCC-1937 cells were exposed to red and infrared lasers at 0.9 and 1.9 J. Cellular viability was assessed using the WST1 method, and a colony formation assay was conducted to evaluate the effects of laser exposure on cell proliferation. Apoptosis and necrosis induction were assessed by flow cytometry using Annexin V and 7AAD, respectively. The oxidative profile was evaluated using the fluorescent marker DCFH-DA detected by flow cytometry. Additionally, the mRNA levels of Superoxide Dismutase (SOD1), catalase (CAT), NAD(P)H quinone Oxidoreductase 1 (NQO1), and Kelch-like ECH-associated Protein 1 (KEAP1) were evaluated by RT-qPCR. Then, protein extracts were separated by SDS-PAGE, incubated with anti-Nrf2 antibody to assess its levels. RESULTS: Proliferation and viability assays did not show statistically significant changes in irradiated cells; however, the clonogenic assay revealed a significant reduction in irradiated conditions. Flow cytometry analysis indicated an increase in apoptosis when cells were exposed to 660 nm at 0.9 J and at 1.9 J. Although it was not statistically significant, we observed an increase in CAT, SOD1, NQO1 and KEAP1 in all laser-exposure conditions. Immunoblotting demonstrated an overexpression of NRF2 at 660 and 808 nm at 1.9 J. CONCLUSION: Our findings suggest that PBM reduces proliferation, induces apoptosis, and the overexpression of genes related to oxidative stress, contributing to the understanding of the mechanisms involved in PBM in BRCA1-deficient tumor cells.

**Keywords:** Breast Cancer, Oxidative Stress, Photomodulation, BRCA1, NRF2.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)



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**RED (660NM) AND NEAR-INFRARED (808 NM) LASER EXPOSURE ACTIVATES PHOSPHO-NF-KAPPA B/P65 IN TRIPLE-NEGATIVE BRCA1-MUTANT HCC-1937 BREAST CANCER CELLS**

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**Abstract**

Background: Breast cancer (BC) is a multifactorial disease that leads to cancer-associated death in women worldwide. A key risk factor for BC is mutation in the BRCA1 gene, which plays a critical role in DNA double-strand repair through homologous recombination. Recent studies have demonstrated photobiomodulation (PBM) as a promising treatment for inflammatory conditions. Thus, we hypothesized whether it could influence NF-kappaB activity and the expression of inflammatory cytokines regulated by this transcription factor in BC. AIM: We sought to investigate the effects of PBM on NF-kappaB signaling in triple-negative BRCA1-mutated breast cancer cells. METHODS: Human BC HCC1937 cells, BRCA1-mutant (c. 5266dupC), were exposed to red (660 nm) and near-infrared (808 nm) lasers at 0.9 and 1.9 J/cm<sup>2</sup> using the Photon Lase III (DMC) device. After 48h, total protein was extracted, separated by SDS-PAGE, transferred to PVDF membranes, and then incubated with anti-NF-kappaB/p65 and anti-phospho NF-kappaB/p65 (Ser536) antibodies, followed by incubation with the appropriate secondary antibody. GAPDH was used as a loading control. Total RNA was isolated from cells using TRIzol. One ug of RNA was reverse-transcribed into cDNA to assess the mRNA levels of the downstream NF-kappaB regulatory targets, including the cytokines IL-1B, IL-6 and IL-8, by RT-qPCR. GAPDH mRNA levels were used as a reference to calculate expression variation using the 2-DeltaDeltaCt method. Statistical analysis (ANOVA, p<0.05 considered significant) was performed using GraphPad Prism 9. RESULTS: Immunoblotting assays showed increased levels of p-p65 (p=0.082) in all conditions in HCC1937. Although it was not statistically significant, we observed upregulation of IL1B (3.23-fold), IL6 (1.69-fold), and IL8 (8.31-fold) in cells exposed to near-infrared (808 nm) at 0.9 J/cm<sup>2</sup> compared to their control counterparts. CONCLUSION: Our experiments demonstrated the upregulation of p-NF-kappaB/p65 and suggest an upregulation of the pro-inflammatory cytokines regulated by this transcription factor in BRCA1-mutant HCC-1937 cells following exposure to near-infrared laser. Altogether, our findings provide the first evidence that near-infrared laser exposure induces NF-kappaB pathway activation in BRCA1-mutant BC cells, which would contribute to the comprehension of the mechanisms involved in photobiomodulation in tumor cells.

**Keywords:** Breast cancer, BRCA, NFkappaB, Laser, Photobiomodulation

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

**TEMPORAL CHARACTERIZATION OF CANDIDA ALBICANS BIOFILMS AND METHYLENE BLUE UPTAKE FOR OPTIMIZING ANTIMICROBIAL PHOTODYNAMIC THERAPY**

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**Abstract**

Candidiasis, a fungal infection mainly caused by *Candida albicans*, is a frequent opportunistic condition that significantly affects immunocompromised individuals, compromising mucosal integrity and quality of life. Despite the availability of antifungal drugs, their effectiveness is increasingly limited by the emergence of resistant strains and the structural protection provided by biofilms, which reduce drug penetration and promote persistent infections. These limitations highlight the urgent need for complementary approaches. Among them, antimicrobial photodynamic therapy (aPDT) stands out as a promising non-invasive strategy that combines a photosensitizer (PS), visible light, and molecular oxygen to generate reactive oxygen species (ROS) capable of destroying microbial cells through oxidative damage without inducing resistance. This study aimed to investigate the temporal development of *C. albicans* biofilms and to determine optimal pre-irradiation conditions for aPDT by analyzing methylene blue (MB) uptake. Biofilms were grown in vitro for 6, 12, and 24 hours and analyzed by optical density (OD) and crystal violet staining to assess growth and maturation. MB internalization was evaluated at concentrations of 0.1 mM and 1 mM after 1, 5, and 10 minutes of incubation, with absorbance measured spectrophotometrically. At 6 hours, biofilm formation was incipient; at 12 hours, growth increased sharply but with high variability among replicates. After 24 hours, biofilms became homogeneous and reached a mature, stable phase, confirmed by crystal violet quantification. The 1 mM MB concentration resulted in greater cellular absorption than 0.1 mM, and uptake increased proportionally with incubation time, with 10 minutes yielding the highest internalization. These findings establish 24 hours as the optimal period for obtaining standardized mature *C. albicans* biofilms and indicate that using 1 mM methylene blue with a 10-minute pre-irradiation enhances PS uptake efficiency. Together, these optimized parameters strengthen the experimental basis for subsequent aPDT assays and may contribute to the development of more effective and resistance-preventive antifungal therapies.

**Keywords:** Biophotonics, Microbial resistance, Photosensitizer.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

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**EFFECT OF BLUE LED PHOTOBIOMODULATION ON TUMOR BEHAVIOR AND CANCER STEMNESS IN ORAL SQUAMOUS CARCINOMA CELL LINES**

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**Abstract**

Oral squamous cell carcinoma (OSCC) is a highly aggressive malignancy characterized by poor prognosis and resistance to conventional therapies. Studies have shown that OSCC tumors contain a subpopulation of cancer stem cells (CSCs), responsible for sustaining tumor growth, metastasis, and contributing to treatment failure. Recently, blue LED photobiomodulation (BL) has demonstrated antitumor effects; however, its impact on OSCC, particularly in the CSC population, remains largely unexplored. Objective: To evaluate the effect of BL photobiomodulation on tumor behavior and CSC properties in OSCC. Methodology: Two OSCC cell lines, SCC9 and HSC3, were irradiated with blue LED (460 nm, 350 mW, 105, 168, and 210 J/cm<sup>2</sup>). After 24 hours, cell viability was evaluated using MTS and crystal violet assays. Necrosis and apoptosis were analyzed by Annexin V and DAPI stain by flow cytometry; migration capacity was assessed through a wound-healing assay; and CSCs properties were examined by the colony and sphere formation assays, RT-qPCR for CSC biomarkers (BMI1, CD44, OCT4, and NANOG), and flow cytometric for CD44 and ESA expression. Results: Cellular viability in both cell lines was reduced after BL irradiation. Apoptosis increased in SCC9 cells with BL exposure but remained the same in HSC3 cells. On the other hand, BL significantly reduced the migration capacity of both cell lines. Regarding CSC properties, BL decreased the number of colonies in SCC9 cells only, at both 105 J/cm<sup>2</sup> and 210 J/cm<sup>2</sup> irradiation parameters, while the number of spheres decreased in both cell lines. Expression of BMI1, OCT4, NANOG and CD44 genes was not altered after BL irradiation. BL also did not affect the frequency of CD44<sup>high</sup>/ESA<sup>high</sup> cells in both cell lines, however, at 210 J/cm<sup>2</sup>, the frequency of CD44<sup>low</sup> cells in SCC9 was higher, which is associated with a more differentiated phenotype. Conclusion: The results indicate that blue LED photobiomodulation exerts antitumor effects on oral squamous cell carcinoma, reducing tumor cell viability, migration, and self-renewal, and increasing apoptosis. It also decreased sphere and colony formation, especially in the SCC9 cell line. These findings suggest that BL can modulate tumor behavior in OSCC without significantly altering CSC-associated gene expression, highlighting its potential as a complementary therapy in controlling OSCC progression and justifying further investigation in preclinical and clinical settings.

**Keywords:** Oral squamous cell carcinoma, photobiomodulation, cancer stem cells, Blue Light.

**Study Type:** Estudo experimental in vitro (células) (Experimental study in vitro - cells)

## EFFECTS OF PHOTOBIOMODULATION ON THE VIABILITY, PROLIFERATION AND MIGRATION OF C2C12 MYOBLASTS EXPOSED TO A HIGH CONCENTRATION OF DEXAMETHASONE

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### Abstract

**Introduction:** Skeletal muscle function depends on balanced proliferation, differentiation, and regeneration, processes that can be impaired by prolonged exposure to medications such as dexamethasone (DEXA), a potent glucocorticoid associated with muscle atrophy. Photobiomodulation (PBM) has recognized anti-inflammatory and regenerative effects, improving muscle cell viability and mitochondrial function. However, its potential to counteract glucocorticoid-induced muscle atrophy remains unclear. **OBJECTIVE:** To investigate the effects of PBM on the viability, proliferation, and migration of C2C12 myoblasts exposed to 200  $\mu$ M DEXA. **METHODS:** C2C12 myoblasts were cultured in DMEM supplemented with 10% fetal bovine serum to promote cell proliferation and 2% horse serum to induce differentiation. Concomitantly with differentiation induction, PBM and dexamethasone were applied according to the experimental groups: Control, PBM, DEXA 200  $\mu$ M, and DEXA 200  $\mu$ M + PBM. PBM was performed using a GaAlAs diode laser (780 nm, 70 mW), delivering a total energy of 1.05 J with an exposure time of 15 seconds. The evaluation periods were 24, 48, and 72 hours for viability (MTT) and proliferation (crystal violet) assays, and 0, 6, 12, and 24 hours for migration (wound healing assay). Three independent experiments were performed, and the results were subjected to statistical analysis (ANOVA/Tukey). **RESULTS:** Treatment with 200  $\mu$ M DEXA significantly reduced the viability and migratory capacity of C2C12 myoblasts, indicating cytotoxic effects associated with the high concentration of the drug. PBM, in both conditions, was unable to significantly modulate these parameters compared to the control. However, in the proliferation assay, a more protective effect of PBM was observed in cells exposed to DEXA at all evaluation periods. **CONCLUSION:** Photobiomodulation therapy (PBM) demonstrated a protective and regenerative role in muscle cells exposed to dexamethasone, promoting increased cell proliferation at all time points analyzed and increasing migratory capacity after 24 hours. These effects indicate that PBM can neutralize the cytotoxic and antiproliferative actions of dexamethasone, mitigating its impact on the regenerative potential of C2C12 myoblasts. In contrast, exposure to a high concentration of dexamethasone (200  $\mu$ M) alone significantly reduced cell viability and migration, consistent with its well-documented catabolic and atrophic effects on skeletal muscle tissue.

**Keywords:** muscle cells, C2C12, photobiomodulation, dexamethasone, atrophy.

**Study Type:** Estudo experimental in vitro (células) (Experimental study in vitro - cells)

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**EFFECTS OF PHOTOBIOMODULATION ON APOPTOSIS AND NECROSIS IN C2C12 CELLS EXPOSED TO JUVENILE AND ADULT BOTHROPS ALTERNATUS VENOM**

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**Abstract**

Snakes of the genus *Bothrops* have great medical and epidemiological importance, especially in Latin America, where they are responsible for about 90% of snakebites. The bites of these snakes cause serious local and systemic effects in their victims, representing an important public health problem. Within this genus, several widely distributed species stand out, among them *Bothrops alternatus*, popularly known as Urutu, which predominantly inhabits the southern regions of South America. In addition, it is known that there are differences in the composition of the venoms of young and adult snakes, which can result in variations in the severity and evolution of the clinical manifestations observed. Photobiomodulation (PBM) has been shown to be an effective adjuvant therapy to serum therapy in reducing the local effects induced by *bothrops* venom. This study evaluated the effect of PBM on C2C12 myoblast cells after exposure to *Bothrops alternatus* (BaV) venom in its juvenile (BaJV) and adult (BaAV) stages. C2C12 cells received either BaJV or BaAV (50 µg/mL) or culture medium alone (control) and were immediately treated with PBM. The treatment was performed with a low-level laser (wavelength 660 nm, 4 J/cm<sup>2</sup>, 100 mW, 0.33 W/cm<sup>2</sup>, 40 seconds). Apoptosis, necrosis, and cytotoxicity were evaluated three hours after exposure to the venom, using LDH assay and flow cytometry for the detection of annexin V (apoptosis) and 7-AAD (necrosis). The results demonstrated that both venoms significantly increased cytotoxicity and induced apoptosis in the cells. Treatment with PBM reduced BaJV-induced apoptosis and necrosis, but had no significant effect on BaJV-induced cytotoxicity, apoptosis, or necrosis. These findings indicate that the juvenile and adult venoms of *B. alternatus* affect C2C12 cells in a different way in magnitude, and that PBM exerts a protective effect against adult venom, suggesting its therapeutic potential in mitigating the cytotoxic effects induced by *bothrops* envenomation.

**Keywords:** Photobiomodulation (PBM); apoptosis; necrosis; *Bothrops alternatus*.

**Study Type:** Estudo experimental in vitro (células) (Experimental study in vitro - cells)



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**EVALUATION OF THE EFFECTS OF LOW-POWER THERAPEUTIC RED LASER AND BLUE LED ON GENOMIC STABILITY AND TELOMERE MAINTENANCE IN HUMAN BREAST CANCER MCF-7 CELLS**

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**Abstract**

Background: photobiomodulation (PBM) induced by radiations emitted from low-power lasers and LEDs (light-emitting diodes) have been used to treat diseases and clinical conditions. Breast cancer is the type of neoplasia that most affects women worldwide. Proliferation, migration, invasion, evasion, and cell death are characteristics of cancer, and these cellular responses are used to evaluate the effects induced by physical and chemical agents on cancer cells. There are doubts about the beneficial effects of PBM on cancer patients, since data are scarce or incomplete, making necessary a better understanding of PBM-induced effects on cancer cells. Aims: To elucidate the effects of a low-power therapeutic laser and a LED on cellular events, reactive oxygen species levels, gene expression related to DNA oxidative lesion repair, genomic stability, telomere maintenance, and length in MCF-7 cells. Methods: Human breast cancer cells MCF-7 were exposed to red laser (658 nm; 23, 46, and 69 J/cm<sup>2</sup>; 0.77 W/cm<sup>2</sup>, 100 mW; spot size of 0.13 cm<sup>2</sup>) and blue LED (470 nm; 160, 321, and 482 J/cm<sup>2</sup>; 5.35 W/cm<sup>2</sup>, 1500 mW; spot size of 0.28 cm<sup>2</sup>), alone and simultaneously, in continuous emission mode. Cell viability, migration, and invasion were assessed using WST-1, Wound Healing, and Transwell Matrigel assays, respectively. Reactive oxygen species (ROS) levels, apoptosis and necrosis were measured by flow cytometry. Furthermore, mRNA levels of DNA repair genes (APTX, POL $\beta$ , and PCNA) and telomere maintenance genes (TRF1 and TRF2) were quantified by RT-qPCR. Telomere length was assessed by qPCR. Results: Cell viability and migration were not significantly altered when compared to the control group. Cell invasion was significantly inhibited after exposure at the laser and LED. The red laser alone significantly increased ROS levels and apoptosis. However, necrosis decreased significantly after exposure to red laser and blue LED, alone and simultaneously. Photobiomodulation induced by low-power red laser and blue LED decreased the mRNA levels of repair genes involved in the base excision repair pathway and genes involved in telomere maintenance. Furthermore, telomere length was significantly increased after simultaneous exposure to red laser and blue LED. Conclusion: These results improve our understanding about effects of PBM on tumors cells, which could be used to increase the safety and efficacy of PBM-based therapeutic protocols targeting cancer patients.

