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Research Article

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Clinical Indications for the Simultaneous Use of Red and Infrared Wavelengths in Photobiomodulation: A Systematic Review and Meta-Analysis

Cintia Regina Andrade Sousa, Lívia Fernandes Cardozo Rodrigues, Franco Arsati, Antônio Luiz Barbosa Pinheiro, Juliana Monteiro Azevedo, Maria Cristina Teixeira Cangussu*

Abstract

Introduction: To identify the clinical indications and effects of the simultaneous use of red and infrared wavelengths in photobiomodulation in adults. Methods: A systematic review was conducted in accordance with PRISMA guidelines and registered with PROSPERO (CRD420251024814). The databases searched were PubMed, Scopus, BVS, Web of Science, and ProQuest, with no language or date restrictions. Studies including participants aged 18 years or older that used the wavelengths simultaneously and compared them with placebo, other therapies, isolated wavelengths, or a before-and-after design were included. Superpulsed/superluminous laser, associations with other wavelengths, and intraindividual comparisons were excluded. Study selection was performed in two stages by independent reviewers. Risk of bias was assessed using the ROB 2 and ROBINS-I V2 tools. The meta-analysis was conducted in Stata/SE 16.1 (random-effects model; REML; I^2). Results: A total of 2916 records were identified, and 28 studies were included. In eight studies, the meta-analysis showed a reduction in pain on the Visual Analog Scale of -2.03 points (95% CI: -2.86 to -1.20; $p<0.001$), with high heterogeneity and an effect direction favoring the intervention. Evidence of benefit was observed for musculoskeletal pain and mucosal/wound conditions. Sports-related outcomes, such as maximum heart rate, perceived exertion, and peak velocity, showed no significant differences. Risk of bias was high/critical in most studies (64.3%). Conclusion: Although the simultaneous application of wavelengths appears promising, the available evidence does not yet support firm clinical recommendations. Multicenter randomized clinical trials with adequately powered samples, standardized protocols, and greater methodological rigor are needed.

Keywords: Low-Level Light Therapy; Photobiomodulation Therapy; Inflammation; Analgesia

Introduction

Photobiomodulation (PBM) is a noninvasive therapy that uses red light (620-700 nm) and near-infrared light (700-1440 nm) to stimulate or inhibit biological processes in various tissues. It is effective in the treatment of immunoinflammatory, musculoskeletal, and neurological disorders, and in promoting the healing of wounds and chronic ulcers. Systematic reviews have reported improvement in pain in several conditions, such as low back pain [1], painful diabetic neuropathy [2], and orofacial pain [3], as well as indications for tissue repair [4]. Studies have shown that low-level laser therapy can modulate inflammatory responses, improve tissue regeneration, and relieve pain associated with inflammatory [5-7].

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The effectiveness of PBM depends on irradiation parameters such as light wavelength (nm), energy density (J/cm²), power density (mW/cm²), power (mW)/irradiation time, and treatment protocol, leading to beneficial outcomes such as pain relief, wound healing, and tissue regeneration [8].

Red and near-infrared light stimulate ATP production by modulating oxidative stress and triggering cellular responses favorable to tissue repair and the modulation of inflammation [9,10]. However, wavelengths in the 600-700 nm range are used to treat superficial tissues, whereas those between 780 and 950 nm penetrate more deeply and are indicated for deeper tissues [11]. In addition, infrared light may enhance tissue perfusion by increasing local circulation and promoting arterial and venous dilation, and it is also associated with pain reduction, thereby expanding its applications in musculoskeletal disorders [12,13].

The choice of wavelength should be determined by the depth of the target tissue and the clinical goal of treatment. Considering that red light acts predominantly on superficial tissues and infrared light reaches deeper tissues, the simultaneous use of these wavelengths may broaden the area of PBM action across different tissue depths.

Furthermore, this combination may favor complementary biological responses related to analgesia, inflammatory modulation, and tissue repair. However, the clinical benefits of this simultaneous application remain poorly described in the literature, especially compared with the isolated or sequential use of the wavelengths.

