

Original Research

Received 28 June 2026

Revised 02 Aug 2026

Accepted 15 Aug 2026

Natural Resources for Human Health 2026, Vol. 6 (17s): 1015–1022

KEYWORDS:

Photobiomodulation; endodontics; low-level laser therapy; biological mechanisms; pain management; pulp regeneration

A Comprehensive Review of Biological Mechanisms and Clinical Applications of Photobiomodulation in Endodontics

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ABSTRACT: Photobiomodulation (PBM) therapy, also known as low-level laser therapy (LLLT), has demonstrated considerable potential as a non-invasive method of treatment in dentistry, particularly in endodontics. It has been established that PBM causes biological effects via interactions between light and cell chromophores, which positively affect mitochondrial functions and lead to ATP formation in the body. In addition, PBM affects the regulation of reactive oxygen species (ROS), intracellular Ca^{2+} ions, and NO, positively affecting cellular functions, inflammatory processes, and tissue regeneration. There are numerous cases of application of PBM therapy in endodontics owing to the favorable qualities of this type of therapy. Firstly, there is substantial evidence proving effectiveness of PBM in reducing post-endodontic pain, promoting periapical healing, and increasing treatment success rates. In addition, PBM therapy has become a subject of research into its regenerative effect on dental pulp stem cells within the framework of regenerative endodontics. This review discusses in detail biological principles underlying photobiomodulation and its possible applications in endodontics.

1. INTRODUCTION

Photobiomodulation (PBM) is a non-invasive technique that promotes tissue repair and healing while reducing inflammation and pain. Clinical evidence supports its use across several dental fields, including oral mucositis, periodontitis, temporomandibular disorders, orthodontics, and endodontics. In endodontic practice, PBM has been investigated for postoperative pain control, modulation of inflammation, periapical tissue healing, and regenerative procedures. This review focuses on the biological mechanisms of PBM and its clinical applications in endodontics [1, 2].

A major development in dental therapy is photobiomodulation (PBM), which uses tailored light energy to modulate tissue repair and discomfort in a non-invasive manner. In dentistry, lasers can be used in different ways, and their growing use has broadened the range of adjunctive approaches available for oral health care. Because PBM includes a range of electromagnetic wavelengths capable of producing photostimulatory or photoinhibitory responses according to the delivered dose, the term “photobiomodulation” more accurately describes these low-power light-based treatments [1, 3].

Photobiomodulation is a non-invasive approach used to support pain control, modulation of inflammation, and tissue healing in several dental fields. Most PBM protocols employ red or near-infrared light, commonly within the 600–1000 nm range. The absorbed light interacts with cellular chromophores, particularly mitochondrial cytochrome c oxidase, and initiates a series of photochemical reactions [2, 4].

PBM uses visible red and near-infrared wavelengths that differ in tissue penetration and optical absorption. These wavelengths can influence cell signaling through reactive oxygen species (ROS), increase adenosine triphosphate (ATP) production, and support regenerative activity without the thermal effects associated with high-power surgical lasers [3, 4].

The biological basis of PBM is the response of cellular photoacceptors to specific wavelengths of red or near-infrared light. Mitochondria are central to this response because their chromophores absorb photons and modify respiratory-chain activity, thereby affecting cellular metabolism and downstream signaling [4, 5].

Adenosine triphosphate (ATP), nitric oxide (NO), reactive oxygen species (ROS), and calcium ions are among the mediators influenced by PBM-related mitochondrial activity. The response is dose dependent; low or appropriate energy levels may stimulate biological activity, whereas excessive exposure can reduce or reverse the intended effect [4, 5].

2. BIOLOGICAL MECHANISMS OF PHOTOBIOMODULATION

Although PBM is increasingly investigated for tissue repair and regeneration, variation in irradiation parameters and incomplete protocol standardization still limit direct clinical translation. At the cellular level, PBM is mainly associated with non-thermal photochemical interactions that influence mitochondrial activity, redox signaling, membrane ion channels, and downstream transcriptional responses (Figure 1) [2, 5].