**Keywords:** Breast cancer. DNA repair. Genomic stability. Laser. Light-emitting diode. Photobiomodulation. Telomere.

**Study Type:** Estudo experimental in vitro (células) (Experimental study in vitro - cells)

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**LOW-POWER INFRARED LASER AND AMBER LED ON CELL VIABILITY, REACTIVE OXYGEN SPECIES, AND DNA REPAIR GENES IN BREAST CANCER CELLS**

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**Abstract**

**Background:** Photobiomodulation (PBM) is a therapy that utilizes low-power lasers and LEDs (light-emitting diodes) to stimulate biological processes. However, the cellular and molecular mechanisms involved in PBM induced by low-power lasers and LEDs are not fully understood. Some studies indicated that reactive oxygen species (ROS) are involved in PBM, which could induce DNA repair mechanisms. Breast cancer is a neoplasm with a high incidence among women worldwide, and despite PBM is considered safe therapy, its use in cancer patients is a topic of controversy. **Aims:** This study evaluated effects of a low-power infrared laser and an amber LED on cell viability, ROS generation, and DNA repair gene expression in breast cancer cells. **Methods:** Cultures of MCF-7 (luminal A) and MDA-MB-231 (triple-negative) breast cancer cells were irradiated with infrared laser (830 nm; 32, 64, and 97 J/cm<sup>2</sup>) and amber LED (617 nm; 358, 716, and 1074 J/cm<sup>2</sup>), either alone or simultaneously, in continuous wave mode. Cell viability was assessed using the WST-1 assay at 24 and 48 h. ROS production was measured by flow cytometry using the DCFH-DA probe. Additionally, the mRNA levels of DNA repair genes (APTX, POLβ, and PCNA) were quantified using quantitative reverse transcription polymerase chain reaction. **Results:** No statistically significant difference ( $p > 0.05$ ) in cell viability were observed in MCF-7 or MDA-MB-231 cells compared to non-irradiated controls. The data obtained show that, exposure to infrared laser (97 J/cm<sup>2</sup>) or amber LED (1074 J/cm<sup>2</sup>) did not alter ROS levels in MCF-7 and MDA-MB-231 cells. However, in MCF-7 cells, simultaneous exposure to infrared laser (97 J/cm<sup>2</sup>) and amber LED (1074 J/cm<sup>2</sup>) at the highest fluences significantly ( $p < 0.05$ ) increased ROS levels. In contrast, no significant change was observed in MDA-MB-231 cells. Regarding DNA repair, neither infrared laser nor amber LED irradiation significantly altered APTX, POLβ, or PCNA mRNA levels in the breast cancer cells. **Conclusion:** PBM with infrared laser and amber LED did not alter cell viability and levels of mRNA from DNA repair genes in both breast cancer cell, but did increase the ROS levels in MCF-7. These findings contribute to a better understanding of PBM effects on tumor cells.

**Keywords:** Breast cancer, DNA repair, laser, LED, photobiomodulation, reactive oxygen species.**Study Type:** Estudo experimental in vitro (células) (Experimental study in vitro - cells)

**ANTIBIOFILM EFFECT OF PHOTODYNAMIC THERAPY MEDIATED BY NANOFORMULATED CURCUMIN AND BLUE LED ON MONOSPECIES BIOFILMS OF METHICILLIN-RESISTANT AND -SENSITIVE STAPHYLOCOCCUS AUREUS**

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**Abstract**

The challenge of photodynamic therapy (aPDT) on mature biofilms of antimicrobial-resistant and sensitive species has been explored. It consists of the occasional disruption of the structural matrix of biofilms, allowing microbial cells to be reached by the therapy. The resistance mechanisms related to mature biofilms include chemical and physical diffusion barriers that hinder the penetration of antimicrobial agents and the cohesive strength between cells, whose disruption is essential for the effectiveness of antimicrobial action. The present study aimed to investigate the antibiofilm and antimicrobial effects of aPDT on mature biofilms of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *S. aureus*, using a nanoformulated curcumin photosensitizer and a 450 nm blue LED. One hundred eighty specimens were inoculated in BHI broth with MRSA (ATCC 43300) and *S. aureus* (ATCC 29213) suspensions and incubated in a BOD chamber for seven days. Experimental groups ( $n = 10$ ) received nanoformulated curcumin at concentrations of 70  $\mu\text{g/mL}$  or 100  $\mu\text{g/mL}$ , followed by irradiation with a blue LED ( $460 \pm 10 \text{ nm}$ ,  $18 \text{ mW/cm}^2$ ) for 3 or 5 minutes ( $3.24 \text{ J/cm}^2$  and  $5.4 \text{ J/cm}^2$ , respectively), resulting in the following aPDT test groups: Cur+70 $\mu\text{g/mL}$ . LED3', Cur+70 $\mu\text{g/mL}$ . LED5', Cur+100 $\mu\text{g/mL}$ . LED3', and Cur+100 $\mu\text{g/mL}$ . LED5'. Control groups included untreated samples (Cur-. LED-), light only (Cur-. LED3' and Cur-. LED5'), and curcumin only (Cur+70 $\mu\text{g/mL}$ . LED- and Cur+100 $\mu\text{g/mL}$ . LED-). Specimens were homogenized in 1 mL of saline using a vortex mixer, and 100  $\mu\text{L}$  aliquots were extracted and plated on BHI agar for 24 hours of incubation in a BOD chamber at  $36.5^\circ\text{C}$ . Colony-forming units (CFU) were counted, converted to Log values, and analyzed using ANOVA (5%). Compared with the control group, the aPDT treatments Cur+70 $\mu\text{g/mL}$ . LED3' and Cur+100 $\mu\text{g/mL}$ . LED3 significantly reduced the Log CFU/mL counts of both *S. aureus* and MRSA. These groups showed statistically significant reductions among all tested conditions for both microorganisms. It was concluded that aPDT effectively reduced the Log CFU/mL values in the 3-minute treatment groups for *S. aureus* and MRSA, regardless of the photosensitizer concentration. Among these, aPDT with 100  $\mu\text{g/mL}$  curcumin and 3-minute exposure produced the most significant reduction against *S. aureus*, demonstrating the highest efficacy in combined antibiofilm and antimicrobial activity.

**Keywords:** CURCUMIN; aPDT; MRSA; MSSA; BLUE LED.

**Study Type:** Estudo experimental in vitro (micro) (Experimental study in vitro - micro)

**IN VITRO EVALUATION OF THE OPTIMIZED PROTOCOL OF ANTIMICROBIAL  
PHOTODYNAMIC THERAPY (aPDT) IN STAPHYLOCOCCUS AUREUS**

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**Abstract**

**Introduction:** *Staphylococcus aureus* (*S. aureus*) is a Gram-positive bacterium commonly found in the human microbiota and associated with several infections. Nasal colonization represents a major risk factor for systemic infections, particularly in immunocompromised patients. Conventional decolonization strategies, such as mupirocin, may induce bacterial resistance when used repeatedly. Antimicrobial Photodynamic Therapy (aPDT) has emerged as a promising alternative, relying on the activation of a photosensitizer by light to produce reactive oxygen species that destroy microorganisms without resistance selection. **Objective:** To evaluate, in vitro, the efficacy of an optimized aPDT protocol using methylene blue (MB) at different concentrations and formulations, with reduced pre-irradiation times, aiming at future clinical application in nasal decolonization. **Methodology:** *S. aureus* ATCC 6538 was cultured in Brain Heart Infusion broth, and the growth curve was monitored by optical density (OD<sub>nm</sub>). The mid-log phase occurred after 5 hours (OD  $\approx$  0. 7;  $\sim 2 \times 10^8$  CFU/mL). The experimental groups were: (1) control, (2) laser only, (3) MB only, and (4) MB + laser (aPDT). MB was tested in liquid (0. 01% and 0. 005%) and gel (0. 01%) formulations, with pre-irradiation times of 3 or 5 minutes in the dark. Samples were irradiated with a 660 nm red laser (400 mW/cm<sup>2</sup>, 5 min, 120 J/cm<sup>2</sup>, 3 mm distance). After treatment, cultures were serially diluted, plated on BHI agar, and incubated at 37°C for 24 h for CFU counting. Data were analyzed using the Kruskal-Wallis test followed by Dunn's post-test ( $p < 0. 05$ ). **Results:** Complete bacterial elimination (0 CFU/mL) was achieved with both MB liquid concentrations (0. 01% and 0. 005%) under 5 min pre-irradiation followed by laser exposure. When pre-irradiation was reduced to 3 minutes, a significant reduction ( $10^3$ – $10^4$  CFU/mL) was observed, indicating partial effectiveness. The MB gel formulation showed no significant reduction compared to controls. Statistical analysis confirmed significant differences between the aPDT-treated and control groups ( $p < 0. 05$ ). **Conclusion:** The optimized aPDT protocol using liquid MB (0. 01% and 0. 005%) demonstrated complete in vitro elimination of *S. aureus* when pre-irradiated for 5 minutes, supporting its potential for clinical application in nasal decolonization. Shorter pre-irradiation times or gel formulations reduced efficacy, suggesting the need for further optimization.

**Keywords:** methylene blue, *Staphylococcus aureus*, antimicrobial photodynamic therapy.

**Study Type:** Estudo experimental in vitro (micro) (Experimental study in vitro - micro)

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**RELATIONSHIP BETWEEN MOLAR-INCISOR HYPOMINERALIZATION (MIH) AND OROFACIAL FUNCTIONS: AN OBSERVATIONAL STUDY**

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**Abstract**

**Introduction:** Molar-Incisor Hypomineralization (MIH) is a qualitative enamel defect that primarily affects the first permanent molars and, occasionally, the incisors. It is characterized by well-defined, asymmetric opacities that range from mild to severe, presenting whitish-yellow or brownish hues. These lesions are often associated with mild to severe hypersensitivity, depending on the type of opacity and the presence of enamel breakdown. Patients with MIH may be more susceptible to orofacial dysfunctions, particularly involving breathing and mastication, although specific data remain scarce. **Objective:** To compare orofacial functions between children with and without MIH. **Methodology:** This cross-sectional study compared orofacial functions using the Nordic Orofacial Test–Screening (NOT-S), which includes both interview and clinical examination, in children with and without MIH. The study followed ethical guidelines for research involving human participants and was approved by the UNINOVE Research Ethics Committee (CAAE: 7. 240. 574; 22/11/2024) and registered at ClinicalTrials.gov (NCT06692257). The sample consisted of 56 children (both sexes), aged 6–12 years, treated at the UNINOVE Dental Clinic. Assessments included MIH diagnosis based on the criteria proposed by Ghanin et al. (2015), dental hypersensitivity (VAS), response to cold air stimulus (SCASS), and orofacial function (NOT-S). **Results:** No significant differences were found between groups regarding age or sex. However, children with MIH showed a higher frequency of moderate/severe hypersensitivity ( $p = 0.035$ ), higher SCASS scores ( $p < 0.001$ ), and greater impairment in the mastication domain (39.3% vs. 10.7%;  $p = 0.029$ ). The MIH group also presented higher total NOT-S scores, with alterations in sensory, respiratory, oral habits, resting facial posture, and motor domains, although no individual item reached statistical significance. Correlation analysis, considering all participants, revealed a positive association between SCASS scores and both the NOT-S interview domain and total NOT-S score ( $p < 0.05$ ). **Conclusion:** Molar-Incisor Hypomineralization negatively affects functional, sensory, and behavioral aspects, influencing children's quality of life and dental management. These findings highlight the need for tailored clinical protocols, multidisciplinary follow-up, and future longitudinal studies.

**Keywords:** Molar-Incisor Hypomineralization, Orofacial functions, Enamel defects, Pediatric dentistry.

**Study Type:** Estudo observacional (humanos) (Observational study - humans)



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**Amber photobiomodulation compared to Tranexamic Acid in the Control of Melasma:  
Pilot Study, Randomized, Controlled, Double-Blind**

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São Paulo, Brazil**Abstract**

**Introduction:** Melasma is a pigmentation disorder which affects approximately 36.3% of the Brazilian population, with 90% of cases occurring in women. Its etiopathogenesis remains not fully understood. Tranexamic acid (TXA) inhibits plasminogen activation, blocks the interaction between melanocytes and keratinocytes, and suppresses tyrosinase activity. Amber photobiomodulation (PBM) has also been shown to activate autophagy, according to in vitro studies. **Objective:** To evaluate the effect of amber PBM compared to TXA in the control of melasma. **Methodology:** This randomized, controlled, double-blind study was divided into two arms. Group 1: PBM with amber LED + placebo cosmetic. Group 2: sham PBM + 5% TXA cosmetic. Participants underwent weekly sessions for 12 weeks, along with daily home application of the assigned cosmetic for 3 months, followed by a 2-month post-treatment follow-up. **Results:** Twenty-one women aged 35 to 50 years were included. For the MASI outcome, the mean values were  $13.8 \pm 2.8$ ,  $11.7 \pm 2.1$ , and  $11.8 \pm 2.2$  in the TXA group, and  $16.4 \pm 3.0$ ,  $16.8 \pm 2.2$ , and  $16.2 \pm 2.0$  in the PBM group. No statistically significant differences were observed between groups at any time point or within groups over time. Global Facial Assessment revealed median scores of 4 [3–4] for TXA and 4 [4–5] for PBM, indicating clinical improvement in both groups. Regarding the MelasQoL questionnaire, scores decreased from  $47.9 \pm 15.6$ ,  $37.0 \pm 17.0$ , and  $19.3 \pm 11.5$  in the PBM group and from  $46.6 \pm 12.9$ ,  $38.1 \pm 9.7$ , and  $26.8 \pm 13.6$  in the TXA group at baseline, week 6, and post-treatment, respectively, showing improved quality of life in both groups. There were no between-group differences in quality-of-life improvement, although a significant intragroup improvement was observed after the sixth week. **Conclusion:** Both treatments led to a significant improvement in participants' quality of life, despite the absence of measurable improvement in melasma severity according to the MASI index. Nevertheless, melasma remained stable without worsening during the 60-day follow-up, with no significant differences between the TXA and PBM treatments.

**Keywords:** photobiomodulation, tranexamic acid, ambar LED, melasma.**Study Type:** Estudo piloto (Pilot study)



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**EFFECTS OF LASER PHOTOBIOMODULATION COMBINED WITH RESISTANCE EXERCISES ON PAIN AND QUALITY OF LIFE IN WOMEN WITH KNEE OSTEOARTHRITIS: A PILOT STUDY**

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**Abstract**

**INTRODUCTION:** Knee osteoarthritis (KOA) is a degenerative and progressive joint disease and one of the main causes of pain, functional disability, and reduced quality of life in adults and older individuals. Photobiomodulation Therapy (PBMT), particularly when delivered by low-level laser, has shown relevant therapeutic potential in modulating inflammation, providing analgesia, and stimulating tissue regeneration. **OBJECTIVE:** To evaluate the preliminary effects of PBMT applied to acupuncture points combined with resistance exercises on pain level and quality of life in women with KOA. **METHODOLOGY:** Twenty-three women with clinically diagnosed KOA were randomized into two groups: Exercise Group (Ex), which performed a resistance exercise protocol only; and Exercise + PBMT Group (ExP), which performed the same exercise protocol combined with PBMT application. Interventions were carried out twice a week for six weeks (12 sessions). The exercise program included warm-up, strengthening of knee and hip flexors and extensors, adductors and abductors, followed by stretching of the main lower limb muscles. PBMT (808 nm, 100 mW, 4 J per point) was applied to five acupuncture points on the affected knee immediately after each session. Functionality and quality of life were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) before and after treatment. **RESULTS AND DISCUSSION:** The ExP group showed a significant improvement in total WOMAC scores compared with the Ex group, indicating reduced pain and improved physical function. The combination of PBMT at acupuncture points with resistance exercise appears to enhance analgesic and functional effects, possibly through photobiological mechanisms related to inflammatory modulation and increased local microcirculation. As this is a pilot study, the findings should be interpreted with caution; however, they indicate a positive trend and support the ongoing randomized controlled clinical trial designed to confirm the efficacy of this combined approach. **CONCLUSION:** PBMT applied at acupuncture points, when combined with a resistance exercise program, was effective in reducing pain and improving quality of life in women with KOA. This pilot study suggests that combining these therapies may represent a promising complementary strategy in the rehabilitation of osteoarthritis, whose efficacy is currently being investigated in a randomized controlled clinical trial.

**Keywords:** Osteoarthritis; knee; Photobiomodulation Therapy; Pain.**Study Type:** Estudo piloto (Pilot study)

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**VASCULAR PHOTOBIOMODULATION AS AN ADJUVANT TO THE TREATMENT OF LOW BACK PAIN: PILOT CLINICAL TRIAL**

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**Abstract**

Low back pain is a prevalent condition that significantly impacts public health. Vascular photobiomodulation demonstrates promising therapeutic effects due to its sedative, antispasmodic, and analgesic properties. Furthermore, interventions such as mobility exercises, abdominal strengthening, and manual therapy have proven effective in the recovery and management of low back pain. The objective of this pilot project was to evaluate the effect of vascular photobiomodulation (MVBP) combined with manual therapy and therapeutic exercises on patients with low back pain during the initial period. Twenty participants completed the Oswestry Disability Index 2.0, Roland Morris Questionnaire, and Pain Analogue Scale (VAS) questionnaires and were divided into two groups: G1 (manual therapy + exercises + sham MVBP) and G2 (manual therapy + exercises + active MVBP). Treatment lasted four consecutive weeks (twice a week) with MVBP application for 30 minutes in each session. Data were analyzed using statistical tests (SAS for Windows). v. 9.4) such as the Student's t-test and chi-square test, and the repeated measures model with the Wald test. In all analyses,  $p < 0.05$  was considered statistically significant. Regarding pain according to the VAS, no statistically significant difference was observed between the groups at the end of treatment ( $p = 0.1398$ ). Responses to the Roland Morris questionnaire ( $p = 0.007$ ) and the Oswestry Index 2.0 ( $p = 0.0322$ ) demonstrated intragroup improvement before and after treatment and between groups ( $p < 0.05$ ). This pilot study concluded that the use of FBMV, in conjunction with manual myofascial release and therapeutic exercises, contributed to the improvement of the participants' daily activities. However, regarding the impact on pain, further studies are needed, considering that FBMV treatment shows promising potential.