Therefore, the objective of this systematic review was to identify potential clinical indications and effects of the simultaneous use of a light source emitting red and infrared wavelengths in PBM.

Methods

Study design

A systematic literature review was conducted in accordance with the PRISMA checklist and included a meta-analysis.

Eligibility criteria

The eligibility criteria for this review included studies involving individuals older than 18 years who received, as the intervention, simultaneous red and infrared wavelengths to promote photobiomodulation. Studies were considered eligible when the comparator group received a placebo, another therapeutic intervention, isolated use of red or infrared light, or a before-and-after therapy design.

The exclusion criteria were studies that used superpulsed lasers or superluminous devices, as well as those in which red and infrared wavelengths were combined with other wavelengths, such as blue, violet, or yellow. Studies that adopted a split-mouth experimental design or compared the effect of the intervention on one side of the body with the opposite side were also excluded.

Data sources

The databases used were PubMed, Scopus, BVS, Web of Science, and ProQuest. No restrictions were applied regarding the language or publication date of the articles searched.

Search strategy

The search strategy was developed based on the PICO acronym (P - individuals older than 18 years; I - low-intensity light at red and infrared wavelengths applied simultaneously; C - placebo, other therapies, or red and infrared light applied in isolation; O - photobiomodulation). Thus, the Medical Subject Headings (MeSH) descriptor "Low-Level Light Therapy" and its synonyms were used and combined with the Boolean operator OR. The free terms "Red" and "Infrared" were added to the search line using the Boolean operator AND. Additionally, sensitivity analysis was performed using the Peer Review of Electronic Search Strategies (PRESS). The specific strategies for each database are described in Supplementary Material 1.

Study selection

References found in the databases were imported into the Rayyan application, which identified and resolved some duplicates; the remaining duplicates were removed manually. The first stage of study selection involved reading titles and abstracts, and the second stage involved full-text review of the selected records. Both stages were performed by two independent, blinded researchers, and any disagreements were resolved by a third researcher.

Data extraction

To streamline initial data extraction, Google AI Studio was used as an auxiliary tool under strict double-check protocols. Subsequently, two independent, blinded reviewers manually verified 100% of the extracted data against the full-text articles to ensure complete accuracy. The prompts are described in Supplementary Material 2. The generative tool was used as an auxiliary resource for the initial organization of information, which was subsequently distributed into five tables in Microsoft Excel 2010: 1 - General characteristics of the studies: article title, author, year of publication, study type, sample size, age, sex, educational level, income, marital status, and ethnicity (Supplementary Material 3); 2 - Intervention characteristics: article title (author, year), type of equipment used, type of light (laser or LED, and the wavelength used), mode of energy emission (pulsed or continuous), energy dose per application point, total energy dose, power, application time, treatment duration, and technique applied (Supplementary Material 4); 3 - Primary

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outcome characteristics: article title (author, year), primary outcome, instruments used to assess the primary outcome, criteria for assessing the primary outcome, and results of the primary outcome (Supplementary Material 5); 4 - Secondary outcome characteristics: article title (author, year), secondary outcomes, instruments used to assess the secondary outcome, criteria for assessing the secondary outcomes, and results of the secondary outcomes (Supplementary Material 6); 5 - Conclusion characteristics: article title (author, year), effects of photobiomodulation in relation to the outcomes, and the overall result of the article (Supplementary Material 7).

Risk-of-bias assessment

Following the Cochrane Collaboration's recommendation, the risk of bias in the selected studies was assessed using the ROB 2 tool for randomized clinical trials and the ROBINS-I V2 tool for interventional clinical studies. ROB 2 comprises 22 questions distributed across five domains (bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result), with a final risk-of-bias classification as: 1 - low risk, 2 - some concerns, and 3 - high risk. ROBINS-I V2 includes 40 questions across seven domains (bias due to confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result), with the following classification: 1 - low risk, 2 - moderate risk, 3 - serious risk, and 4 - critical risk.