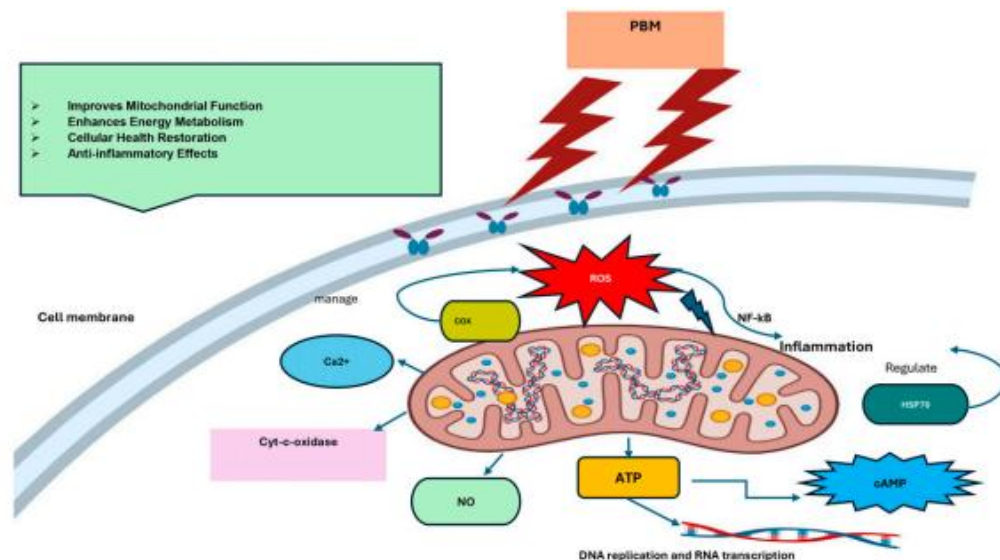


Figure 1: Mechanisms of photobiomodulation (PBM) at the cellular level. *Source: Babrami et al., 2025 [2].*

Photobiomodulation has been reported to influence the proliferation, migration, survival, and differentiation of several cell populations, including mesenchymal stem cells, gingival fibroblasts, and dental pulp stem cells. These cellular responses are relevant to the regenerative potential of PBM, although their magnitude depends on the biological state of the cells and the irradiation protocol [6, 7].

The biological response to PBM is strongly dependent on wavelength, power, irradiance, energy density, pulse characteristics, exposure time, and the optical properties of the target tissue. Red and near-infrared wavelengths remain the most frequently used because they can reach deeper tissues with relatively limited water absorption, whereas shorter wavelengths can produce different cellular responses [3, 8].

2.1 Mitochondrial Activation and ATP Production

The mitochondrial respiratory chain is a principal target of red and near-infrared PBM. Cytochrome c oxidase (CCO), located in complex IV, can absorb incident photons and modify electron transport. This interaction supports formation of the proton gradient and can increase mitochondrial activity and ATP production, providing additional energy for cellular repair and biosynthesis [5, 7].

2.2 Reactive Oxygen Species (ROS) Signaling

PBM can produce a transient increase in reactive oxygen species (ROS), which at controlled concentrations can act as second messengers rather than only as damaging oxidants. Redox-sensitive signaling influences transcription factors, growth-related pathways, and adaptive stress responses. Because excessive ROS is harmful, the therapeutic effect remains closely linked to the delivered dose and the biological condition of the target tissue [5, 9].

Recent mechanistic work has shown that PBM-induced redox signaling can coordinate inflammatory and tissue-healing pathways. In normal oral keratinocytes, PBM was associated with coordinated NF- κ B, TGF- β 1, and ATF-4 signaling together with downregulation of inflammatory and apoptotic pathways, supporting a regulated rather than indiscriminate oxidative response [9].

2.3 Nitric Oxide and Calcium-Dependent Signaling

Nitric oxide (NO) is also involved in the mitochondrial response to PBM. Photon absorption may displace inhibitory NO from cytochrome c oxidase, facilitating respiratory activity and ATP synthesis; changes in NO availability may also contribute to local vascular and signaling effects [4, 5].

Near-infrared irradiation can also influence light-sensitive ion channels and intracellular calcium (Ca^{2+}) flux. Calcium signaling interacts with ROS, NO, and cyclic AMP (cAMP) and this cross-talk can activate transcription factors involved in migration, proliferation, and differentiation. These secondary signals help explain why different wavelengths and doses may produce different biological effects [4, 10].