**Keywords:** low back pain, vascular photobiomodulation, myofascial release, exercises.

**Study Type:** Estudo piloto (Pilot study)

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**MANAGEMENT OF MAGNESIUM SULFATE EXTRAVASATION INJURY USING  
PHOTOBIOMODULATION IN A PEDIATRIC PATIENT**

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**Abstract**

**Introduction:** Extravasation of vesicant medications constitutes a relevant complication in intravenous therapy, especially in pediatric patients, whose tissues are more susceptible to chemical injuries. Once tissue damage occurs, nursing action is essential. Photobiomodulation (PBM) is a promising therapeutic resource for wound healing and reducing the inflammatory process. **Objective:** To describe the nursing management using PBM in a chemical lesion. **Method:** Case report of a pediatric patient treated in the outpatient clinic of a hospital in Southern Brazil. The follow-up totaled 5 consultations over a period of 15 days, with data obtained from the electronic medical record. Study approved CAAE 51607721. 9. 0000. 5327. **Results:** A male patient, 1 year old, received magnesium sulfate via a peripheral venous access on the dorsum of the foot during hospitalization in an intensive care unit. He presented with a blistering vesicant lesion and an adjacent erythematous area after extravasation during the infusion. The protocol of topical care and PBM application was initiated on the 2nd and 7th days. After discharge, in outpatient treatment, PBM was applied during consults. In the first session, 3J/cm<sup>2</sup> of red (R) and infrared (IR) laser was applied over the central point of the lesion, in addition to 1J/cm<sup>2</sup> (R + IR) in the perilesional areas, in order to control the inflammatory process and stimulate regeneration. In the subsequent session, the dose was adjusted to 2J/cm<sup>2</sup> (R + IR) on the central lesion and 1J/cm<sup>2</sup> (R + IR) in a scanning motion over the perilesional regions, maintaining the same protocol until the penultimate consultation. The topical treatment consisted of cleaning with 0. 9% saline solution, using compresses with polyhexamethylene biguanide, zinc oxide on the perilesional areas, covering with paraffin gauze, simple gauze, and a bandage. Throughout the sessions, a progressive reduction in the lesion was observed, with decreased slough, tissue reorganization, and improved coloration and integrity of the skin in adjacent areas. In the last session, the affected area was 100% epithelialized, and only a single punctual application of PBM at 2J/cm<sup>2</sup> (R + IR) and a barrier cream for skin protection were performed. Full healing allowed for outpatient discharge without sequelae or scars. **Conclusion:** The management of magnesium sulfate extravasation in a pediatric patient using PBM and appropriate dressings proved effective in tissue recovery, promoting healing.

**Keywords:** Low-Level Light Therapy, Wound Healing, Magnesium Sulfate, Nursing.

**Study Type:** Relato de caso (Case report)

**PHOTOBIMODULATION IN THE MANAGEMENT OF A FACIAL CHEMICAL BURN**

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**Abstract**

**Introduction:** Chemical burns represent a challenge in occupational health, especially in hospitals, due to exposure to harmful substances. Facial burns can result in severe compromises with a risk of mortality if associated with airway injuries. These injuries require immediate management, irrigation with cold water, specialized monitoring, estimation of the affected area, and identification of systemic toxicity. **Objective:** To describe the nursing management of a facial chemical burn. **Method:** Case report treated with photobiomodulation in an outpatient clinic of a hospital in the south of Brazil, conducted by the dermatological nurse, totaling 6 consultations over 12 days. The data were extracted from the medical record. The study was approved by CAAE 51607721. 9. 0000. 5327. **Results:** A 51-year-old man suffered a facial burn from methanol and formic acid while working as a safety technician. He was wearing protective glasses and a mask. Attended by the Occupational Medicine Service, he reported pain of 7 on the Verbal Categorical Scale, described as burning. He received intravenous analgesia and irrigation with water for 15 minutes. During first consultation, he presented with a superficial second-degree burn covering 1% of the total body surface area: on the forehead, from the hairline to the left malar region, with violaceous erythema, erosions, and non-blanching areas. Photobiomodulation (PBM) was started less than 2 hours after the accident, with 6j/cm<sup>2</sup> of red and infrared laser, opting for higher doses due to the intensity of the pain and significant dermal damage. Antiseptic compresses, non-adherent dressing, and topical corticosteroid after medical evaluation were used. Consultations occurred every 48 hours, with progressive improvement of erosions and pain (2 and 0). PBM was maintained and, with progressive improvement, the dose was reduced to 4j/cm<sup>2</sup>. In the areas of neoepithelialization, an ointment based on zinc oxide was associated. A normotrophic scar was observed where the burn occurred, and the patient was cleared to return to work activities in less than 2 weeks. **Conclusions:** Early specialized intervention, associated with almost immediate PBM assisted in pain reduction and tissue repair. With continuous monitoring, there was healing, aesthetic rehabilitation, and valorization of the worker. A rapid and effective scar evolution in a protocol using higher doses of red and infrared laser is also highlighted.

**Keywords:** Burns, Low-Level Light Therapy, Nursing.

**Study Type:** Relato de caso (Case report)

**PHOTOBIOMODULATION-ENHANCED ALVEOLAR RIDGE PRESERVATION IN A SYSTEMICALLY COMPROMISED BARIATRIC PATIENT: A CASE STUDY**

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**Abstract**

**Introduction:** Patients undergoing bariatric surgery often develop nutritional deficiencies and altered bone metabolism, which can severely compromise alveolar ridge preservation and subsequent dental rehabilitation. Photobiomodulation (PBM) has emerged as a promising adjunct therapy capable of stimulating bone regeneration and accelerating soft tissue healing. **Objective:** This study reports the outcomes of combining bone grafting with low-level PBM for alveolar ridge preservation and implant rehabilitation in a bariatric patient with severe malnutrition and osteoporosis. **Methods:** A 65-year-old female patient with a history of bariatric surgery, chronic malnutrition, and osteoporosis underwent the extraction of teeth 24, 25, and 26. Ridge preservation was performed using a bovine-derived xenograft (Lumina-Bone®) and a collagen membrane. Following suturing, a PBM protocol was applied weekly for 26 sessions using a semiconductor diode system emitting simultaneous red (InGaAlP) and infrared (AlGaAs, 808 nm) light directed at the vestibular, lingual, and occlusal regions. Clinical progress and bone formation were evaluated through computed tomography at different stages of treatment. **Results:** Despite her compromised systemic condition, the combination of xenograft and PBM promoted favorable bone healing. Tomographic analysis indicated an average gain of 1.5 mm in bone height during treatment. After six months, reductions in ridge thickness were 26.55% (tooth 24), 34.45% (tooth 25), and 51.42% (tooth 26). These values were similar or lower than those reported in eutrophic patients who underwent grafting without PBM. Implants showed excellent osseointegration, allowing complete and uneventful oral rehabilitation. **Conclusion:** This case demonstrates the ability of PBM to modulate biological repair processes and enhance regenerative outcomes in systemically compromised individuals. The synergistic effect of bone grafting and PBM effectively limited bone resorption and promoted osseointegration, even under severe nutritional deficiency. PBM's biostimulatory action was essential to accelerate bone neoformation, preserve alveolar dimensions, and ensure successful implant-supported rehabilitation. The findings emphasize the clinical relevance of biophotonics as an adjunctive tool to optimize bone regeneration and implant success in bariatric patients with impaired healing potential.

**Keywords:** bariatric, bone grafting, osteoporosis, dental implant, photobiomodulation, biophotonic;

**Study Type:** Relato de caso (Case report)



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**USE OF VASCULAR PHOTOBIOMODULATION AS ADJUVANT THERAPY IN CHRONIC RHINOSINUSITIS WITH NASAL POLYPS: 22-MONTH FOLLOW-UP THERAPEUTIC PROTOCOL**

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**Abstract**

Vascular photobiomodulation (VPBM) has proven to be a promising strategy in the treatment of various diseases, such as in the management of chronic sinonasal inflammation, promoting inflammation modulation. The balance between M1 and M2 macrophage phenotypes is essential for promoting effective immune responses. When imbalanced, it leads to the onset of various diseases, such as chronic rhinosinusitis with nasal polyps (CRSwNP). This multifactorial disease involves immunological and epithelial barrier alterations, resulting in persistent inflammation of the sinonasal mucosa. The objective of this study is to demonstrate the efficacy of VPBM as adjuvant therapy in a patient with eosinophilic asthma, CRSwNP, and bronchiectasis, receiving monthly treatment with the immunobiological tezepelumab for 22 months. Patient R. T. T. , a 66-year-old female, weighing 51 kg, had symptoms beginning 20 years ago, with headache, postnasal discharge, continuous obstruction, recurrent bacterial sinusitis, and nasal polyps. During conservative therapy, the patient underwent antrostomy and septoplasty to remove polyps. The VPBM protocol consisted of a diode laser (ECCO ILIB PLUS), P: 100 mW, wavelength 660 nm, under the radial artery for 40 min, and a total energy of 240 J. VPBM was administered intranasally, simultaneously with a red and infrared laser for 10 min in each nostril, and a diode laser (Laser Duo – MMO), P: 50 mW, irradiance of 3.33 W/cm<sup>2</sup>, and total energy: 60 J. Using the same laser equipment, the intestinal region was irradiated simultaneously with 660 and 808 nm at nine points, P: 50 mW, E: 6 J/point, and radiation exposure: 100 J/cm<sup>2</sup>. This protocol was performed weekly for 22 months, resulting in improved quality of life, no surgery, no complications, and no hospitalizations. A computed tomography scan performed during this period revealed a stable sinonasal region without polyps. VPBM combined with irradiation of the intestinal axis, as adjuvant therapy, was effective in the treatment of chronic rhinosinusitis, modulating the inflammatory process and improving immunity, as evidenced by the patient's progress during this period. The use of VPBM in patients with chronic rhinosinusitis involves understanding the pathophysiology and the interaction between light and tissue, allowing for the development of an individualized protocol and providing a safe and effective adjuvant therapeutic approach.

**Keywords:** M1 and M2 macrophages, Vascular photobiomodulation; Chronic rhinosinusitis with nasal polyps; Tezepelumab.

**Study Type:** Relato de caso (Case report)



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**EFFECTS OF PHOTOBIOMODULATION WITH SUPERPULSED AND DUAL WAVELENGTH LASER (810nm + 980nm) IN CHILDREN AND ADOLESCENTS WITH SYMPTOMS OF FACIAL MUSCLE PAIN AND HEADACHE: CASE SERIES.**

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**Abstract**

Orofacial pain and tension headaches are prevalent in children and adolescents, negatively impacting their development and quality of life. The aim is to analyze the efficacy of Photobiomodulation (PBM) as a non-pharmacological therapeutic alternative, using a dual-wavelength superpulsed laser (810 nm + 980 nm) to control these painful symptoms. This study is a case series of children (aged 6 to 17 years). They will be divided into two groups: the intervention group (G1), which will receive local active PBM in eight sessions (two per week) on the masseter, temporalis, trapezius, and TMJ muscles, and the control group (G2), which will undergo a sham procedure (placebo). Pain will be assessed using The Faces Pain Scale and ICHD-3 questionnaires. A crucial secondary objective is to investigate the correlation between anthropometric variables (BMI, skin type) and laser energy penetration, aiming to optimize dosimetry for each individual. Partial results demonstrate that the protocol is safe and promising. One reported case indicated clinical improvement in migraine and orofacial pain after the sessions, eliminating the need for analgesics. Analysis of the measured temperature and power confirmed the delivery of adequate energy to deep tissues without excessive heating, reinforcing the importance of considering anthropometry in PBM.

**Keywords:** children, adolescents, headache, facial pain, photobiomodulation

**Study Type:** Série de casos (Case series)

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**ANTIMICROBIAL PHOTODYNAMIC THERAPY ON BACTERIAL CELLULOSE MEMBRANES  
CONTAMINATED WITH CANDIDA ALBICANS: AN INNOVATIVE APPROACH FOR BURN  
TREATMENT**

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**Abstract**

**Introduction:** Burns are severe injuries that compromise skin integrity, promoting infections and delaying the healing process. The rupture of the skin barrier allows colonization by pathogenic microorganisms such as *Candida albicans*, frequently associated with hospital infections and resistant biofilms. Given the growing antifungal resistance, the search for alternative, safe, and accessible therapies becomes essential. **Objective:** To evaluate the efficacy of Antimicrobial Photodynamic Therapy (aPDT) applied to bacterial cellulose membranes contaminated with *C. albicans*, verifying its antimicrobial action and the preservation of the structural and regenerative properties of the biomaterial. **Methodology:** The research was conducted under controlled laboratory conditions. Samples of bacterial cellulose membranes were contaminated with *C. albicans* and subjected to the application of the photosensitizer methylene blue, followed by irradiation with red light ( $\lambda = 660$  nm). After treatment, microbiological analyses (CFU count), and mechanical resistance tests were performed to verify the effectiveness of aPDT and the maintenance of material integrity. **Results:** The results showed a significant reduction in fungal load on membranes treated with aPDT, confirming the photodynamic action of methylene blue under red light. Mechanical analysis revealed preservation of cellulose structure and resistance, demonstrating that the process did not compromise the regenerative properties of the biomaterial. These findings reinforce the potential of the CB + aPDT association as a promising approach for managing contaminated wounds, especially burns, reducing infection risk and dependence on conventional antifungal agents. **Conclusion:** The combination of bacterial cellulose membranes and Antimicrobial Photodynamic Therapy proved effective in reducing *C. albicans* without compromising the structure and physical properties of the dressing. This is an innovative, safe, and low-cost strategy with potential application in hospitals and burn treatment centers, representing progress in infection control and tissue regeneration.

**Keywords:** Burns, Antimicrobial Photodynamic Therapy, Bacterial Cellulose, *Candida albicans*, Hospital Infection.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

**BIOFILM DISCLOSING AGENTS AS PHOTOSENSITIZERS IN ANTIMICROBIAL  
PHOTODYNAMIC THERAPY (APDT) FOR BIOFILM CONTROL IN CHILDREN AGED 3–5  
YEARS: A RANDOMIZED CLINICAL TRIAL**

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**Abstract**

Dental caries is one of the most prevalent chronic diseases in childhood, resulting from the activity of an acidogenic oral biofilm that promotes demineralization of dental tissues. This condition represents a clinical challenge, especially in children aged 3 to 5 years, due to behavioral limitations at this age and the high risk of disease progression. In this context, minimally invasive, safe, and well-accepted strategies have been increasingly explored, such as antimicrobial photodynamic therapy (aPDT). This approach combines the application of a photosensitizing dye with a light source of compatible wavelength, leading to the formation of reactive oxygen species capable of selectively inactivating pathogenic microorganisms without affecting healthy tissues. This study aims to evaluate the efficacy of aPDT with blue LED in reducing the microbial activity of cariogenic biofilm in children aged 3 to 5 years classified as high risk for caries. It will be conducted as a randomized clinical trial with three parallel groups: Group 1 (control), subjected to blue LED irradiation (VALO Grand) without dye application; Group 2, treated with erythrosine + blue LED; and Group 3, treated with GC TriPlaque ID Gel + blue LED. The sample will consist of 71 children (approximately 24 per group), a number defined by sample size calculation indicating a minimum of 63 participants to maintain 80% statistical power, increased by 12% to account for potential losses. Screening will be based on the CAMBRA protocol, adapted for children, and inclusion will depend on classification as high caries risk. Biofilm will be collected before and after the intervention using a sterile auricular curette applied to the cervical vestibular surface of the deciduous molar. The collected material will be transferred to sterile microtubes containing Stuart transport medium and kept at 4 °C until microbiological processing. Colony-forming unit (CFU) counts will allow comparison of microbial load before and after the intervention. The results are expected to support the clinical validation of aPDT with blue LED as a safe and effective alternative for controlling the oral microbiota in young children, offering an additional microbiological management protocol in preventive pediatric dentistry.

**Keywords:** Terapia fotodinâmica, cárie dentária, LED azul, eritrosina, Dental Plaque.

**Study Type:** Ensaio clínico (Clinical trial)

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**COMPARATIVE STUDY OF PHOTODYNAMIC THERAPY WITH LED AND PROBIOTICS IN THE TREATMENT OF HALITOSIS: PROTOCOL FOR A RANDOMISED CONTROLLED CLINICAL TRIAL**

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**Abstract**

Introduction: Halitosis is a term that defines any unpleasant odour smell originating from the oral cavity and may have a local or systemic origin. Objective: This project aims to determine the effectiveness of treatment involving antimicrobial photodynamic therapy (aPDT) combined with treatment using probiotics at reducing halitosis. Methodology: 92 individuals from 18 to 60 years of age with a diagnosis of halitosis (sulfide  $\geq 112$  ppb, gas chromatography) will be selected. The participants will be randomly allocated to four groups (n=23). Group 1 (control): brushing, dental floss and tongue scraper; group 2: brushing, dental floss, tongue scraper and aPDT with blue Light Emitting Diode (LED) +annatto; group 3: brushing, dental floss, tongue scraper and aPDT with blue Light Emitting Diode (LED) +annatto and probiotic lozenges containing *Streptococcus salivarius* K12 (BLIS K12); and group 4: brushing, dental floss, tongue scraper and probiotic lozenges containing *S. salivarius* K12 (BLIS K12). Comparisons will be made of the respiratory analysis results before and immediately after the first treatment session, at the end of the 30-day treatment period and again 60 days after the treatment initiation. Microbiological analysis (counts of colony-forming units of viable bacteria from coated tongue) will be performed at the same time. The microbiome analysis will be conducted before treatment, 30 days after treatment completion and 60 days after treatment initiation, following DNA extraction. All groups will receive oral hygiene instructions as well as brushes, toothpaste and dental floss. Data normality will be checked using Shapiro-Wilk test. In the case of normality, analysis of variance is used for the comparisons. In the case of non-parametric data, Kruskal-Wallis test will be used. Wilcoxon test will be used to analyse the results of each treatment between two assessment times.