Data analysis

The meta-analysis was performed using Stata/SE 16.1, applying a random-effects model for quantitative data and the restricted maximum likelihood estimator to estimate the summary measure and its respective confidence intervals. I^2 was used to assess study heterogeneity, and values above 60% were considered high. All pain scores were normalized to a 0-10 scale prior to calculating the mean differences.

Research protocol

The review plan was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420251024814, after no records on this topic were found.

Results

According to the database searches, 2916 articles were identified. After the exclusion of duplicates and articles excluded during the title and abstract screening phase, 105 articles were selected for full-text reading. Of these, 28 texts met the eligibility criteria (Figure 1).

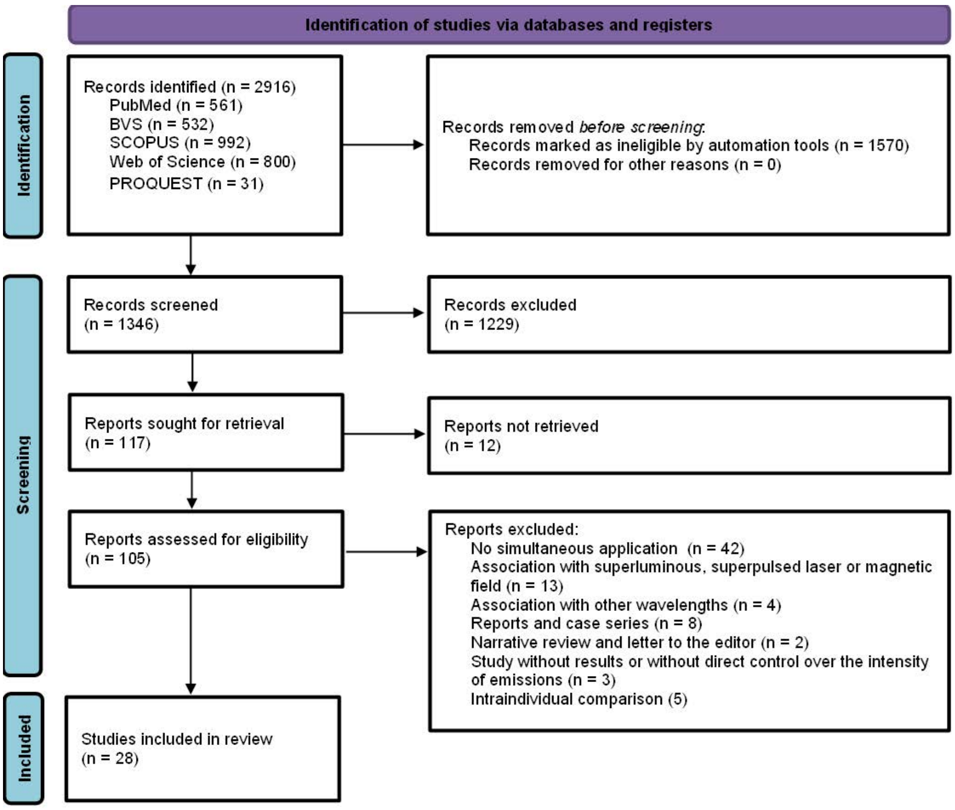

Figure 1: Flow diagram of article selection.

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Sousa CRA, et al., J Biotechnol Biomed 2026
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Of the 28 selected studies, 96.4% were randomized clinical trials, and 60.8% of publications were concentrated between 2021 and 2025. Regarding sample size, there was equivalence between groups with up to 30 participants (39.3%) and those with 31 to 60 participants (39.3%) (Table 1).

Regarding the type of light used, LED was the most prevalent (50.0%), followed by laser (39.3%). Regarding the emission mode, continuous emission was observed in 35.7% of interventions and pulsed emission in 17.9%, while 39.3% of studies did not report this variable (Table 1).

Table 1: General characteristics of the studies.