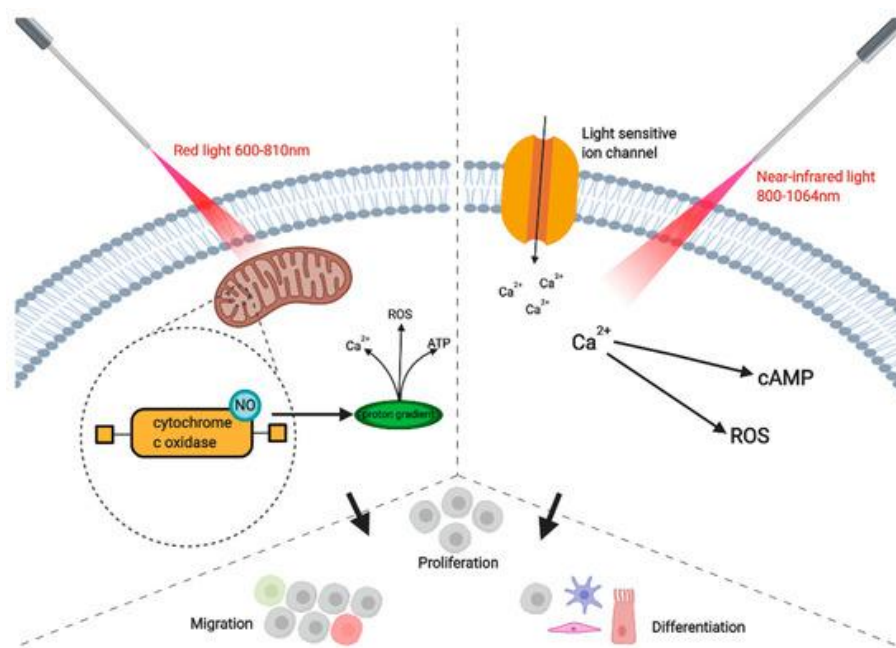


Figure 2: Red light (600–810 nm) can be absorbed by cytochrome c oxidase in the mitochondrial respiratory chain, promoting nitric oxide displacement, proton-gradient formation, and changes in ATP, ROS, and Ca^{2+} signaling. Near-infrared light (810–1064 nm) can also affect light-sensitive ion channels and calcium-dependent pathways involved in cell proliferation, migration, and differentiation. Created with BioRender. *Source: Hernández-Bule et al., 2024 [10].*

3. THERAPEUTIC EFFECTS OF PHOTOBIO-MODULATION

3.1 Anti-inflammatory Effects

The anti-inflammatory effect of PBM is related to modulation of cellular signaling rather than simple suppression of the inflammatory response. Changes in mitochondrial redox state, local microcirculation, and transcriptional activity can reduce excessive inflammatory signaling while preserving pathways required for repair. This provides a biological basis for using PBM as an adjunct when inflammation contributes to pain or delayed healing [9, 11].

Inflammatory mediators are an important part of this response. Prostaglandin-dependent signaling, cyclooxygenase activity, cytokine pathways, and redox-sensitive transcription factors contribute to nociceptor sensitization and tissue inflammation. PBM has been associated with modulation of these mediator networks, including NF- κ B/TGF- β 1-linked signaling, although the magnitude of the response varies with dose, timing, wavelength, and tissue condition [9, 11].

3.2 Analgesic Effects

Post-endodontic pain is influenced by mechanical, chemical, microbial, and inflammatory factors affecting pulpal and periapical tissues. PBM has therefore been investigated as a non-pharmacological adjunct for pain control, but the clinical response is not uniform across all endodontic conditions [12, 13].

Clinical trials illustrate this variability. Naseri et al. reported that 808-nm irradiation applied from both buccal and lingual aspects reduced postoperative pain more effectively than sham treatment in symptomatic irreversible pulpitis. In a 2025 retreatment trial, a combined Er:YAG and 635-nm PBM protocol was associated with lower early pain scores and improved periapical healing [14, 15].

More recent randomized trials have not shown a consistent analgesic advantage. Machado et al. found no significant reduction in pain after single-visit treatment of maxillary molars with 808-nm PBM, while Freitas-Júnior et al. reported no significant overall treatment effect after emergency pulpectomy [16, 17].

A 2026 randomized controlled study of endodontic surgery likewise found no clear postoperative pain advantage for PBM over the comparator regimen, further indicating that clinical setting and dosimetry can materially influence the observed analgesic effect [18].

3.3 Pulp Regeneration

PBM is also relevant to regenerative endodontics because cellular responses to light can influence migration, proliferation, survival, and differentiation of stem/progenitor cells. Dental pulp stem cells are particularly important in this context because their bioenergetic state and differentiation capacity contribute to dentin-pulp tissue repair [7, 19].

Experimental studies indicate that PBM can alter ATP production, growth-related signaling, and osteogenic or odontogenic differentiation in dental-derived stem cells. The response is not uniformly stimulatory, however, because wavelength, energy density, cell stress, culture conditions, and exposure schedule can change the direction and magnitude of the effect [7, 20].

A 2026 study using human dental pulp stem cells showed that 810-nm near-infrared PBM combined with allogeneic fibrin serum enhanced later osteogenic marker expression and matrix mineralization at an appropriate energy density. PBM alone did not produce a uniformly positive early response, again emphasizing the importance of biological context and dose selection in regenerative protocols [21].

Taken together, the regenerative literature supports a potential role for PBM in pulp-dentin complex repair, but the evidence remains protocol dependent. Translation from laboratory models to predictable clinical pulp regeneration will require consistent reporting of wavelength, power, irradiance, energy density, exposure time, application geometry, and treatment frequency [8, 19].