**Keywords:** Anti-Bacterial Agents, Bacteriology, Drug Combinations, Medicine, Antimicrobial photodynamic therapy.

**Study Type:** Protocolo (Protocol)

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**EFFECTS OF TALAPORFIN-MEDIATED PHOTODYNAMIC THERAPY IN LEWIS LUNG CARCINOMA AND HUMAN A549 ADENOCARCINOMA MODELS: AN IN VITRO STUDY**

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**Abstract**

Lung cancer remains one of the leading causes of cancer-related mortality worldwide, characterized by high biological heterogeneity and frequent therapeutic resistance. Photodynamic Therapy (PDT) is a promising and minimally invasive strategy that combines a photosensitizer (PS), light of a specific wavelength, and molecular oxygen to generate reactive oxygen species (ROS), promoting selective cell death and immune activation. Talaporfin sodium, a third-generation PS, presents advantages such as a shorter plasma half-life and reduced cutaneous phototoxicity, increasing its safety and clinical applicability. However, comparative studies investigating its effects across different lung cancer models remain limited, particularly between murine and human cell lines, and in three-dimensional (3D) cultures that better recapitulate the tumor microenvironment. Objective: To evaluate in vitro the effects of Talaporfin-mediated PDT in two lung carcinoma models—Lewis Lung Carcinoma (LLC) and human A549 adenocarcinoma—using 3D culture systems. Methodology: LLC and A549 cell lines will be cultured under standard conditions (37°C, 5% CO<sub>2</sub>, 95% humidity), with LLC maintained in RPMI-1640 medium and A549 in DMEM supplemented with 10% fetal bovine serum and 1% antibiotic/antimycotic. 3D spheroids will be generated using the hanging drop method, in which 15–30 µL drops containing 1×10<sup>4</sup> cells are placed on the inverted lid of culture plates. After 5–7 days, compact spheroids of 200–300 µm in diameter will be obtained. The experimental groups will include: (1) control, (2) Talaporfin only, (3) Laser only, and (4) PDT (Talaporfin + Laser). PDT will be performed 24 h after incubation with 0.75 mM Talaporfin, followed by irradiation at 660 nm (6 J/cm<sup>2</sup>) using a diode laser (40 mW) for 2 minutes and 30 seconds. Cell viability will be assessed using MTS and crystal violet assays; spheroid growth and morphology will be monitored microscopically and analyzed using ImageJ. Clonogenic potential, sphere formation, and cell migration (wound healing) will also be evaluated. Levels of IL-1β, IL-6, TNF-α, IFN-γ, IL-10, TGF-β, VEGF, PD-L1, arginase-1, and iNOS will be quantified by ELISA. Statistical analysis will be performed using ANOVA followed by Tukey's test (p < 0.05).

**Keywords:** Lung carcinoma, A549 adenocarcinoma, Lewis carcinoma, Photodynamic therapy, Talaporfin, 3D spheroids, Cell culture.

**Study Type:** Estudo experimental in vitro (Experimental study in vitro)

## EFFECTS OF PHOTOBIMODULATION ON HUMAN PLATELETS: CHARACTERIZATION OF THE ABSORPTION SPECTRUM AND ANALYSIS OF CELL VIABILITY

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### Abstract

**Introduction:** Human platelets play an essential role in hemostasis, immune response, and tissue repair processes. However, during storage, they undergo biochemical and functional changes that may compromise their therapeutic quality in transfusion medicine. Strategies aimed at preserving platelet viability and functionality are highly relevant. Photobiomodulation (PBM)—the application of low-intensity light to modulate biological processes—is considered a promising approach to maintaining cell functionality during storage. **Objective:** To characterize the absorption spectrum of human platelets and evaluate the effects of PBM on cell viability. **Methodology:** Platelet concentrates obtained by apheresis from healthy donors will be provided by the Fundação Pró-Sangue (São Paulo Blood Center Foundation), School of Medicine, University of São Paulo, Brazil. The dosimetric parameters for each irradiated group will be defined based on the initial spectrophotometric analysis. Each experimental group will be subjected to the following evaluations: absorption spectrophotometry; cell viability (trypan blue exclusion method); platelet morphology (optical microscopy); nitric oxide dosage (Griess method) and total protein quantification (Bradford method); and apoptosis analysis (Annexin staining by flow cytometry). This project will be approved by the Research Ethics Committee of Universidade Nove de Julho (opinion No. 7, 619, 499).

**Keywords:** photobiomodulation, platelets, cell viability.

**Study Type:** Protocolo (Protocol)



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# **EFFECTS OF PHOTOBIMODULATION ON THE RELAXATION OF LARYNGEAL MUSCULATURE IN INDIVIDUALS WITH FUNCTIONAL LARYNGEAL HYPERFUNCTION: RANDOMIZED CONTROLLED CLINICAL TRIAL PROTOCOL**

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## **Abstract**

**Introduction:** The growing appreciation of the voice as an expressive and functional resource, together with the expansion of digital media, has increased the demand for vocal health care, especially among voice professionals. Functional laryngeal hyperfunction is one of the main causes of vocal disorders in this group, with standard treatment consisting of exercises aimed at relaxing the laryngeal musculature. Although effective, these exercises often face low patient adherence. Considering that light-based therapies have been investigated for muscle relaxation in different contexts, the hypothesis of this study is to verify whether this effect also occurs in the laryngeal musculature, thus assisting in the treatment of functional laryngeal hyperfunction. **Objective:** To evaluate the effect of photobiomodulation on the relaxation of the laryngeal musculature in individuals with functional laryngeal hyperfunction using surface laryngeal electromyography (sEMG). **Methodology:** Eighty participants will be randomized into two groups: PBM Group (n = 40), receiving PBM + vocal relaxation exercise, and Control Group (n = 40), performing vocal relaxation exercise + PBM sham. The primary outcome will be muscle activity measured by sEMG. Secondary outcomes will include acoustic analysis of vocal emission, spectrographic voice analysis, application of the VHI-10 protocol, the Vocal Tract Discomfort Scale (VTDS) and/or Visual Analogue Scale (VAS), maximum phonation time (MPT), harmonic-to-noise ratio (HNR), fundamental frequency (f0), perceptual-auditory voice evaluation (GRBAS scale), presence of laryngeal pain or discomfort, and time to perceived clinical improvement. Variables will be measured at baseline, one hour after intervention, three days after, and one week after treatment. Data will be analyzed for normality using the Shapiro–Wilk test. For normally distributed variables, repeated-measures ANOVA with Bonferroni post-hoc test will be applied; for non-parametric variables, Friedman and Mann–Whitney tests will be used. Statistical significance will be set at  $p < 0.05$ . All analyses will be conducted using SPSS v25.0. **Keywords:** photobiomodulation, laryngeal hyperfunction, sEMG Outcomes and Assessment Methods (Summary) Acoustic Analysis of Vocal Emission Objective assessment of the voice (frequency, intensity, noise). How to measure: Sustained emission (e.g., /a/); software such as Praat or VoxMetria. VHI-10 (Voice Handicap Index – 10) Impact of the voice on the patient's life (physical, emotional, functional). How to measure: Questionnaire with 10 items (0 to 4); total score from 0 to 40. VTDS (Vocal Tract Discomfort Scale) Laryngeal discomfort (burning, itching, pain, tension). How to measure: Frequency and intensity of 8

symptoms. Spectrographic Voice Analysis Visualization of vocal frequency over time. How to measure: Spectrogram generated by software (e. g. , Praat). sEMG (Surface Laryngeal Electromyography) Laryngeal muscle activity during speech. How to measure: Electrodes placed on the skin; measures electrical signal during phonation. Maximum Phonation Time (MPT) Duration for which the vowel /a/ can be sustained. How to measure: Simple stopwatch timing during emission. Harmonic-to-Noise Ratio (HNR) Quality of vocal emission (clear vs. hoarse voice). How to measure: Acoustic software calculates the harmonic/noise ratio. Fundamental Frequency (f<sub>0</sub>) Pitch of the voice (low or high). How to measure: Frequency measurement of the emission; software such as Praat. GRBAS Scale Perceptual assessment of vocal quality by specialists. How to measure: Score from 0 (normal) to 3 (severe) for G, R, B, A, and S. Reduction of Laryngeal Pain or Discomfort Subjective improvement in symptoms such as pain or tightness. How to measure: VAS scale (0 to 10) or Vocal Tract Discomfort Scale (VTDS). Time to Perceptible Clinical Improvement When the patient or therapist perceives improvement. How to measure: Self-report or clinical record throughout treatment.

**Keywords:** Photobiomodulation, laryngeal hyperfunction, sEMG.

**Study Type:** Protocolo (Protocol)

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**EFFECTS OF TRANSCUTANEOUS VASCULAR LASER IRRADIATION ON VENOUS ULCERS: A  
RANDOMIZED CONTROLLED TRIAL PROTOCOL**

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**Abstract**

**Introduction:** Transcutaneous Vascular Photobiomodulation (VPBM), also known as Intravascular Laser Irradiation of Blood (ILIB), is a low-intensity laser therapy that modulates oxidative stress, attenuates inflammation, and enhances microcirculation. It has shown potential benefits in chronic wounds such as venous ulcers, which are marked by persistent inflammation, oxidative imbalance, and systemic dysfunction. **Objective:** To investigate the systemic and local effects of VPBM applied to chronic venous ulcers, clinically evaluating healing, as well as morphological changes in peripheral blood and thermal patterns (thermography) of compromised skin, correlating the primary outcome to these findings. **Methodology:** A prospective, randomized, controlled trial will follow SPIRIT guidelines, registered in REBEC, and approved by the Ethics Committee. The study will be conducted at the outpatient service of the Universidade Estadual do Piauí (UESPI), Brazil. Sample size was calculated based on randomized trials of local photobiomodulation in venous ulcers. **Inclusion criteria:** 34 patients aged 18–70 years, with unilateral VU >6 months and area of 25cm<sup>2</sup>. **Exclusion criteria:** hematological disorders, severe systemic disease, active infection, continuous corticosteroid therapy, photosensitivity, or cognitive impairment. Participants will be randomized into two groups: Control Group (standard care+VPBM placebo) and Intervention Group (standard care+active VPBM). VPBM will be applied transcutaneously over the radial artery with the following parameters: 660nm, continuous mode, 100 mW, 1800s (30min/session), 180 J, radiant exposure 6. 428J/cm<sup>2</sup>, beam area 0. 028 cm<sup>2</sup>, twice weekly for four weeks (8 sessions). **Outcomes:** The primary outcome is wound healing, assessed weekly by the Leg Ulcer Measurement Tool (LUMT). Secondary outcomes include peripheral blood live microscopy (dark-field and bright-field DFM) and local skin infrared thermography patterns. Evaluations will occur at baseline, Day 7, 14, and 21. Epidemiological data will be collected, and adverse effects monitored. **Statistical analysis:** Data normality will be tested with Kolmogorov-Smirnov. Two-way repeated measures ANOVA with Bonferroni post-hoc will be used for interim analysis, and Generalized Estimating Equations (GEE) for final comparisons. Pearson correlation will be applied between primary and secondary outcomes. Significance will be set at  $p < 0.05$  (SPSS, IBM, USA). Anonymized data will be analyzed.

**Keywords:** Intravascular laser irradiation of blood (ILIB), peripheral blood microscopy, vascular photobiomodulation (VPBM), infrared thermography, venous ulcer.

**Study Type:** Protocolo (Protocol)

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**EFFECTS OF PHOTOBIOMODULATION WITH RED AND INFRARED LEDS IN INDIVIDUALS UNDERGOING RHINOPLASTY: PROTOCOL FOR A RANDOMIZED, DOUBLE-BLIND, CONTROLLED CLINICAL TRIAL**

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**Abstract**

Edema and ecchymosis are common after rhinoplasty and may delay recovery. Photobiomodulation (PBM) has been shown to have analgesic, anti-inflammatory, and regenerative effects; however, its role in rhinoplasty remains underexplored. Objectives: This study aims to evaluate the effectiveness of PBM in reducing periorbital edema in patients undergoing rhinoplasty. Methodology: Sixty patients will be randomized into two groups: Control (n = 30), who will undergo sham PBM before surgery, and PBM (n = 30), who will receive preoperative PBM followed by rhinoplasty. Treatment will be delivered with a cluster device containing three red (660 nm, 150 mW each) and three infrared (808 nm, 150 mW each) diodes, applying 12 J per point (per laser) over 80 seconds at three standardized sites (nasal dorsum and bilateral frontal processes of the maxilla). The intervention (PBM or sham) will be applied one hour before surgery. Edema will be assessed using the Hoffmann scale and standardized photographs, which will be analysed with ImageJ software. Secondary outcomes include edema at additional time points, ecchymosis, pain (as measured by the visual analog scale - VAS), skin thickness (as assessed by nasal tip assessment), and analgesic use. The SCHNOS will be used for aesthetic and functional evaluation. Follow-up will occur at 3, 7, 30, 60, and 90 days, as well as at 6 and 12 months. Adverse events will also be analyzed. Data will be tested for normality (Shapiro–Wilk) and analysed with ANOVA or Friedman and Mann-Whitney tests, as appropriate; and chi-square/Fisher's exact test for SCHNOS data. This trial was approved by the Research Ethics Committee of Irmandade da Santa Casa de São Paulo (protocol number: 7, 503, 097) and registered at ClinicalTrials.gov (NCT07033039 – last update: 06/13/2025). This study may support the use of PBM as an effective, safe, and accessible adjuvant therapy in aesthetic surgical practice.

**Keywords:** Rhinoplasty, Photobiomodulation, Edema, Postoperative, Clinical trial, Low-level laser therapy.

**Study Type:** Protocolo (Protocol)

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**EFFICACY OF PHOTODYNAMIC THERAPY IN INFECTIONS RELATED TO SCHANZ PINS AND KIRSCHNER WIRES: A RANDOMIZED CONTROLLED CLINICAL STUDY**

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**Abstract**

**Background:** Infections associated with external fixators and orthopedic implants remain a clinical challenge due to biofilm formation and bacterial resistance. Systemic antibiotics show limited efficacy because of poor biofilm penetration and the rise of resistant strains, while chlorhexidine may impair tissue repair. These limitations emphasize the need for adjuvant, safe, and effective antimicrobial approaches. Antimicrobial photodynamic therapy (aPDT) stands out for its selective microbial action, lack of resistance induction, low cost, and ease of use, making it a promising adjunct for orthopedic infections. **Aim:** To evaluate the efficacy of aPDT combined with standard treatment for infections related to Schanz pins and Kirschner wires, compared with standard care alone. **Methods:** This randomized, controlled, double-blind clinical trial will include 72 participants with external fixators or orthopedic implants, allocated into two groups (n=36). The Experimental Group will receive standard wound care (debridement, cleansing with 2% chlorhexidine, and systemic/local antibiotics when indicated) plus aPDT using a 660 nm diode laser (400 mW, continuous mode, 5 min exposure, 120 J/cm<sup>2</sup>, 4 points around each pin, single session) after pre-irradiation with 0.01% methylene blue. The Control Group will receive identical care combined with sham photobiomodulation. Treatments will occur twice weekly for two weeks, performed by the same investigator. **Outcomes:** The primary outcome is the reduction of the infected area, measured by the Bates-Jensen Wound Assessment Tool (13–65 points) until infection resolution. Secondary outcomes include wound healing (PUSH Tool 3.0), pain intensity (VAS), analgesic consumption, bacterial load, antibiotic use, local temperature (infrared thermography), pH of the insertion site, and quality of life (EQ-5D-3L and SF-36). Adverse events related to aPDT will be recorded. Wound area and volume will be quantified via ImitoWound® for standardized digital analysis. **Statistical analysis:** Data will undergo normality testing and be analyzed using two-way ANOVA or Kruskal–Wallis, with categorical variables compared via chi-square or Fisher’s exact test. Kaplan–Meier curves and log-rank tests will assess time to infection resolution. Statistical significance is set at  $p < 0.05$ .

**Keywords:** aPDT, photodynamic therapy, lasers, orthopedics, wounds caused by orthopedic conditions, phototherapy.

**Study Type:** Protocol (Protocol)

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**EXPERIMENTAL STUDY OF PHOTOBIOMODULATION ASSOCIATED WITH OPIOID DRUG USE  
IN PAIN CONTROL IN A COLLAGENASE-INDUCED TENDINITIS MODEL**

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Saúde (1);**Abstract**

Tendinopathies are inflammatory conditions of the tendon, which may present as acute or chronic and represent a therapeutic challenge due to their high incidence. Traditional treatment is still mainly pharmacological, with limited efficacy and well-known adverse effects. Photobiomodulation (PBM) is considered a safe therapy for the management of joint and tendon disorders, capable of modulating inflammation and pain. The aim of this study is to evaluate the effect of PBM combined with an opioid drug on pain mechanisms, assessing histological and biochemical parameters related to nociceptive modulation. Methodology: Wistar rats will be anesthetized, and tendinitis will be induced by transcutaneous injection of type I collagenase. The animals will be allocated into healthy controls (CTL) or tendinitis groups: untreated (NT), treated with photobiomodulation (PBM), with tramadol (OP), or with the combination of both therapies (PBM+OP). Additional groups will receive the opioid antagonist naloxone combined with PBM (NL+PBM) or tramadol (NL+OP). Twelve hours after tendinitis induction, the animals will be euthanized, and the tendons collected for histological (inflammatory infiltrate) and biochemical analyses (MPO activity and gene expression of pain receptors). This study aims to investigate the effects of PBM on central pain control mechanisms through the evaluation of opioid receptor expression.

**Keywords:** tendinopathies, photobiomodulation, opioids, MOR, chronic pain.**Study Type:** Protocolo (Protocol)



## PHOTOBIOMODULATION IN STAGE 1 AND 2 PRESSURE INJURIES: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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### Abstract

Pressure injuries (PIs) are recognized as common adverse events following hospitalization, ranking among the five leading causes of harm to inpatients. Recent studies have demonstrated that photobiomodulation (PBM) is a promising intervention for wound healing, reducing inflammation, and stimulating tissue regeneration. Although PBM has already been applied in the treatment of advanced-stage PIs, its use in early stages (stages 1 and 2) remains underexplored. This study hypothesizes that early PBM intervention may prevent the progression of PIs to more severe stages, reducing the risk of complications and improving patients' quality of life. Therefore, this study aims to evaluate the treatment success rate of stage 1 and 2 PIs in hospitalized patients through PBM application. This is a randomized controlled clinical trial including patients with stage 1 and 2 PIs and a Braden scale score < 14. A total of 224 participants will be randomly allocated into two groups: PBM Group (n = 112), which will receive irradiation on the pressure injuries using a 660 nm continuous-wave laser, with an output power of 100 mW and irradiance of 35. 388 mW/cm<sup>2</sup>. The application technique will be punctual, with 16 irradiated points, resulting in a radiant exposure of 1. 769 J/cm<sup>2</sup> and 5 J of energy per point. The exposure time will be 50 seconds per point, totaling 80 J of energy per session. The intervention will be applied five times per week for three weeks (15 sessions). The Control Group (n = 112) will receive the PBM simulation. Both groups will receive standard care, including cleansing, debridement, and dressings. The primary outcome will be the incidence of progression of PIs to more advanced stages. Secondary outcomes will include: time to PI development, local pain intensity (measured using the Visual Analog Scale – VAS), healing score (as assessed by the PUSH tool), health-related quality of life (measured using the EQ-5D questionnaire), number of dressing changes, adverse events related to PBM, and patient satisfaction with the treatment. Outcome variables will be assessed at baseline, in the first and second weeks after the beginning of the intervention. Data will be analysed with a 5% significance level (p < 0. 05), following the intention-to-treat principle. Progression of lesions (categorical variable) will be compared between groups using Fisher's exact test or chi-square test. Continuous variables (VAS, PUSH, and EQ-5D) will be tested for normality using the Shapiro-Wilk test and compared between groups using Student's t-test or Mann-Whitney test, according to distribution. Intraindividual changes over time will be analyzed using repeated-measures ANOVA or the Friedman test, as applicable.