General Characteristics of the Studies	N (28)	%
Design		
Randomized Clinical Trial	27	96.4
Prospective Clinical Study	1	3.6
Year of Publication		
2010 to 2015	2	7.1
2016 to 2020	9	32.1
2021 to 2025	17	60.8
Sample Size		
≤ 30	11	39.3
> 30 and ≤ 60	11	39.3
> 60	6	21.4
Light Type		
Laser	11	39.3
LED	14	50.0
Laser + LED	2	7.1
Not specified	1	3.6
Emission Mode		
Continuous	10	35.7
Pulsed	5	17.9
Continuous + Pulsed	2	7.1
Not reported	11	39.3
Primary Outcome*		
Physical and functional performance		
Strength and torque	4	10.5
Sports and running performance	3	7.9
Mobility and range of motion	3	7.9
Cardiorespiratory function		
Ventilatory capacity and respiratory strength	1	2.6
Physiological responses during exercise and recovery	3	7.9
Tissue healing and regeneration		
Wound and ulcer healing	2	5.3
Regeneration and markers of muscle injury	2	5.3
Inflammatory conditions of the mucosa	2	5.3
Pain management and associated disability		
Localized musculoskeletal pain	5	13.2
Pain in neurological conditions	1	2.6
Analgesia in procedures and childbirth	1	2.6
Specific clinical conditions		
Allergic rhinitis	2	5.3
Diabetic peripheral neuropathy	1	2.6
Changes in taste	1	2.6
Metabolism and biochemistry		
Body composition and abdominal fat	2	5.3
Oxidative stress and biochemical markers	2	5.3
Cognitive functions and overall well-being		
Sleep and daytime function	1	2.6
Cognitive function and manual dexterity	1	2.6
Quality of life and well-being	1	2.6
Secondary Outcome**		
Physical and functional performance		
Strength and torque	3	5.8
Mobility and range of motion	3	5.8
Balance and functional independence	1	1.9
Fatigue and recovery	1	1.9
Cardiorespiratory function		
Maximal and submaximal heart rate	3	5.8
Subjective perception of exertion	2	3.8
Fetal well-being based on cardiorespiratory parameters	1	1.9
Tissue healing and regeneration		
Wound and ulcer healing	3	5.8
Skin regeneration	1	1.9
Oral conditions (salivary flow, tooth mobility)	1	1.9
Pain management and associated disability		
Musculoskeletal pain	4	7.7
Oral and mucosal pain	2	3.8
Pain-related disability	1	1.9
Use of analgesics	2	3.8
Specific clinical conditions		
Control of respiratory symptoms (rhinitis)	1	1.9
Improvement of alopecia	1	1.9
Condition of amniotic membranes/delivery	1	1.9
Edema	2	3.8
Metabolism and biochemistry		

Sousa CRA, et al., J Biotechnol Biomed 2026
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Body weight and BMI	3	5.8
Overall functional status (ECOG)	1	1.9
Gastrointestinal effects	1	1.9
Associated metabolic markers (lactate)	1	1.9
Change in skin temperature	3	5.8
Cognitive functions and overall well-being		
Psychometric scales	1	1.9
Quality of life and general health	1	1.9
Satisfaction and acceptability	6	11.5
Diaries and self-assessments	2	3.8
Risk of Bias		
Low risk	6	21.4
Some concerns	4	14.3
High risk	17	60.7
Critical	1	3.6
* (n=38) Several articles had more than one primary outcome.		
** (n=52) Several articles had more than one secondary outcome.		

In the synthesis of 28 studies, PBM showed a predominance of findings compatible with anti-inflammatory actions (20/28; 71.4%), followed by evidence related to analgesia (10/28; 35.7%) and tissue repair/healing (10/28; 35.7%).

In the included studies, outcomes were mainly concentrated on pain, physical function, and physiological responses. Among primary outcomes, pain control and associated disability were prominent, especially localized musculoskeletal pain (n = 5; 13.2%), followed by strength and torque (n = 4; 10.5%) and mobility/range of motion and sports performance (n = 3; 7.9%). Among secondary outcomes, musculoskeletal pain predominated (n = 4; 7.7%), followed by strength and torque and mobility/range of motion (n = 3; 5.8%), as well as satisfaction and acceptability measures (n = 6; 11.5%). Overall, the findings show that the literature prioritizes outcomes related to pain reduction, functional improvement, and assessment of treatment response. Regarding risk of bias, 64.3% of the studies were classified as high/critical risk (Table 1).