4. CLINICAL APPLICATIONS IN ENDODONTICS

In endodontics, PBM has been investigated mainly for postoperative pain control, modulation of periapical inflammation, support of soft- and hard-tissue healing, and regenerative procedures. Its non-invasive nature makes it suitable as an adjunct rather than a replacement for established chemomechanical disinfection, obturation, surgical, or vital-pulp-treatment procedures [22–26].

Recent clinical evidence is particularly relevant to periapical disease and retreatment. In a 2025 randomized trial, the combined use of Er:YAG laser-activated irrigation and 635-nm PBM was associated with reduced early pain and greater reduction in periapical lesion size at six months compared with conventional retreatment. Because the intervention combined two laser modalities, the findings are better interpreted as evidence for the combined protocol rather than PBM alone [15].

Evidence for postoperative analgesia remains mixed across primary treatment, retreatment, emergency pulpectomy, and endodontic surgery. This heterogeneity is clinically important because target tissues, inflammatory burden, application sites, and irradiation schedules differ considerably between studies [13, 17].

Accordingly, clinical interpretation should focus on the complete PBM protocol rather than wavelength alone. Direct comparison between studies requires attention to power, irradiance, fluence, energy per point, exposure time, treatment frequency, application geometry, and the clinical diagnosis being treated [8, 11].

5. CLINICAL PROTOCOLS AND PARAMETERS OF PBM

The efficacy of PBM depends on a set of interrelated parameters rather than a single laser setting. Wavelength affects optical penetration, while power, irradiance, radiant exposure, application time, delivery mode, number of points, and treatment schedule determine the dose received by the target tissue. A biphasic dose-response is commonly described, so both insufficient and excessive energy may reduce the intended biological response [8, 11].

Recent endodontic trials demonstrate substantial protocol heterogeneity and correspondingly mixed clinical outcomes. **Table 1** summarizes representative studies from the last six years, including recent randomized trials, and illustrates how differences in wavelength, dose, application geometry, and clinical indication complicate direct comparison between protocols [8, 13].

Table 1. Recent clinical PBM protocols and outcomes in endodontics.

Author	Year	Laser	Parameters	Main Result
Naseri et al. [14]	2020	808-nm diode	100 mW; 600- μ m fiber; 70 J/cm ² ; 80 s; buccal only or buccal + lingual irradiation.	Buccal + lingual PBM reduced postoperative pain versus placebo at 4, 8, 24, and 48 h and reduced analgesic use.
Kolberg-Babrzyńska et al. [15]	2025	635-nm diode PBM + Er:YAG LAI	PBM: 400 mW; 5 s/point; 2 J/point; 4 J/cm ² ; 2 apical points; sessions at 0, 24, 48, and 96 h.	Combined laser protocol reduced VAS pain at 24–48 h and produced greater periapical lesion reduction at 6 months.
Machado et al. [16]	2025	808-nm diode	100 mW; 3 J/point; 3 points over molar apices; 9 J total; single post-treatment application.	No significant benefit versus sham for spontaneous pain at 4, 8, 12, or 24 h, percussion/palpation pain, or OHIP-14 outcomes.
Freitas-Júnior et al. [17]	2026	808-nm AsGaAl	100 mW; continuous mode; contact/perpendicular; 1 J per point for 10 s; up to 6 points immediately after emergency pulpectomy.	Pain decreased over time in both groups, but PBM was not associated with a significant overall postoperative analgesic benefit.
Cirisola et al. [18]	2026	808-nm diode	100 mW; 4 J/cm ² ; 5 vestibular points; applications immediately after endodontic surgery, at 24 h, and at 7 days.	PBM did not show a clear postoperative pain advantage over conventional analgesic management after endodontic surgery.

6. CONCLUSION

In summary, photobiomodulation is a promising adjunct in endodontics because its biological effects involve mitochondrial activation, ATP production, redox signaling, nitric oxide, calcium-dependent pathways, and modulation of inflammatory responses. These mechanisms provide a scientific basis for applications in pain control, periapical tissue healing, and pulp-regenerative strategies. Clinical findings, however, are not uniformly positive: recent randomized trials report both beneficial

and neutral outcomes, particularly for postoperative pain. The principal limitation remains the marked variation in wavelength, power, energy density, application site, treatment schedule, and clinical indication. Future trials should therefore use standardized dosimetry and reporting frameworks and should evaluate diagnosis-specific protocols before PBM can be incorporated into routine endodontic guidelines.

ACKNOWLEDGEMENTS

None

FUNDING

The authors declare that no funds, or other support were received during the preparation of this manuscript.

AUTHOR CONTRIBUTIONS

All authors contributed to the review design and conception. All authors read and approved the final review. Data collection and analysis were performed by [M.H.N. & L. A]. the first draft of review was written by M.H.N. The critical review and editing of the review for its intellectual content was performed by [M.H.N &L.A].

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

Not applicable. This is a narrative review of published literature and involved no human participants or animals.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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