**Keywords:** photobiomodulation, pressure injury prevention, pressure injuries, wound healing, laser therapy.

**Study Type:** Protocolo (Protocol)

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**PHOTOBIOMODULATION FOR PREVENTING SURGICAL-SITE INFECTION IN CORONARY ARTERY BYPASS GRAFTING. A RANDOMIZED, DOUBLE-BLIND CLINICAL TRIAL WITH A 30-DAY FOLLOW-UP.**

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**Abstract**

**Introduction:** Surgical site infection in cardiac surgeries is a serious complication with high mortality, especially when it progresses to mediastinitis. It represents a significant challenge for patient safety and the sustainability of the healthcare system. Recent data from the state of São Paulo indicate that the surgical site infection rate in coronary artery bypass grafting surgeries reached 7.93% in 2024, highlighting the magnitude of the problem. This scenario is associated with prolonged hospital stays, increased hospital costs, increased demand for antibiotics and additional interventions such as new surgical approaches, and significantly impacts patient quality of life. Given this problem, it is necessary to investigate adjuvant therapeutic strategies that can act preventively to reduce postoperative complications. Photobiomodulation presents a promising alternative by stimulating healing, modulating inflammatory and immunological responses, and favoring an environment less conducive to bacterial colonization. **Methodology:** This study will be a randomized, double-blind, sham-controlled clinical trial involving 194 patients undergoing coronary artery bypass grafting (CABG) and followed up to postoperative day 30. Participants will be divided into two groups: laser and sham, receiving transcutaneous applications parallel to the surgical incisions from the first to the fifth postoperative day. The protocol will be conducted using an Ecco Reability Cluster Dual Laser device, consisting of three 660 nm diodes and three 808 nm diodes, with a power of 150 mW per diode, with simultaneous emission totaling 18 J in 20 seconds, resulting in an energy density of 2 J/cm<sup>2</sup> per cycle. The first two applications will be performed over a standard dressing, and a dosimetry adjustment of 60% transmittance will be used. **Objectives:** The primary outcomes of this study will include the incidence of surgical site infection and wound dehiscence, while secondary outcomes will include pain intensity, analgesic use, length of hospital stay, and treatment costs. Statistical analysis will be conducted to compare the groups regarding clinical and laboratory variables, ensuring the robustness of the findings. The results are expected to confirm the potential of photobiomodulation as an adjuvant strategy in preventing surgical complications, favoring patient recovery, reducing hospital stays, and optimizing hospital resources.

**Keywords:** Photobiomodulation, low-level laser therapy, coronary artery bypass grafting, CABG, surgical site infection prevention, wound dehiscence, sustainability of the health system.

**Study Type:** Protocolo (Protocol)

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**IMPACT OF PHOTODYNAMIC THERAPY WITH 5-ALA ON A549 LUNG ADENOCARCINOMA  
AND LEWIS LUNG CARCINOMA CELL LINES**

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**Abstract**

Lung cancer, particularly adenocarcinoma, is one of the leading causes of mortality worldwide, characterized by high aggressiveness and low survival rates in advanced stages. Photodynamic therapy (PDT) has emerged as a promising approach that combines a photosensitizer activated by light at a specific wavelength, in the presence of oxygen, to generate reactive oxygen species (ROS). These species induce cell death and modulate the tumor microenvironment. This study investigates the effects of PDT on lung adenocarcinoma cell lines A549 (human) and LLC (murine, Lewis Lung Carcinoma), using 5-aminolevulinic acid (5-ALA) as the photosensitizer. The experimental model employs three-dimensional (3D) spheroid cultures, which more accurately reproduce the tumor microenvironment, allowing a realistic assessment of cellular interactions and treatment responses. The 3D spheroids will be formed using the hanging drop method, in which 15–30  $\mu\text{L}$  drops containing  $1 \times 10^4$  cells are placed on the inverted lid of culture plates; after 5–7 days, compact spheroids of 200–300  $\mu\text{m}$  in diameter will be obtained. The experiment includes eight groups: (1) Control (lung adenocarcinoma – unmanipulated cells maintained under the same conditions as the other groups); (2) Photosensitizer (exposure to 5-ALA); (3) LED (irradiation with 660 nm LED, 6  $\text{J}/\text{cm}^2$ , 122 s); and (4) PDT (exposure to 5-ALA followed by LED irradiation under the same parameters). These groups will be assessed in both cell lines (A549 and LLC). Analyses will include cell viability, spheroid size, colony-forming ability, cell migration, modulation of signaling pathways, and the profile of pro- and anti-inflammatory cytokines (IL-6, TNF- $\alpha$ , IL-1 $\beta$ , IL-10, and IFN- $\gamma$ ), aiming to elucidate the immunological mechanisms associated with tumor response. Statistical analysis will be performed using one-way ANOVA followed by the Student-Newman-Keuls post-test, with GraphPad Prism 5.0 software (USA). The results are expected to contribute to understanding the impact of PDT on tumor viability reduction and immunological microenvironment reprogramming, promoting antitumor responses.

**Keywords:** Photodynamic therapy, Lung adenocarcinoma, 5-ALA, Pulmonary inflammation.

**Study Type:** Protocolos (Protocols)

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**THE USE OF PHOTOBIOMODULATION AND ANTIMICROBIAL PHOTODYNAMIC THERAPY IN THE MANAGEMENT OF PRESSURE INJURIES: SCOPING REVIEW AND CONSENSUS BY THE MODIFIED DELPHI METHOD**

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**Abstract**

**Introduction:** Pressure injuries are highly prevalent in hospital and long-term care settings, especially among bedridden, elderly, or mobility-impaired patients. They result from prolonged pressure on the skin and underlying tissues, often exacerbated by shear forces, friction, and moisture, leading to significant clinical consequences such as pain, infection, prolonged hospitalization, and even sepsis or death. Among innovative therapeutic approaches for managing these injuries, photobiomodulation (PBM) and antimicrobial photodynamic therapy (aPDT) have shown promising outcomes. PBM employs low-intensity light to stimulate cellular metabolism and tissue repair, while aPDT combines light and a photosensitizer to generate reactive oxygen species capable of eliminating pathogenic microorganisms. However, current literature reveals heterogeneity in protocols, dosimetric parameters, and clinical indications, underscoring the need for standardization. **Objective:** To conduct a scoping review of the scientific literature, followed by the development of an expert consensus on the use of PBM and aPDT in pressure injuries, using the modified Delphi method. **Methodology:** This protocol involves two sequential phases: (1) a scoping review conducted according to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guideline, aiming to map existing evidence on the use of PBM and aPDT in the treatment of pressure injuries; and (2) a modified Delphi consensus, in which a panel of experts in nursing and related health fields will participate in iterative rounds to establish agreement on key parameters, indications, and application strategies for both therapies. The results will be organized into practical recommendations according to lesion stage and therapeutic objective, contributing to the improvement of clinical practice and research in multidisciplinary health contexts.

**Keywords:** photodynamic therapy, photobiomodulation, low-level laser therapy, pressure ulcer, nursing, consensus, Delphi technique.

**Study Type:** Protocolos (Protocols)



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**BIOPHOTONIC TECHNOLOGIES IN THE CLINICAL MANAGEMENT OF MALAR ERYTHEMA**

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**Abstract**

Malar erythema is a characteristic manifestation of systemic lupus erythematosus (SLE), marked by inflammation, vasodilation, and facial tissue damage. The controlled application of biophotonic technologies, including pulsed lasers and intense pulsed light, both high-power sources, has shown significant therapeutic potential. These modalities can reduce inflammation, modulate immune activity, and stimulate cellular regeneration, promoting tissue repair, restoring the skin barrier, and decreasing facial redness. Such effects contribute to improved quality of life and self-esteem in patients. The objective was to evaluate the therapeutic efficacy of these biophotonic technologies in treating malar erythema in SLE, focusing on their impact on inflammation and skin regeneration. Methods: This is an exploratory narrative literature review, where searches were conducted in the PubMed, SciELO, and Web of Science databases, using the descriptors "photobiomodulation", "light therapy", "malar erythema", "lupus erythematosus", and "treatment". Clinical trials, observational studies, and reviews involving human SLE patients with cutaneous manifestations were included. Results: From clinically relevant studies published in the last 22 years, seven were initially selected. Four studies were excluded for focusing on systemic SLE rather than skin lesions, leaving three studies that were descriptively analyzed for therapeutic interventions in malar erythema. In one study evaluating direct intervention on erythema, specifically outcomes of reduced hyperemia and clinical improvement of facial erythema, the use of Pulsed Dye Laser (PDL) (585-595 nm, radiant exposure 5–7.75 J/cm<sup>2</sup> and 6–13 J/cm<sup>2</sup>) was the main approach, showing significant clinical improvement of facial erythema greater than 60% and reduction in pruritus. The second study used the Nd:YAG laser, resulting in reduced hyperpigmentation and improved scar aesthetics. The third study evaluated UVA-1 irradiation (340–400 nm; radiant exposure 60 J/cm<sup>2</sup>), which modulated vascular and inflammatory responses, reduced hyperemia, induced HO-1, and promoted antioxidant, anti-inflammatory effects, and aesthetic improvement. Conclusion: From this perspective, the analysis indicates that biophotonic technologies demonstrated effectiveness in the management of malar erythema, with significant clinical improvement, a low incidence of adverse effects, and a favorable tolerability profile, reinforcing their therapeutic safety.

**Keywords:** Photobiomodulation, Light therapy, Malar erythema, Lupus erythematosus, Treatment.

**Study Type:** Revisão (Review)

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**BLUE LIGHT PHOTOTHERAPY IN THE MANAGEMENT OF EARLY ENAMEL LESIONS IN CHILDREN**

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**Abstract**

Early enamel demineralization is a frequent clinical finding in pediatric dentistry, particularly in patients with poor hygiene or orthodontic appliances. Conventional remineralization methods rely mainly on topical fluoride and casein phosphopeptide–amorphous calcium phosphate (CPP-ACP). Recent evidence suggests that blue light phototherapy (405–470 nm) may enhance enamel remineralization and reduce bacterial biofilm activity through photochemical and photothermal effects, offering a non-invasive adjunct for early lesion management. AIM: This literature review aimed to evaluate the efficacy of blue light phototherapy in the management and remineralization of early enamel lesions in children. METHODS: A comprehensive literature search was performed in PubMed, Scopus, and Web of Science databases for studies published between 2018 and 2025 using the terms “blue light,” “phototherapy,” “enamel demineralization,” “remineralization,” and “pediatric dentistry.” In vitro and in vivo studies involving primary or permanent teeth with initial white spot lesions were included. Data on lesion depth, mineral gain, bacterial reduction, and light parameters were analyzed. RESULTS: Blue light phototherapy demonstrated significant antibacterial effects against *Streptococcus mutans* and *Lactobacillus acidophilus*, leading to reduced biofilm formation. When combined with fluoride or CPP-ACP, the therapy enhanced remineralization and decreased lesion progression. Studies using wavelengths between 440–470 nm with power densities of 100–250 mW/cm<sup>2</sup> showed optimal results. No adverse effects on enamel structure or pulp vitality were reported. CONCLUSION: Blue light phototherapy represents an innovative, non-invasive adjunct for managing early enamel lesions in children. Its antimicrobial and remineralizing properties can complement conventional preventive strategies. Further randomized clinical trials are required to standardize parameters and confirm long-term outcomes in pediatric populations.

**Keywords:** “Blue light,” “phototherapy,” “enamel demineralization,” “remineralization,” and “pediatric dentistry.”

**Study Type:** Revisão (Review)

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**EFFECT OF THE ASSOCIATION OF VASCULAR AND LOCAL PHOTOBIOMODULATION ON THE ACUTE INFLAMMATORY PROCESS CAUSED BY BOTHROPIC ENVENOMATION**

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**Abstract**

**Introduction:** Envenomation by venomous snakes represents a global public health problem, affecting millions of people and causing deaths and disabilities. In Brazil, about 90% of snakebites are caused by snakes of this genus. Although antivenom serotherapy is the standard and highly effective treatment against the systemic effects of Bothrops envenomation, it is ineffective against the local effects of the venom (at the bite site), which can lead to limb loss in the most severe cases and other sequelae. Photobiomodulation (PBM) therapy has proven to be a promising therapeutic resource in cases of Bothropic envenomation, by reducing the local effects related to toxicity and by promoting muscle regeneration. **Objective:** In the present study, we intend to evaluate the combined effects of local photobiomodulation (PBM) and vascular photobiomodulation (VPBM) on the acute inflammatory process caused by Bothrops atrox venom in an animal model. **Methodology:** For this purpose, Balb/C mice will receive the venom and will be treated with antivenom, local PBM, and VPBM, alone or in combination. The parameters used in local and vascular PBM will be a wavelength of 660 nm, power of 100 mW (power density of 0.33 W/cm<sup>2</sup>), beam area of 0.028 cm<sup>2</sup>, with an energy of 4 J, fluence of 44 J/cm<sup>2</sup>, for 40 s. Muscle edema, cell migration to the muscle, hyperalgesia, and pro- and anti-inflammatory cytokines will be analyzed. To assess muscle edema, the envenomed muscle will be measured relative to the control muscle; hyperalgesia will be measured by von Frey filaments; and migration will be assessed by total and differential leukocyte count and cytokine dosage by ELISA. **Conclusion:** The aim is to establish an integrated approach that enhances the beneficial effects of local FBM, offering a complementary alternative to antivenom therapy. This innovative strategy is expected to broaden treatment possibilities for both local and systemic manifestations of envenomation, resulting in significant advances in the clinical management of these conditions.

**Keywords:** Fotobiomodulação, inflamação, edema, hiperalgesia, Bothrops atrox.**Study Type:** Revisão (Review)

**EFFECTS OF LASER THERAPY ON AUTISM SPECTRUM DISORDER: A SYSTEMATIC REVIEW**

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**Abstract**

**Background:** Autism Spectrum Disorder (ASD) is characterized by neurodevelopmental impairments that affect several areas of human life, such as social interaction, behavior, and communication. Recently, there has been growing interest in non-pharmacological interventions for ASD, such as transcranial laser photobiomodulation and laser acupuncture. **AIM:** This study aims to evaluate the effects of laser therapy (transcranial photobiomodulation or laser acupuncture) in individuals with autism. **METHODS:** This study is a systematic literature review based on articles available in PubMed and Lilacs databases that evaluated children and adults undergoing transcranial laser therapy or laser acupuncture. Application parameters, behavioral scales, and biomarkers were analyzed. Six articles were selected from the literature search. Eligibility criteria were as follows: full text; time frame within the last 5 years; languages in English and Spanish; and relevant to the topic. **RESULTS:** In autistic individuals, laser therapy increases neurogenesis and synaptogenesis; promotes neuroprotection; modulates neuroinflammation; influences the production of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF); stimulates serotonin production; increases cognitive function, concentration, and attention; improves sleep; decreases irritability and stereotypical behaviors; and improves language and social interaction. Reported adverse effects were minimal. **CONCLUSION:** Laser therapy is promising and safe as a complementary intervention in ASD. However, randomized clinical trials with larger sample sizes and standardized protocols are recommended to confirm the observed effects.

**Keywords:** Laser therapy, Photobiomodulation, Autism Spectrum Disorder, Neuroplasticity, Complementary therapies.

**Study Type:** Revisão (Review)

**EFFECTS OF LASER THERAPY ON INTESTINAL DYSBIOSIS: LITERATURE REVIEW**

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**Abstract**

**Background:** Intestinal dysbiosis, characterized by microbiota imbalance, is associated with inflammatory, metabolic, and neurological processes, highlighting the importance of the gut-brain axis. Low-level laser therapy (LLLT) has been investigated as a non-invasive therapeutic strategy capable of modulating the intestinal microbiota and reducing systemic inflammation. **AIM:** This study aimed to review the available evidence on the effects of laser therapy on intestinal dysbiosis, with an emphasis on experimental and clinical studies. **METHODS:** This is a literature review based on articles indexed in PubMed and Lilacs, which evaluated the influence of LLLT on microbial composition, inflammatory cytokines, and intestinal mucosal integrity in humans and animals. **RESULTS:** LLLT, which involves the use of red (630-700 nm) and infrared (700 and 1200 nm) light, reduced inflammation by decreasing pro-inflammatory cytokines (IL-6, IL-8, IL-12, and TNF- $\alpha$ ), in addition to affecting the circadian rhythm, restoring microbiota balance, and promoting gut-brain axis communication. The exact mechanism by which light interacts with the microbiota has not yet been elucidated. In addition to chromophores located in cells, a diversity of bacterial species (gram-positive and gram-negative) and fungal cells (including yeast) have been shown to respond to laser therapy. Specifically, LLLT increased the number of Lactobacillus and Bifidobacterium, both essential for maintaining intestinal homeostasis, reducing inflammation and strengthening the intestinal epithelial barrier. Furthermore, laser therapy promoted a positive change in the Firmicutes/Bacteroidetes ratio and a decrease in the number of Helicobacter pylori in the gut microbiota. **CONCLUSION:** Laser therapy has promising therapeutic potential in the treatment of intestinal dysbiosis, but requires standardized protocols (effective doses, application frequency, session duration, application site - transcranial, intranasal, abdominal, vascular photobiomodulation) and more robust clinical studies to confirm its efficacy and safety. Furthermore, it is essential to evaluate the effect of LLLT on various disorders related to the gut microbiota that have not yet been studied.