PBM performed simultaneously with red and infrared wavelengths showed an analgesic effect. Several trials reported pain reduction in different clinical and functional contexts, including after flexor tendon repair, myofascial pain of the masseter, knee pain with improved mobility, pain during gait, and reduction of pain in other musculoskeletal and neurological conditions [14-21].

Eight studies were selected for the meta-analysis, with the mean difference in pain level measured on the visual analog pain scale.

In the meta-analysis of mean differences (random-effects model), the intervention reduced pain on the VAS by -2.03 [-2.86, -1.20] points, with statistical significance ($p<0.001$), compatible with clinical relevance (2.03 points on the VAS). Heterogeneity among studies was high, indicating that pain was assessed in diverse clinical contexts and with varied methodologies, which warrants caution when interpreting the summary estimate.

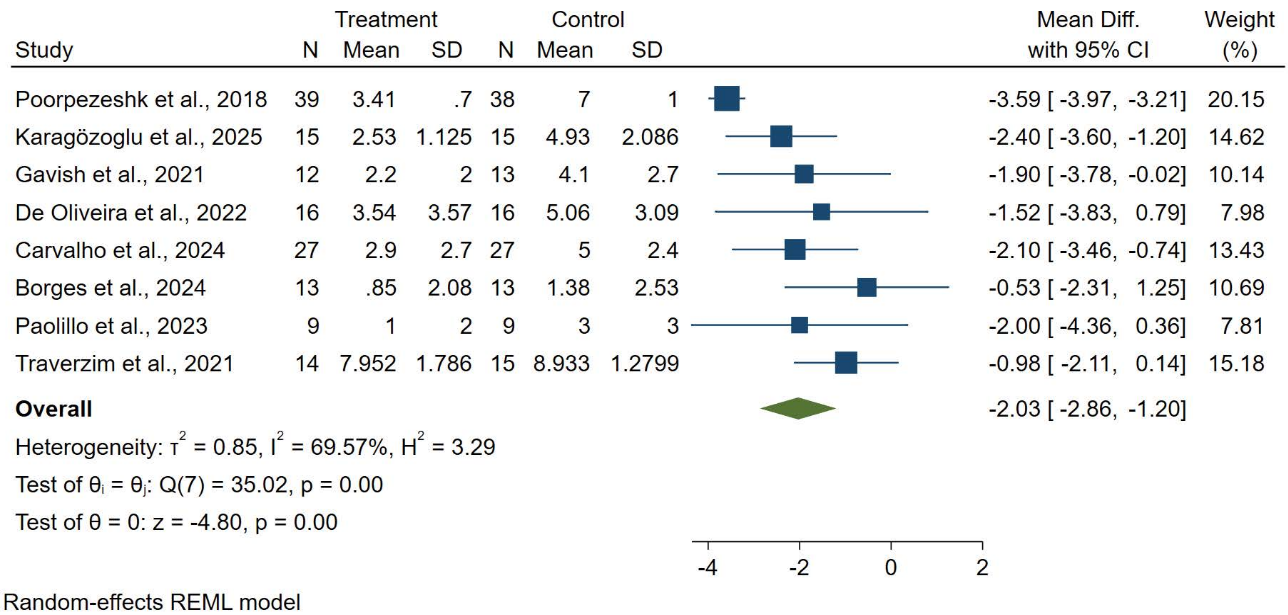

Figure 2: Meta-analysis of the mean difference in pain level.