**Keywords:** Laser therapy, Photobiomodulation, Dysbiosis, Intestinal microbiota, Brain-gut axis.

**Study Type:** Revisão (Review)



**EFFECT OF PHOTOBIOMODULATION THERAPY ON SLEEP QUALITY IN DIFFERENT HEALTH CONDITIONS: A LITERATURE REVIEW**

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**Abstract**

**Introduction:** Sleep is a fundamental pillar of health, yet insomnia is highly prevalent and negatively impacts quality of life. Conventional pharmacological therapies have significant limitations, including side effects and dependence potential, justifying the search for new approaches. Photobiomodulation (PBM), a non-invasive therapy using low-intensity light to modulate biological processes, emerges as a promising alternative for improving sleep quality. **Aim:** To analyze and synthesize scientific evidence on the use of photobiomodulation (PBM), or low-power laser, for improving sleep quality, addressing its potential mechanisms of action and the results of clinical studies. **Methods:** A literature review was conducted in the PubMed database using the descriptors "(Sleep quality) AND ((photobiomodulation) OR (Low level laser))", with filters for full-text, free-access studies. 36 articles were identified; 13 met inclusion criteria: addressing the PBM-sleep relationship. Study protocols and paid-access articles were excluded. **Results:** The analyzed literature indicates a strong association between PBM therapies and improved sleep outcomes across diverse health conditions. Transcranial PBM (t-PBM) repeatedly demonstrated efficacy, improving subjective sleep quality (measured by PSQI) in patients with psychiatric conditions (Major Depressive Disorder, Generalized Anxiety Disorder, persistent anxiety). Similar positive outcomes were seen in children with Autism Spectrum Disorder. The potential extends beyond t-PBM; one RCT using a low-level LED helmet found significantly reduced insomnia scores in shift-work nurses. Laser acupuncture also reduced sleep onset latency and night awakenings in chronic insomnia. Systemic applications, like whole-body PBM for Fibromyalgia and intravascular laser irradiation for Guillain-Barré syndrome, also reduced sleep disturbances. This evidence is supported by systematic reviews confirming PBM's potential to enhance sleep, possibly by modulating cerebral glymphatic function. **Conclusion:** Photobiomodulation, especially its transcranial form, shows consistent positive effects on sleep quality in healthy individuals and patients with diverse neurological, psychiatric, and clinical conditions. While promising, methodological heterogeneity and limited RCTs indicate the need for standardized research to confirm efficacy, define optimal parameters, and fully understand the involved mechanisms.

**Keywords:** Sleep quality, Photobiomodulation, Low level laser

**Study Type:** Revisão (Review)

## IMPACT OF PHOTOBIOMODULATION ON MYOCARDIAL REGENERATION FOLLOWING INFARCTION: A NARRATIVE REVIEW

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### Abstract

**Introduction:** A Myocardial Infarction (MI) causes irreversible heart muscle cell death, leading to fibrosis and progressive ventricular remodeling that often results in heart failure. Photobiomodulation (PBM), a noninvasive therapy using low-level laser or LED light, is emerging as a strategy to boost cellular metabolism, angiogenesis, and tissue repair. Recent findings suggest that PBM can reduce post-infarction damage and support myocardial healing by activating mitochondria and modulating molecular pathways. **Objective:** To assess the preclinical evidence on the effects of PBM on myocardial regeneration following infarction. **Methods:** This narrative review searched PubMed for studies on “photobiomodulation” OR “low-level laser therapy” OR “LLLT” OR “LED therapy” OR “laser therapy” AND “myocardial infarction” OR “heart regeneration” OR “cardiac repair.” Eligible studies (January 2021–October 2025) included randomized trials, experimental animal studies, or systematic reviews assessing PBM effects on myocardial regeneration in animal models or adults ( $\geq 18$  years). Outcomes included cardiac function improvement, tissue regeneration, reduced fibrosis, expression of regenerative markers, and enhanced hemodynamic parameters. **Results:** Screening identified 17 articles, with 7 meeting inclusion criteria. PBM has shown benefits in myocardial regeneration, including reduced infarct size and collagen deposition, attenuated fibrosis, and preserved ventricular wall integrity. Functional improvements were observed, with enhanced ejection fraction and fractional shortening. 4 studies used red-light PBM (630–660nm; 15mW; 0.9 J), 2 applied LED irradiation at 630 nm, and one used near-infrared light (850nm), all studies related directly to injured tissue. 3 out of 7 studies have shown that PBM promoted angiogenesis, 3 studies demonstrated evidence about cardiomyocyte proliferation. 2 articles also enhanced the increased mitochondrial ATP synthesis, while 3 of them showed suppressed inflammatory and pro-fibrotic mediators (IL-6, TGF- $\beta$ 1, collagen I/III), and regulated remodeling-associated microRNAs (downregulating miR-136-5p, miR-34c, and miR-93), supporting myocardial repair. **Conclusion:** PBM demonstrates cardioprotective and regenerative effects after myocardial infarction by enhancing mitochondrial function, reducing fibrosis and inflammation, and improving ventricular function. Standardized protocols and more human studies are needed to confirm its safety and efficacy.

**Keywords:** Photobiomodulation, Myocardial Infarction, Cardiac Regeneration, Tissue repair.

**Study Type:** Revisão (Review)

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**INFRARED LED-BASED DEVICE WITH OPTICAL DOSIMETRY CONTROL FOR  
PHOTOBIOMODULATION IN DIABETIC FOOT ULCERS**

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**Abstract**

Photobiomodulation (PBM) research explores the interaction between light and biological tissues and has been applied in recent decades to treat various diseases. It stands out for being a non-invasive and low-cost method with positive results in a short period of time. This study aims to develop a prototype based on a cluster of infrared Light Emitting Diode (LEDs) for PBM in the treatment of diabetic foot ulcers, a global health concern. The system consists of 48 infrared LEDs with emission at 940 nm (mod. L-51AEIR1BC), and optical power of 20 mW/LED, where the cluster was designed for a total radius of 4.5 cm (circular shape), being divided into three levels: 1.5, 2.5 and 3.5 cm, where each of them contains 8, 16 and 24 LEDs respectively, totaling areas of 7.07; 19.63 and 38.48 cm<sup>2</sup>. The levels were subdivided into sections of 8 LEDs in series, each polarized by resistors to control the electric current, as simulated in the LTspice® software, ensuring stable optical operation and electrical safety. Electronic control was provided by an ATmega328p single-chip microcontroller, programmed in C language, with the human-machine interface using an SSD1306 I2C display for operation selection (initialization, level selection, time selection, fluence calculation, and irradiation time counting). Dosimetry adjustment was performed using three buttons (SELECT, UP, and DOWN), which select advance, return, and change variable values. The exposure time was set between 30 and 300 seconds, in 30-second increments. Based on the chosen level and exposure time, energy density (fluence) can be varied between 0.68 and 7.48 J/cm<sup>2</sup>, which falls within the optical therapeutic window, as determined by a literature review conducted. The prototype was designed in both 2D and 3D using Autodesk Fusion® software and subsequently 3D printed with a white PLA filament, resulting in an attractive and ergonomic aesthetic with a low weight of only 210 grams. The innovative optoelectronic system not only controlled optical dosimetry but also allowed for adjustments in the irradiation area and time elapsed to irradiate the wound size being treated throughout the wound healing process. This approach differs from some devices on the market, which typically only display the remaining irradiation time. The results obtained demonstrate the system's ability to control optical dosimetry, combining practicality and functionality, and support its future potential for clinical evaluation.

**Keywords:** Photobiomodulation, LED, Diabetic Foot Ulcer**Study Type:** Desenvolvimento de equipamento (Development of Equipment)

**LIGHT-BASED THERAPIES IN THE PREVENTION AND TREATMENT OF SURGICAL SITE INFECTIONS: A SYSTEMATIC REVIEW**

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**Abstract**

**Introduction:** Surgical site infections (SSIs) cause significant postoperative morbidity, worsened by antimicrobial resistance. Light-based therapies such as antimicrobial photodynamic therapy (aPDT), blue light (405nm), UV-C, and photobiomodulation (PBM) reduce microbial load, disrupt biofilms, and promote healing without chemicals. **Objective:** To evaluate light-based therapies for SSI prevention and treatment, focusing on application parameters (photosensitizer, wavelength, dose/exposure), mechanisms of action, clinical outcomes, methodological limitations, and guidance for future research. **Methods:** A narrative review was conducted using PubMed and SciELO and the descriptors "photobiomodulation" OR "low-level laser therapy" OR "photodynamic therapy" OR "antimicrobial photodynamic therapy" OR "aPDT" OR "laser therapy" AND "surgical site infection" OR "surgical wound" OR "postoperative infection" OR "infected wound" OR "surgery" NOT dentistry OR dental OR tooth OR oral OR periodontal). Studies from January 2018 to October 2025 using red, blue, infrared, or UV-C light for SSI prevention or treatment, including clinical trials, observational/experimental studies, and systematic reviews, were included. Screening identified 11 studies, with data on application parameters, populations, and outcomes (microbial reduction, healing, safety) extracted and analyzed. **Results:** Among the 11 studies, four used red light (630–660nm), three blue light (405–470nm), two UV-C (254nm), and two multi-wavelength PBM (450–850nm). Radiant exposures varied from 2 to 50J/cm<sup>2</sup>, with treatment times of 30 seconds to 10 minutes per area. Outcomes included infection rates, healing time, pain and edema reduction, and local histological or microbiological changes. Most studies showed significant bacterial load reductions, especially in *Staphylococcus aureus* and *Pseudomonas aeruginosa*, improved healing, and less necrotic tissue. Blue light had direct antimicrobial effects, while red and infrared light stimulated fibroblasts and collagen, supporting tissue repair. UV-C was effective in surface and instrument decontamination, though tissue damage risks depend on dose, penetration, and exposure. Multi-wavelength PBM accelerated soft tissue recovery and reduced inflammation in bone fractures. **Conclusion:** Light-based therapies are promising for managing SSIs, but methodological differences and limited trials require standardized protocols and further studies to confirm efficacy and safety.

**Keywords:** Surgical site infection, Photodynamic therapy, Photobiomodulation, Methylene blue, UV-C, Blue light

**Study Type:** Revisão (Review)

**LASER IN THE TREATMENT OF ACNE: MECHANISMS, LIGHT SOURCES, AND RECENT EVIDENCE IN PATIENTS UNDER 18 YEARS OF AGE**

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**Abstract**

**Introduction:** Photobiomodulation uses non-ionizing light sources, such as lasers and LEDs, to treat acne vulgaris, a chronic inflammatory disorder of the sebaceous glands. Different wavelengths modulate local inflammation and act directly on lesions, while high-power sources provide antimicrobial, anti-inflammatory, and thermal effects. Recent studies support its efficacy, highlighting its potential as a complementary or alternative treatment, particularly in patients under 18 years. **OBJECTIVE:** To conduct a narrative literature review on the efficacy and safety of laser considering photobiomodulation and high power sources in the treatment of acne lesions in patients under 18 years of age. **METHODS:** This narrative review followed the PRISMA guidelines. A search of PubMed and ScienceDirect using the terms “photobiomodulation AND acne” yielded 164 publications. Exclusion criteria removed studies with participants aged 18 years or older, those lacking detailed dosimetric parameters, published before 2020, involving animal models, or not original scientific articles. **RESULTS:** Five studies evaluated the efficacy and safety of laser and light therapies for acne vulgaris. Fluorescent light therapy combined with isotretinoin improved moderate-to-severe acne, while pulsed dye (595 nm) and diode (577 nm) lasers were effective for inflammatory lesions and comedones. Comparative studies showed 577 nm diode and 1064 nm Nd:YAG lasers to be safe, well-tolerated, and effective across skin phototypes. In a randomized trial with 52 patients, both lasers significantly reduced inflammatory lesions ( $p < 0.001$ ), with similar Acne Severity Index responses (26.9% diode, 28.8% Nd:YAG), high satisfaction, and mild, transient adverse events. A retrospective study of 225 patients treated with 1064nm Nd:YAG (650ms pulse) found 48% achieved an ablative effect after three sessions, with limited side effects and 80% avoiding isotretinoin; median IGA score at six months was 1.0. In 12 patients treated with fluorescent light energy plus low-dose isotretinoin or tetracycline for 52 weeks, rapid improvement in redness, edema, and overall skin appearance was observed, with no severe adverse effects, confirming safety and efficacy even with potentially photosensitizing drugs. **CONCLUSION:** Photobiomodulation, particularly using the 577nm yellow diode and 1064nm Nd:YAG lasers, is a safe and effective therapeutic option for acne vulgaris, with only mild and transient adverse effects.

**Keywords:** Photobiomodulation, Low-Level Light Therapy, Laser Therapy, Acne vulgaris, Inflammation



**Study Type:** Revisão (Review)

**LOW-LEVEL LASER THERAPY IN ACCELERATING TOOTH ERUPTION AND ROOT FORMATION IN PEDIATRIC DENTISTRY**

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**Abstract**

**BACKGROUND:** Delayed tooth eruption and incomplete root formation are common developmental concerns in pediatric dentistry and orthodontics. These conditions may result from local trauma, systemic disorders, or genetic factors, potentially affecting occlusion and craniofacial growth. Low-Level Laser Therapy (LLLT), or photobiomodulation therapy (PBMT), has demonstrated the ability to stimulate osteogenic and odontogenic activity by promoting mitochondrial function, cellular proliferation, and angiogenesis, suggesting potential benefits in accelerating tooth eruption and enhancing root development. **AIM:** This literature review aimed to analyze the biological effects and clinical outcomes of low-level laser therapy on tooth eruption rate and root formation in pediatric patients. **METHODS:** A literature search was performed in PubMed, Scopus, and Web of Science databases for studies published between 2018 and 2025 using the keywords “low-level laser therapy,” “photobiomodulation,” “tooth eruption,” “root formation,” and “children.” Experimental and clinical studies involving primary or permanent teeth in eruption were included. The main outcomes evaluated were eruption rate, root length, bone remodeling, and cellular response. **RESULTS:** LLLT increased osteoblastic differentiation, collagen synthesis, and vascularization in the pericoronal follicle region. Wavelengths ranging from 780 to 850 nm and energy densities between 3–8 J/cm<sup>2</sup> were associated with enhanced tooth eruption velocity and root elongation in animal and pediatric models. Studies also reported elevated alkaline phosphatase activity and upregulation of genes related to dentin and bone formation (Runx2, BMP-2, and OCN). Clinically, PBMT reduced the latency phase of eruption and improved eruption symmetry without adverse effects on pulp or periodontal tissues. **CONCLUSION:** Low-level laser therapy represents a promising adjunct in the management of delayed tooth eruption and root development in pediatric dentistry. Its biostimulatory effect on bone remodeling and odontogenesis supports its potential inclusion in orthodontic and interceptive protocols. Further controlled trials are required to define standardized parameters and long-term outcomes.

**Keywords:** “low-level laser therapy,” “photobiomodulation,” “tooth eruption,” “root formation,” “children.”

**Study Type:** Revisão (Review)

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**LOW-LEVEL LASER THERAPY IN NIPPLE TRAUMA: DEVELOPMENT AND VALIDATION OF A STANDARD OPERATIONAL PROTOCOL**

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**Abstract**

**INTRODUCTION:** Nipple trauma is a frequent complication in the early stages of breastfeeding, with prevalence rates of up to 96%, including excoriations, fissures, and erosions. These injuries cause pain, increase the risk of infection, compromise breastfeeding continuity, and may lead to early weaning. Low-level laser therapy (LLLT) is a photobiomodulation technique that uses low-energy monochromatic light to stimulate cellular repair, reduce inflammation, and promote analgesia. Despite its potential, the incorporation of LLLT into maternal and child health services requires structured protocols to ensure safety, reproducibility, and professional autonomy. **AIM:** To develop a Standard Operational Protocol (SOP) for the use of LLLT in the management of nipple trauma in lactating women. **METHODS:** This is a report of technological innovation regarding an educational intervention practice developed for a municipal health service to support women with nipple trauma during breastfeeding, to be carried out by nurses. The study resulted from activities of a doctoral course conducted between September and October 2024. The proposal sought to critically analyze an institutionalized process in the workplace of the doctoral students and propose an improvement that would generate a product eligible for copyright registration. The process was structured in stages: literature review, SOP development, validation by field experts, institutional approval, and copyright registration. **RESULTS:** The SOP was structured as a quality management tool, aiming to standardize the use of LLLT in nipple trauma. The document describes, step by step, the clinical assessment, contraindications, technical parameters, and follow-up of breastfeeding women. Validation by experts confirmed clarity, scientific consistency, and clinical feasibility. The protocol received approval from the institution's nursing technical manager and was registered as an authored work. **CONCLUSION:** The development of the SOP reinforces the importance of standardizing clinical practices to ensure maternal safety, promote breastfeeding continuity, and strengthen nursing autonomy in the use of photobiomodulation. This product represents an innovative, dynamic, and replicable tool for health systems, aligned with contemporary trends in biophotonics and quality management.

**Keywords:** Enterostomal Therapy, Low-Level Light Therapy, Breastfeeding, Nursing Care**Study Type:** Revisão (Review)

**PHOTOBIOMODULATION AS A NON-INVASIVE THERAPEUTIC STRATEGY FOR ALZHEIMER'S DISEASE**

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**Abstract**

**Introduction:** Alzheimer's disease (AD) is a progressive neurodegenerative condition that initially manifests as mild memory loss and later leads to declines in cognitive, behavioral, and language functions. It mainly affects elderly individuals (>65 years). Despite the high prevalence of AD and decades of research, there are still no effective treatments capable of halting or reversing its progression. In this context, photobiomodulation (PBM) emerges as a promising therapeutic approach that uses low-power, non-ionizing light sources primarily in the red and near-infrared (NIR) wavelengths, to modulate cellular processes. **Objective:** To conduct a narrative review to assess the potential of PBM as a non-invasive therapeutic alternative, addressing its biological mechanisms and clinical applications in the prevention and treatment of Alzheimer's disease manifestations. **Methods:** A search was conducted in PubMed, MEDLINE, and SciELO using the keywords "Alzheimer's disease (AD)" and "photobiomodulation (PBM)." Studies were excluded if they lacked a description of PBM parameters or presented duplicated results. **Results:** Five studies were initially identified, with four meeting the inclusion criteria and analyzed in full. PBM demonstrated beneficial effects in both experimental and clinical studies on Alzheimer's disease. Clinical improvements included enhanced cognitive function in patients with mild to moderate dementia treated with PBM 810nm for 12 weeks. In preclinical studies, transgenic mice exposed to 810nm light three times per week for six months showed reduced beta-amyloid plaque deposition along with improved mitochondrial and behavioral function. The most commonly used wavelengths range from 600–670nm (red) and 800–1100nm (infrared), with fluences of 0.5–10J/cm<sup>2</sup>, applied two to five times per week, producing positive effects on oxidative stress, inflammation, and neuronal function. These findings highlight the potential of photobiomodulation as a promising therapeutic strategy for the management of Alzheimer's disease. **Conclusion:** PBM represents a non-invasive, safe, and potentially effective therapy capable of improving cognition and quality of life through neuroprotective and brain-restorative effects. However, detailed and long-term clinical trials are still needed to confirm its efficacy and to establish standardized treatment protocols.