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Sousa CRA, et al., J Biotechnol Biomed 2026
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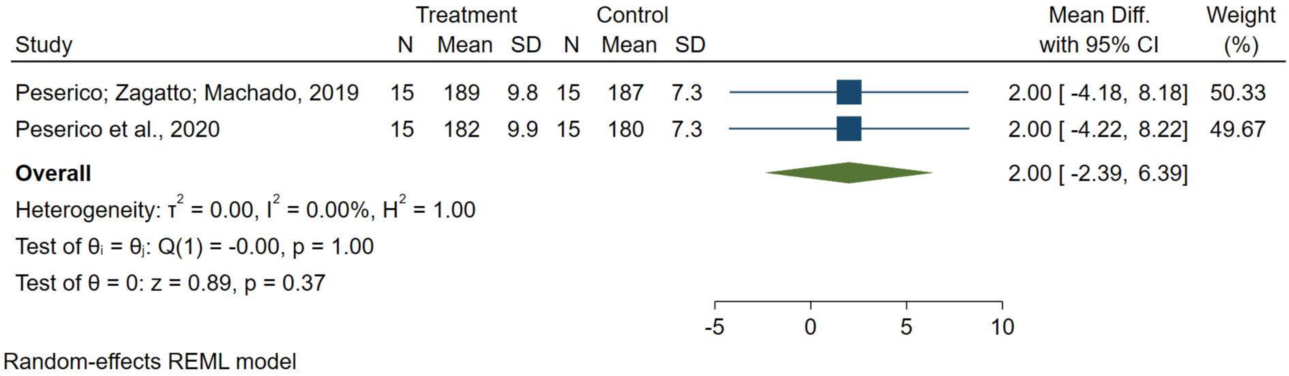

Figure 3: Meta-analysis of the mean difference in maximum heart rate.

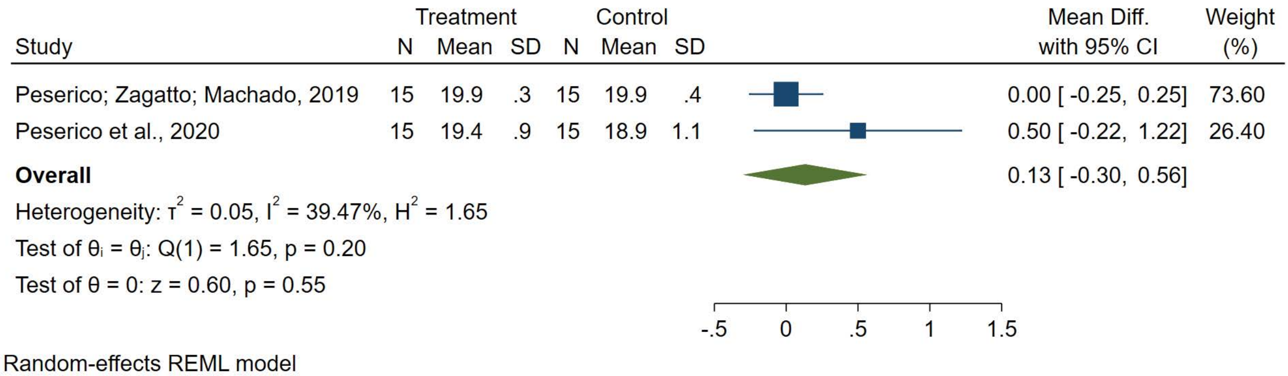

Figure 4: Meta-analysis of the mean difference in perceived exertion.

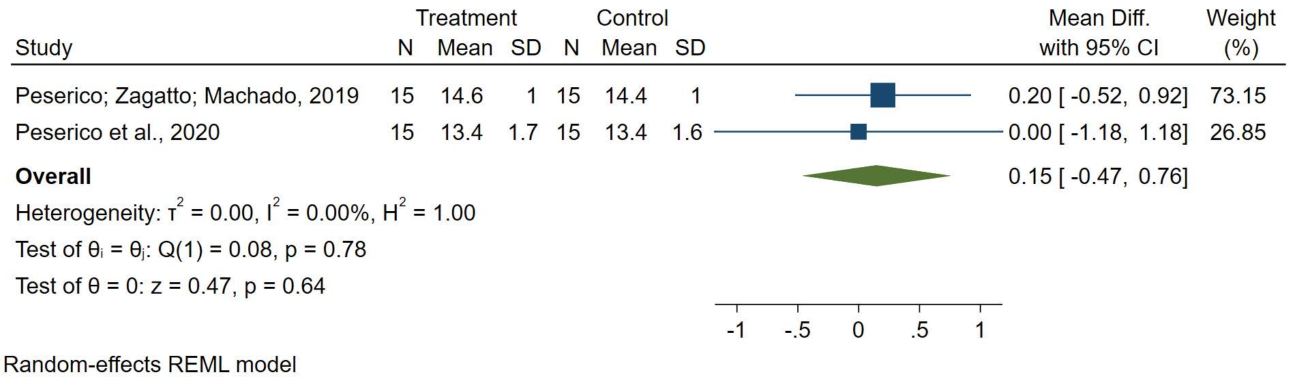

Figure 5: Meta-analysis of the mean difference in peak velocity.

Although the direction of effect favored the intervention, the synthesis included distinct clinical conditions, including musculoskeletal, neurological, and obstetric conditions, as well as tissue injuries, which may limit the clinical interpretation of a single summary estimate of pain.

In the sports context, the technique reduces immediate fatigue by preserving torque after intense exercise [22], and modulates oxidative stress by limiting the increase in oxidized glutathione (GSSG) induced by training [23]. However, in the meta-analyses of mean differences from only two studies, with an independent sample, no statistically significant differences were observed between the intervention and control groups for maximum heart rate (Figure 3), perceived exertion (Figure 4), and peak velocity (Figure 5) in the incremental treadmill test. Thus, these findings should be interpreted as insufficient evidence to confirm benefit in these outcomes, and not as a conclusive demonstration of the absence of effect.

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Sousa CRA, et al., J Biotechnol Biomed 2026
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Tissue repair appeared more consistently in healing and regeneration outcomes, with reductions in ulcer area and depth and improvement in clinical classification, as well as reductions in the grade of oral mucositis and manifestations associated with tissue damage [24-28].

The anti-inflammatory dimension was supported both by direct results (e.g., reduction of local edema/inflammation and decreases in eosinophils and neutrophils in nasal lavages) and by biological plausibility involving modulation of pro- and anti-inflammatory cytokines [22,24,29-33].

Some studies did not demonstrate statistically significant benefits in their primary outcomes with the simultaneous use of red and infrared wavelengths, although some of them indicated trends toward moderate clinical improvement or favorable effects in secondary outcomes [30,31,34-37].

Discussion

The results of the meta-analysis indicate that the intervention reduced pain on the VAS by -2.03 [-2.86, -1.20] points, with statistical significance ($p<0.001$) [14-21,24,38], especially with the association of wavelengths, which promoted pain relief superior to infrared alone [14,18].

The simultaneous use of red and infrared wavelengths was more effective than isolated protocols in reducing the grade of mucositis and, in one investigation, also reduced the need for analgesics compared with the isolated red wavelength at the same dose [25,27]. However, in the study by Borges et al. [14], the analyses suggested that infrared alone could be as effective as, or more effective than, the combination for reducing ulcer area.

In androgenetic alopecia, the device that combined two wavelengths produced a slightly greater increase in hair density than the red-only device, although both were superior to the control [39]. In outcomes evaluating musculoskeletal, physical, and functional performance, the wavelength association was not more effective than isolated applications, probably due to dose parameters that are not yet optimized, short-duration protocols, the absence of systematic association with structured training programs, small sample sizes, and clinical variability among participants [18,34,40].

The interpretation of these findings may be supported by the biological plausibility of combining wavelengths. Both red light (620-700 nm) and near-infrared light (700-900 nm) are known to be absorbed by intracellular chromophores, mainly in the mitochondrial respiratory chain. This leads to biochemical responses that alter cellular signaling, resulting in changes in ATP levels and reactive oxygen species (ROS), and the activation of transduction pathways. These changes modulate neuronal excitability and gene expression, thereby reducing nociceptive transmission. In addition, PBM alters neurotransmission and the release of peptides and peripheral opioids, such as increased expression of beta-endorphins and modulation of substance P signaling, contributing to local and systemic analgesia [41-45].