**Keywords:** Photobiomodulation, near-infrared light (NIR), Alzheimer's disease, neuroprotection, non-invasive therapy

**Study Type:** Revisão (Review)

**PHOTOBIMODULATION AND MUSCLE FATIGUE IN ADULTS: A LITERATURE REVIEW**

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**Abstract**

**INTRODUCTION:** Muscle fatigue is a multifactorial physiological condition characterized by reduced force generation and performance after intense or prolonged activity. It involves peripheral and central mechanisms associated with metabolite accumulation, oxidative stress, and mitochondrial dysfunction. Photobiomodulation (PBM) has been investigated as a non-invasive intervention capable of modulating cellular metabolism, increasing ATP production, and reducing reactive oxygen species, thus promoting faster recovery and improved muscle performance. **OBJECTIVE:** To review the scientific literature on the effects of photobiomodulation on muscle fatigue in adults, focusing on physiological mechanisms, dosimetric parameters, and functional outcomes related to performance and recovery. **METHODS:** An exploratory search was conducted in PubMed and the Virtual Health Library (VHL), considering publications from 2020 to 2025 in English. The descriptors “Photobiomodulation,” “Muscle Fatigue,” and “Adults” were used with the Boolean operator AND. Randomized controlled trials (RCTs) investigating PBM effects on muscle fatigue in adults were included. Two independent reviewers selected studies, resolving discrepancies by consensus. Duplicates and unrelated records were excluded. **RESULTS:** Four articles met the inclusion criteria. All studies were conducted in adult participants, evaluating the effects of single and multiple PBM sessions (laser or LED) in both healthy individuals and patients with medical conditions. A wide heterogeneity in PBM parameters was observed, with wavelengths ranging from 632 to 1064 nm, as well as expressive differences in other dosimetric variables such as emission mode, emitter power, number of emitters, beam area at the target tissue (cm<sup>2</sup>), exposure time (s), radiant exposure (J/cm<sup>2</sup>), radiant energy (J) per point, application sites, total energy, number and frequency of sessions, and application technique. Overall, PBM demonstrated therapeutic potential in reducing muscle fatigue and promoting functional recovery, although the lack of standardized protocols limits direct comparison across studies and the consolidation of robust evidence. **CONCLUSION:** The use of PBM shows promising evidence in reducing muscle fatigue in adults. However, due to the limited number of available studies and the high variability of dosimetric parameters, current evidence remains insufficient to standardize optimal wavelength and energy settings.

**Keywords:** Photobiomodulation, Laser therapy, Muscle fatigue, Muscle recovery, Adults.

**Study Type:** Revisão (Review)



## PHOTOBIOMODULATION AS AN ADJUNCT THERAPY IN DIABETIC PERIPHERAL NEUROPATHY: A SYSTEMATIC REVIEW OF EVIDENCE AND LIMITATIONS

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### Abstract

Diabetic peripheral neuropathy (DPN) is a common and disabling diabetes complication that impairs quality of life and increases the risk of ulcers, infections, and amputations. Despite available treatments, pain control and nerve regeneration remain difficult. Photobiomodulation (PBM) with lasers or LEDs has emerged as a non-invasive option to promote neural recovery, but studies show inconsistent results regarding its efficacy and mechanisms. Objective: This study aimed to conduct a narrative systematic review to assess the efficacy of photobiomodulation therapy for diabetic peripheral neuropathy, identifying key application parameters, mechanisms of action, and clinical effects on pain, nerve regeneration, and functionality, to consolidate current evidence and guide future research. Methods: A comprehensive search was conducted in PubMed and PMC using terms related to photobiomodulation and diabetic peripheral neuropathy. Eligible studies (2018–2025) included randomized trials, observational studies, or systematic reviews evaluating PBM with lasers or LEDs as an adjuvant therapy for adults with type 1 or type 2 diabetes. Outcomes analyzed were neuropathic pain, sensory function, quality of life, and neurophysiological parameters. From 19 identified studies, 10 met the inclusion criteria for detailed analysis, while others were excluded for irrelevance, limited access, or lack of significant findings. Results: The 10 included studies demonstrated that PBM is an effective and safe therapy for diabetic peripheral neuropathy. Most studies used wavelengths from 630 to 810 nm, with five studies in the 630–660 nm (red), four in the 780–810 nm (infrared), and two combining 660/808 nm or 660/850 nm. The radiant exposure ranged from 3 to 30 J/cm<sup>2</sup>, with exposure time sessions lasting 10–20 minutes, applied two to three times per week for 8–15 sessions. Main outcomes included reduction in neuropathic pain in nine studies, improved sensory function in seven, nerve regeneration in five (associated with increased NGF, NSE, and CGRP expression), and enhanced functionality and quality of life in six. Conclusion: Photobiomodulation (PBM) has emerged as a safe and promising adjuvant therapy for diabetic peripheral neuropathy, providing pain relief and promoting nerve regeneration. However, the heterogeneity of protocols underscores the need for standardization and multicenter clinical trials to consistently confirm its therapeutic efficacy.

**Keywords:** Diabetic peripheral neuropathy, Photobiomodulation, Laser therapy, Nerve regeneration, Neuropathic pain, Systematic review

**Study Type:** Revisão (Review)

**PHOTOBIOMODULATION IN BRAIN DISORDERS: PARKINSON'S DISEASE**

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**Abstract**

**Introduction:** Parkinson's disease (PD) continues to challenge modern medicine with its silent, irreversible, and devastating progression. Despite advances in symptomatic management, no current therapy can halt the degeneration of dopaminergic neurons that characterizes this condition. In this context, photobiomodulation (PBM) has emerged as an innovative, non-invasive, and safe therapeutic strategy with neuroprotective potential. By using low-intensity, non-ionizing light sources at specific wavelengths, PBM has demonstrated, in both experimental models and preliminary clinical studies, the ability to modulate mitochondrial processes, reduce neuroinflammation, and stimulate synaptic plasticity. **Objective:** To conduct a narrative literature review of current scientific evidence on the use of PBM as an adjuvant therapeutic strategy in PD, highlighting its neuroprotective mechanisms, potential clinical benefits, and remaining limitations in the literature. **Methods:** A PubMed search for articles published between 2019 and 2024 using the terms "photobiomodulation" and "Parkinson's disease" identified 50 studies. Four were selected for directly addressing PBM in experimental models or PD patients. Duplicates, studies lacking clinical or dosimetric data, and those on other neurodegenerative diseases were excluded. **Results:** The included studies used wavelengths of 670–940nm, applied transcranially or transabdominally, with a power of 0.16mW (160W) and 0.4 to 0.5W and an irradiance of 50mW/cm<sup>2</sup>. Outcomes showed improvements in motor function, balance, cognition, and tremor reduction after 2–3 months, along with mitochondrial neuroprotection and reduced inflammation in experimental models. In a five-year longitudinal study with eight participants, seven continued home-based PBM therapy three times per week; six demonstrated significant gains in gait, balance, cognition, and motor scores, which remained stable or improved in 83% of participants, with no reported adverse effects. Overall, PBM appears to restore mitochondrial function, reduce oxidative stress, and prevent neuronal apoptosis, representing a safe, non-invasive, and potentially effective therapy for slowing Parkinson's disease progression. **Conclusion:** PBM is a promising, non-invasive therapy for PD, enhancing mitochondrial function and reducing inflammation to slow symptom progression, improve quality of life, and confirm its efficacy and safety through broader controlled studies.

**Keywords:** Photobiomodulation, Parkinson's disease, Light-based therapy, Neuroinflammation, Non-invasive therapies

**Study Type:** Revisão (Review)

**PHOTOBIOMODULATION IN BURN WOUND HEALING: LITERATURE REVIEW**

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**Abstract**

**Introduction:** Burn wound healing represents a significant clinical challenge due to the complexity of inflammatory responses, the risk of infection, and the development of hypertrophic scars, factors that compromise both functional and aesthetic recovery of the tissue. In this context, photobiomodulation (PBM) has emerged as a non-invasive and promising approach capable of modulating cellular and molecular processes involved in tissue regeneration. Irradiation with light at specific wavelengths stimulates ATP production, cell proliferation, angiogenesis, and collagen synthesis, in addition to reducing oxidative stress and local inflammation. **Objective:** This study aims to review scientific literature on the effects of PBM in the burn wound healing process, gathering the main experimental and clinical evidence that supports its therapeutic application. **Methodology:** A search was conducted in the PubMed database using the Boolean search strategy ("photobiomodulation" OR "low-level laser therapy") AND ("burn wound" OR "skin graft" OR "laser therapy" OR "LED"). Filters included studies published in English from 2014 to 2024, involving human subjects (randomized clinical trials, clinical trials, and case reports). Studies employing high-power lasers or conducted exclusively in animal models were excluded. Data were extracted regarding study design, population, irradiation parameters, treatment frequency, and main outcomes. **Results:** Thirteen clinical studies on the use of PBM in burn wound healing were identified, of which five met the inclusion criteria and were analyzed. There was wide heterogeneity in PBM parameters, with wavelengths ranging from 655 to 808 nm, as well as differences in other dosimetric variables such as emission mode, emitter power, number of emitters, beam area on the target tissue (cm<sup>2</sup>), exposure time (s), radiant exposure (J/cm<sup>2</sup>), radiant energy (J) per point, application sites, total energy, number and frequency of sessions, and application technique. Some studies did not report all parameters necessary to ensure protocol reproducibility. Overall, PBM accelerated epithelialization, improved graft adherence, enhanced collagen organization, and reduced pain and pruritus, with no adverse effects reported. PBM demonstrated relevant therapeutic potential in tissue repair and in improving scar tissue quality. **Conclusion:** PBM appears to be a safe and effective adjuvant for enhancing burn wound healing and graft integration. Despite the favorable outcomes, there is still a lack of standardized clinical parameters regarding wavelength, energy dose, and application frequency. Further randomized controlled trials are required to establish

evidence-based protocols and strengthen its routine clinical use. Keywords: burns; photobiomodulation; low-level laser therapy; wound healing; skin graft.

**Keywords:** burns, photobiomodulation, low-level laser therapy, wound healing, skin graft.

**Study Type:** Revisão (Review)

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**PHOTOBIOMODULATION IN PAIN CONTROL DURING LOCAL ANESTHESIA IN PEDIATRIC PATIENTS: A NON-PHARMACOLOGICAL ANALGESIC APPROACH**

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**Abstract**

**BACKGROUND:** Local anesthesia is essential in pediatric dental procedures but often triggers anxiety, fear, and pain perception, which may hinder cooperation and increase physiological stress responses. Conventional approaches to minimize discomfort rely mainly on topical anesthetics and behavioral techniques. Photobiomodulation therapy (PBMT) has emerged as a non-pharmacological strategy to modulate nociception by enhancing mitochondrial activity, releasing endorphins, and regulating inflammatory mediators. **AIM:** This literature review aimed to evaluate the efficacy of photobiomodulation in reducing pain and discomfort during local anesthesia administration in children. **METHODS:** An integrative literature review was performed through PubMed, Scopus, and Web of Science databases, including studies published between 2018 and 2025. The search terms used were “photobiomodulation,” “low-level laser therapy,” “pain control,” “local anesthesia,” and “pediatric dentistry.” Clinical and experimental studies evaluating pain perception, physiological responses, or anxiety indicators were included. **RESULTS:** PBMT significantly reduced pain scores measured by Wong–Baker and FLACC scales during anesthesia injection. Studies reported decreased heart rate and improved cooperation in pediatric patients receiving laser preconditioning before infiltration. Wavelengths between 808–830 nm and fluences of 3–6 J/cm<sup>2</sup> provided optimal analgesic outcomes by modulating nociceptor thresholds and reducing prostaglandin E2 release. Some trials demonstrated that PBMT application 60 seconds before injection produced immediate hypoalgesic effects comparable to topical anesthetics. No adverse reactions were reported. **CONCLUSION:** Photobiomodulation represents a safe, non-invasive, and effective adjunct for pain control during local anesthesia in pediatric dentistry. Its biostimulatory action on neural and inflammatory pathways contributes to better patient cooperation and comfort. Further randomized clinical studies are required to standardize parameters and confirm long-term benefits in pediatric populations.

**Keywords:** photobiomodulation,” “low-level laser therapy,” “pain control,” “local anesthesia,” “pediatric dentistry.”

**Study Type:** Revisão (Review)



**PHOTOBIMODULATION IN THE MANAGEMENT OF ORAL MUCOSITIS IN PEDIATRIC  
CANCER PATIENTS: LITERATURE REVIEW**

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**Abstract**

**Introduction:** Oral mucositis is a frequent and debilitating adverse effect of cancer therapy, characterized by intense pain, dysphagia, and significant impairment of quality of life. Photobiomodulation (PBM), which employs non-ionizing low-intensity red or near-infrared light, modulates cellular processes by reducing pro-inflammatory cytokines, stimulating ATP synthesis, and promoting tissue repair. It has shown positive effects on pain, inflammation, edema, and wound healing. Recently, the Brazilian Ministry of Health officially included PBM in the Unified Health System (SUS) procedure table for the prevention and treatment of radio or chemotherapy-induced oral mucositis in outpatient and hospital settings, ensuring standardized access and funding. **Objective:** To assess scientific evidence on photobiomodulation (PBM) and other light-based approaches, such as photodynamic therapy (PDT), for managing oral mucositis in pediatric cancer patients, focusing on mechanisms of action, clinical outcomes, and quality-of-life improvement. **Methods:** This narrative, descriptive, and comparative review analyzed studies published between 2013 and 2025, retrieved from PubMed and Google Scholar using the terms “oral mucositis,” “pediatric oncology,” and “low-level laser therapy.” Duplicate articles, studies lacking detailed PBM parameters, and those involving non-pediatric populations were excluded. **Results:** Eleven studies were initially identified, and five met the inclusion criteria. PBM, alone or combined with photodynamic therapy (PDT) or vascular PBM (VPBM), proved effective in reducing the severity of oral mucositis in pediatric cancer patients ( $p < 0.05$ ). Main outcomes included pain reduction (3 studies), lower mucositis grade (4), prevention of progression (3), absence of adverse effects (3), and faster healing (1). Four studies used red light, four near-infrared, and two combined wavelengths. In two studies, PDT preceded PBM, with one reporting superior results for the combined protocol. Blue LED and VPBM were also applied as adjuncts, both showing positive effects. No adverse events were reported. **Conclusion:** PBM and other light-based therapies, including photodynamic therapy (PDT), are safe and effective for managing oral mucositis in pediatric cancer patients, providing pain relief, faster healing, and improved quality of life, with standardized protocols needed to optimize clinical use.

**Keywords:** “oral mucositis,” “pediatric oncology,” and “low-level laser therapy.”

**Study Type:** Revisão (Review)

**PHOTOBIOMODULATION IN THE POSTOPERATIVE PERIOD OF RHINOPLASTY, SEPTOPLASTY, AND TURBINECTOMY: A LITERATURE REVIEW**

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**Abstract:**

**Introduction:** Adequate postoperative management in otorhinolaryngological surgeries is essential to optimize healing, reduce complications, and improve patient comfort. Photobiomodulation (PBM) has been investigated as an adjuvant therapy for tissue repair, inflammation control, and cellular regeneration. **Objective:** To review the scientific literature on the effects of PBM in the postoperative period of nasal surgeries, including rhinoplasty, septoplasty, and turbinectomy. **Methodology:** An exploratory search was conducted in PubMed, Scopus, and LILACS databases for publications from 2007 to 2025 in English, Portuguese, and Russian. The descriptors “laser therapy, ” “low-level laser therapy, ” “phototherapy, ” and “photobiomodulation” were combined with “septoplasty, ” “turbinectomy, ” “rhinoplasty, ” “nasal surgery, ” “healing, ” “post-surgery, ” and “wounds. ” Study selection was performed by two independent reviewers, and disagreements were resolved by a third evaluator. Original articles describing irradiation parameters and in vitro studies were included, while reviews and studies without a control group were excluded. **Results:** Twenty-three articles were identified, and nine met the inclusion criteria. Considerable heterogeneity was observed in PBM parameters, with wavelengths ranging from 632 to 1064 nm and variations in emission mode, power, beam area (cm<sup>2</sup>), exposure time (s), radiant exposure (J/cm<sup>2</sup>), energy per point (J), application sites, total energy, number and frequency of sessions, and technique. Several studies did not report all parameters required for reproducibility. Overall, PBM showed therapeutic potential in tissue repair by stimulating collagen synthesis and deposition, accelerating epithelialization, and reducing inflammation, edema, and pain. PBM may promote faster recovery and greater comfort after nasal surgeries; however, protocol variability limits comparisons and the establishment of robust evidence. **Conclusion:** The application of PBM in the postoperative period of nasal surgeries still requires stronger evidence and parameter standardization, highlighting the need for further experimental and randomized controlled clinical studies.