Moreover, PBM reduces pro-inflammatory mediators such as PGE2, COX-2, IL-1β, and TNFα, which decreases cellular infiltration, edema, and tissue damage. It also modulates central inflammatory pathways, with suppression of NF-κB and iNOS/NOS2, and reduced expression of COX-2 and pain-related receptors, achieving anti-inflammatory efficacy comparable to that of NSAIDs in selected models [46]. In parallel, it increases mitochondrial ATP, favoring metabolism and cellular recovery [41,43,47], and improves redox status and oxidative stress [46]. These effects, together with improved perfusion and lymphatic drainage [46,48], result in less pain, less edema, and better healing within specific therapeutic dose windows [41,43].

Each wavelength, however, has specific characteristics. Regarding light penetration depth, red wavelengths are absorbed in superficial tissues (skin and mucosa), whereas infrared reaches deeper tissues due to lower scattering and absorption (muscles, joints, nerves, and underlying tissues) [49,51]. Regarding metabolic responses, red light induces responses that are generally more durable, accelerates collagen maturation, restores the dermoepidermal junction, and promotes superficial vasodilation, whereas infrared stimulates mitochondrial activity, differential gene expression in fibroblasts and keratinocytes, and promotes deeper vascular and connective-tissue remodeling [52-55]. Consequently, the simultaneous use of both wavelengths broadens the mode of action and the volume of stimulated tissue, potentially generating additive or synergistic effects.

The results indicate that this occurs in situations in which inflammatory modulation, analgesia, and healing of superficial and underlying tissues determine the clinical outcome. Concomitant action at different depths and cellular targets could potentiate the photobiomodulatory response, resulting in greater pain relief and better tissue repair [14,16,18,25,27-29,38].

In contrast, for outcomes dependent on systemic and chronic adaptations, such as functional and muscular performance, physiological parameters in the incremental running test, or abdominal fat reduction, the evaluated protocols - generally acute or short-term - appear insufficient to generate clear advantages of the wavelength association over isolated protocols or placebo, although isolated effects indicate a possible role as an adjunct [22,23,30,34-38,40].

As strengths, this systematic review stands out for being conducted according to PRISMA guidelines and for registration in PROSPERO, in addition to presenting a meta-analysis of the analgesic effect of the intervention. However, the clinical applicability of the findings should be interpreted

Sousa CRA, et al., J Biotechnol Biomed 2026
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with caution. Clinical and methodological heterogeneity, associated with the high risk of bias in most studies, still limits the strength of this inference; 64.3% of the included studies presented a high/critical risk of bias due to lack of adequate blinding, deficient randomization, and incomplete data. This situation may lead to overestimation of the effects of photobiomodulation, especially for subjective outcomes such as pain. In addition, many studies included small samples: only 21.4% had more than 60 participants, which reduces statistical power, widens confidence intervals, and increases the likelihood of false-negative results.

In contrast, for outcomes dependent on systemic and chronic adaptations, such as functional and muscular performance, physiological parameters in the incremental running test, or abdominal fat reduction, the evaluated protocols - generally acute or short-term - appear insufficient to demonstrate clear advantages of the wavelength association over isolated protocols or placebo. In addition, the quantitative synthesis of these outcomes was based on a very small number of studies, which limits the strength of the conclusions.

Conclusion

The observations reinforce the clinical relevance of the red-infrared combination, which appears to be greater in painful, inflammatory, and healing conditions, whereas evidence for physical performance remains limited. Multicenter randomized clinical trials with adequately powered samples, standardized protocols, and greater methodological rigor are needed.

Authors' Contributions

C.S., L.R., F.A., M.C., J.A. e A.P researched the literature. C.S. wrote the original draft. F.A., M.C., J.A. e A.P reviewed and supervised the writing of the article. All authors have read and agreed to the published version of the article.

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Declaration Of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

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Sousa CRA, et al., J Biotechnol Biomed 2026
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