**Keywords:** Photobiomodulation, Postoperative care, Rhinoplasty, Septoplasty, Turbinectomy.

**Study Type:** Revisão (Review)

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**PHOTODYNAMIC THERAPY (PDT) AND PAIN ATTENUATION IN CUTANEOUS NEOPLASTIC AND PRE-NEOPLASTIC LESIONS: A LITERATURE REVIEW**

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**Abstract**

Introduction: Oncological pain represents a complex and persistent challenge in cancer treatment, significantly impacting patients quality of life. Given this scenario, photodynamic therapy (PDT), which uses lasers and photosensitizers, has been utilized as a promising therapeutic modality due to its minimally invasive nature and high selectivity for tumor tissues and pre-cancerous lesions, such as Basal Cell Carcinoma and Actinic Keratosis. Objective: To search the literature for studies relating the use of PDT to pain attenuation in patients presenting with cutaneous tumor and pre-tumor lesions. Methods: For the literature review, the descriptors "PDT", "Cancer" and "pain" were searched in "Pubmed" (2025/10). Articles published within the last 5 years, with full, free text, were considered. The search resulted in 20 titles, which were selected based on their correlation with the theme. Only 8 dealt with pain attenuation in neoplastic and pre-neoplastic skin lesions, and these were used for the analysis. Results: The analyzed studies demonstrated that PDT plays a relevant role not only in tumor control but also in reducing the pain associated with the treatment and with the cutaneous neoplastic and pre-neoplastic lesions. A systematic review on oral mucositis evidenced significant pain relief and clinical improvement with the use of PDT. Strategies such as "painless PDT" and light fractionation proved effective in diminishing discomfort without compromising therapeutic efficacy. Jet-injection assisted PDT presented higher tolerability and less local pain in patients with basal cell carcinoma. In parallel, nanotechnological advancements, such as the use of redox-sensitive and folate receptor-mediated nanophotosensitizers, contributed to increasing tumor selectivity and reducing post-procedure inflammation and pain. Collectively, the findings reinforce the trend of PDT toward more selective, effective, and comfortable protocols, consolidating its therapeutic and analgesic potential. Conclusion: PDT emerges as a promising and evolving therapeutic option for skin neoplasms and inflammatory conditions. Advances such as jet-injection delivery, painless PDT, and nanotechnology-based photosensitizers<sup>8</sup> have improved tolerability, increased selectivity, and reduced procedure-related pain and inflammation. These findings highlight the progressive refinement of PDT toward more effective and better-tolerated protocols, reinforcing its therapeutic and analgesic potential.

**Keywords:** Skin Neoplasms, Precancerous Conditions, Cancer Pain, Photochemotherapy**Study Type:** Revisão (Review)

**PHOTODYNAMIC THERAPY IN NEOPLASTIC CELLS: A LITERATURE REVIEW**

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**Abstract**

**Introduction:** Photodynamic therapy (PDT) is a minimally invasive therapeutic modality that combines the use of a photosensitizer, light at a specific wavelength, and molecular oxygen to generate reactive oxygen species (ROS) capable of inducing selective cell death in neoplastic cells. In addition to its direct effects on tumor cells, PDT promotes vascular damage and stimulates an antitumor immune response. However, variability in the uptake and type of photosensitizer, specific affinity with tumor cells, tissue heterogeneity, and activation of cellular resistance mechanisms still limit its clinical efficacy. **Objective:** To critically analyze the evidence published over the past ten years on photodynamic therapy (PDT) in neoplastic cells, with emphasis on the factors influencing its effectiveness. **Methodology:** An exploratory search was performed in PubMed using the terms (“photodynamic therapy AND neoplastic cells” OR “PDT in cancer cells”), covering 2014–2024. Initially, 22 studies were identified, including reviews and originals, of which 13 met the inclusion criteria and were analyzed in depth. Eligible articles addressed PDT mechanisms, cellular resistance, nanomaterials, subcellular targeting, and radiometric parameters. Duplicates, papers lacking methodological or radiometric details, and those unrelated to the topic were excluded. **Results:** A wide heterogeneity was observed in the types of photosensitizers, cell lines studied, dosimetric and radiometric parameters, exposure times, and experimental strategies. The efficacy of PDT varied according to the photosensitizer, wavelength, and mode of application. In general, PDT induced apoptosis, necrosis, and immunogenic cell death, associated with the production of ROS and the activation of mitochondrial and lysosomal pathways. Approaches that optimize intracellular oxygen distribution, the use of type I photosensitizers, and coupling with bioactive nanoparticles have shown promise in overcoming resistance in hypoxic microenvironments. **Conclusion:** It is concluded that the application of PDT in neoplastic cells has shown promising results in recent studies, demonstrating relevant therapeutic potential. However, there is still a need for more robust evidence and standardization of radiometric parameters and types of photosensitizers, making it essential to conduct new experimental studies and controlled, randomized clinical trials to consolidate its therapeutic efficacy and safety.

**Keywords:** Photodynamic therapy, Neoplastic cells, Photosensitizers, Reactive oxygen species, Cell death.

**Study Type:** Revisão (Review)

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**TRANSABDOMINAL PHOTOBIOMODULATION AND THE GUT-BRAIN AXIS: AN INTEGRATIVE REVIEW ON MECHANISMS AND EVIDENCE IN NEURODEGENERATIVE DISEASES**

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Pós-Graduação em Engenharia Biomédica, São Paulo/SP, Brasil (2)**Abstract**

**INTRODUCTION:** The gut-brain axis is a bidirectional communication pathway between the central nervous system and the gastrointestinal tract, mediated by neural, immune, hormonal, and metabolic mechanisms. Recent evidence suggests that therapies capable of modulating the gut microbiota may positively influence inflammatory and neuroplastic processes. Photobiomodulation Therapy (PBMT) is a non-invasive intervention that uses low-intensity light in the red and near-infrared spectra, with demonstrated effects on cellular bioenergetics and microbiome modulation. Preclinical and clinical studies indicate that transabdominal PBMT can modify microbiota composition and reduce neuroinflammation, representing a novel approach termed photobiomics. **OBJECTIVE:** To conduct an integrative review of the literature on the effects of transabdominal PBMT in modulating the gut-brain axis in neurodegenerative diseases. **METHODOLOGY:** An integrative literature review was performed using PubMed, SciELO, LILACS, ScienceDirect, and Scopus databases, including studies between 2014 and 2024 in Portuguese, English, and Spanish. Clinical and preclinical studies addressing transabdominal PBMT in relation to the gut-brain axis, intestinal microbiota, or neurodegenerative diseases were included, while studies without consolidated results or focused solely on analgesia were excluded. Extracted data were organized descriptively according to study design, PBMT parameters, and main outcomes. **RESULTS AND DISCUSSION:** Five studies met the inclusion criteria. Overall, transabdominal PBMT increased the proportion of beneficial bacteria (such as Firmicutes), reduced pathogenic species, improved cognition, and decreased neuroinflammatory markers. Clinical studies involving patients with Alzheimer's and Parkinson's disease reported functional improvements and favorable changes in microbiome composition. Moreover, recent reviews suggest a synergistic effect between transcranial and transabdominal PBMT, enhancing modulation of the gut-brain axis. Despite the limited number of studies, evidence supports PBMT as a promising, safe, and integrative intervention for neurodegenerative disease. **CONCLUSION:** Transabdominal PBMT demonstrated modulatory potential over the gut-brain axis, promoting microbial homeostasis and neuroprotection. Although preliminary, these findings highlight the need for controlled clinical trials to validate this emerging therapeutic approach in neurodegenerative disorders.

**Keywords:** Gut-brain axis, Intestinal microbiota, Neurodegenerative Diseases, Photobiomodulation.

**Study Type:** Revisão (Review)



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**THE USE OF PHOTOBIOMODULATION IN THE TREATMENT OF VAGINAL CANDIDIASIS:  
REVIEW OF EVIDENCE, MECHANISMS AND PERSPECTIVES**

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Paulo, Brazil**Abstract:**

Caused primarily by *Candida albicans*. It is characterized by itching, pain, discharge, and inflammation of the vaginal mucosa. It is estimated that up to 75% of women experience at least one episode in their lifetime, with approximately 5% developing a recurrent form. The clinical, psychological, and quality-of-life impact is significant. Resistance to traditional antifungals and high recurrence rates justify the search for alternative therapies. Objective: To review the available scientific evidence on the use of photobiomodulation, especially antimicrobial photodynamic therapy (aPDT), as an alternative therapy for the treatment of vaginal candidiasis. Methodology: A narrative review of the literature was conducted on the mechanisms, efficacy, and prospects of aPDT in the treatment of vaginal candidiasis, including laboratory studies, animal models, and initial clinical applications. The effects of aPDT with various light-activated photosensitizers (LED or laser), their interactions with fungal biofilms, and their impact on gene expression and inflammation were considered. Results: aPDT demonstrated significant action against *C. albicans*, promoting fungal membrane destruction, biofilm inactivation, and reduced virulence. Studies with methylene blue, curcumin, and Photodithazine® showed a reduction in fungal viability and inflammatory burden in murine models of oral and vaginal candidiasis. aPDT also positively modulated the local inflammatory response. Conclusion: Photodynamic therapy appears to be a promising approach in the treatment of vaginal candidiasis, with antifungal and anti-inflammatory effects documented in preclinical models. Its mechanisms of action, distinct from conventional antifungals, make it a potentially effective option for resistant and recurrent cases. Further clinical studies are needed to validate its large-scale

**Keywords:** Photosensitizer, Photodynamic Antimicrobial Chemotherapy (PACT)**Study Type:** Revisão (Review)

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**THE EFFECTIVENESS OF PHOTOBIMODULATION IN THE PREVENTION AND TREATMENT OF HYPERTROPHIC SCARS: A REVIEW OF THE LITERATURE**

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**Abstract**

**Background:** Hypertrophic scars are characterized by an abnormal response during the tissue repair process, marked by excessive fibroblast proliferation and exaggerated collagen deposition, without invading the surrounding healthy tissue. Current established treatments for hypertrophic scars include silicone sheets, compression therapy, intralesional corticosteroid injections, cryotherapy, and high-power lasers. However, these methods present limitations regarding efficacy, cost, and safety. Consequently, a therapeutic gap remains, underscoring the need for safe, effective, and non-invasive alternatives. In this context, Photobiomodulation (PBM) has emerged as a promising technology. Nevertheless, there is still a lack of parameters that consolidate the effectiveness of PBM for hypertrophic scars, which hinders appropriate clinical management. **Aim:** To analyze and synthesize the available scientific evidence on the efficacy and safety of PBM as a therapeutic modality for the prevention and treatment of hypertrophic scars. **Methods:** Narrative review carried out in October 2025 in the PubMed/MEDLINE database, using the descriptors “low-level light therapy”, “laser therapy”, “cicatrix, hypertrophic”, and “burns”, combined by Boolean operators “AND”, “OR” and “NOT”. Original articles, systematic reviews, randomized clinical trials and meta-analyses published between 2021 and 2025, available in full text and in English, Portuguese or Spanish, were included. Duplicate studies, case reports, experimental studies, burn wounds and high-power laser treatments were excluded. At the end of the search, 28 articles were identified; however, only 1 was included, as it met the established inclusion and exclusion criteria. **Results:** 21 of the 43 patients comprised the treatment group, which received an 830 nm light-emitting diode (LED). Scar assessment using a 3D skin imaging system evaluating color, height, pigmentation, and vascularization showed no significant improvement with PBM. However, evaluations based on satisfaction and pain scores, the Global Assessment Scale, and the Vancouver Scar Scale demonstrated significantly better outcomes in the laser-treated group. **Conclusion:** PBM with an 830 nm LED showed promising results in improving patient satisfaction and reducing pain. The scarcity of studies on this topic highlights the need for further research with larger sample sizes and standardized PBM protocols, especially those focused on hypertrophic scars.

**Keywords:** "Laser Therapy", "Low-Level Light Therapy", "Cicatrix, Hypertrophic".

**Study Type:** Revisão (Review)

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**THE USE OF ANTIMICROBIAL PHOTODYNAMIC THERAPY (APDT) IN THE TREATMENT OF PERIODONTAL DISEASE - LITERATURE REVIEW**

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**Abstract**

Introduction: Periodontitis is an infection of the periodontium, the supporting tissue of the teeth, which triggers an inflammatory response and induces alveolar bone resorption because of microbial aggression. Conventional treatment, based on scaling and root planing, aims to reduce the bacterial load; however, it may be limited by the anatomical complexity of the root surface. The use of systemic antimicrobials, although effective, is associated with adverse effects and the increased risk of bacterial resistance. In this context, antimicrobial photodynamic therapy (aPDT) emerges as a promising adjunctive alternative, reducing the need for systemic agents. aPDT involves the topical application of a photosensitizer into periodontal pockets which, when activated by light under specific parameters, promotes the generation of reactive oxygen species (ROS), such as singlet oxygen, which are toxic to microorganisms. OBJECTIVE: To evaluate the effectiveness of aPDT as an adjunctive therapy in the treatment of periodontitis, as well as aspects related to its application and mechanisms of action. METHODOLOGY: This study consists of a literature review conducted in the PubMed and ScienceDirect databases, including studies that investigated the efficacy of aPDT in periodontal therapy. RESULTS: The most commonly used photosensitizer in dentistry is methylene blue, a planar heterocyclic dye whose dimer aggregation may reduce singlet oxygen production. Studies have reported a 96% bacterial reduction using methylene blue in a surfactant vehicle and laser irradiation for five minutes, while shorter exposure times altered microbial growth patterns. Some authors reported no significant reduction in bacterial load, whereas others observed results dependent on the medium and the bacterial species analyzed. CONCLUSION: aPDT proves to be a promising approach in the management of periodontitis. However, factors such as dosimetric parameters, concentration, and aggregation state of the photosensitizer influence the outcomes, and no standardized clinical protocol has been established so far. Moreover, differences between in vitro studies and clinical conditions—such as variations in oxygen tension and the presence of blood in gingival fluids—may affect the therapeutic response. Further studies are needed to elucidate the ideal parameters and to develop new photosensitizers applicable to antimicrobial photodynamic therapy.

**Keywords:** Phonotiazine, photosensitizers, photodynamic antimicrobial chemotherapy (PACT).**Study Type:** Revisão (Review)

**TRANSCRANIAL PHOTOBIOMODULATION AND MENTAL HEALTH: A THERAPEUTIC APPROACH FOR DEPRESSION AND ANXIETY**

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**Abstract**

**Introduction:** Depression and anxiety are leading causes of disability worldwide, affecting over 580 million people. Conventional treatments often show limited efficacy, with about 30% of patients being resistant. Transcranial Photobiomodulation (tPBM), which uses low-intensity near-infrared (NIR) light to modulate brain metabolism, has emerged as a promising, non-invasive therapy. Acting on mitochondrial cytochrome-c oxidase, tPBM enhances ATP production, improves neuroplasticity, and reduces neuroinflammation, offering potential benefits for mood regulation and cognitive function. **OBJECTIVE:** To investigate the effects of transcranial photobiomodulation on mental health, emphasizing its therapeutic potential for depression and anxiety. **METHODOLOGY:** A systematic review was conducted following the PRISMA 2020 protocol. Searches were performed in PubMed and EMBASE for studies published between 2015 and 2025 using the terms "Transcranial Photobiomodulation," "Depression," "Anxiety," and "Mental Health." Twelve eligible studies were included, comprising randomized clinical trials, pilot studies, and experimental models. **RESULTS:** The studies showed heterogeneity in parameters but consistent positive outcomes. The most used wavelengths ranged from 810–1064 nm, irradiance 30–250 mW/cm<sup>2</sup>, fluence 9–60 J/cm<sup>2</sup>, with sessions of 20–30 minutes, two to five times per week for four to eight weeks, targeting mainly the prefrontal cortex. tPBM increased mitochondrial ATP and BDNF levels, improved sleep, mood, and cognition, and reduced oxidative stress, inflammatory cytokines, and cortisol. Dose-dependent effects were observed, with moderate NIR intensities yielding the best results. No severe adverse events were reported, confirming tPBM's safety and tolerability. **CONCLUSION:** tPBM shows significant neuroprotective, anti-inflammatory, and neuromodulatory effects, improving mood and stress regulation by restoring mitochondrial and neuroendocrine balance. Its non-invasive nature, favorable safety profile, and clinical versatility make it a promising adjunct in mental health care. However, further large-scale randomized trials are needed to standardize dosimetry and confirm long-term efficacy. Overall, tPBM bridges neuroscience and clinical practice, offering an innovative, evidence-based approach to treating depression and anxiety.

**Keywords:** Low-Intensity Laser Stimulation, Emotional Dysregulation, Anxious Behavior, Emotional Health.

**Study Type:** Revisão (Review)

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**Effects of Photobiomodulation on J774A.1 Macrophages under Oxidative Stress in vitro**

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**Abstract**

**Introduction:** Oxidative stress is a key factor in the pathogenesis of chronic inflammatory diseases, leading to cellular dysfunction and increased production of pro-inflammatory mediators. Macrophages play a central role in the immune response, and their activation under oxidative conditions significantly contributes to inflammation. The J774A.1 murine macrophage lineage is a well-established in vitro model for studying inflammatory responses and oxidative stress. Photobiomodulation (PBM), using low-level laser therapy, has demonstrated anti-inflammatory and antioxidant effects in several cellular models by modulating mitochondrial activity and reducing reactive oxygen species (ROS) generation. However, its specific effects on macrophages under controlled oxidative stress conditions remain underexplored. **Objectives:** To investigate whether PBM can attenuate the inflammatory and oxidative damage induced by hydrogen peroxide ( $H_2O_2$ ) in J774A.1 macrophages. **Methodology:** Cells will be exposed to different  $H_2O_2$  concentrations (50, 100, and 200  $\mu M$ ) to induce oxidative stress and will be treated or not with PBM using a red laser (660 nm, 50 mW, 3 J/cm<sup>2</sup>, 60 s/well). Cell viability (MTT assay), morphological changes, and the production of inflammatory markers (TNF- $\alpha$ , IL-6, iNOS) and nitric oxide (NO) will be analyzed. Based on previous evidence, PBM parameters are suitable for biostimulation and immune modulation. It is expected that PBM will reduce cell death and decrease the release of pro-inflammatory cytokines and NO in  $H_2O_2$ -challenged macrophages, supporting its protective and anti-inflammatory potential. This ongoing study may contribute to understanding PBM mechanisms as a non-pharmacological strategy for managing oxidative stress-related inflammatory conditions.

**Keywords:** Photobiomodulation; Oxidative stress; Macrophages; Inflammation; Hydrogen peroxide.

**Study Type:** Estudo In Vitro (In vitro study)