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Review

Effects of Photobiomodulation in Association with Biomaterials on the Process of Guided Bone Regeneration: An Integrative Review

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Abstract

Photobiomodulation (PBM) has been widely studied for its regenerative and anti-inflammatory properties. Its application, combined with biomaterials, is emerging as a promising strategy for promoting tissue regeneration. Considering the diversity of available evidence, this study conducted an integrative literature review, aiming to critically analyze and synthesize the effects of PBM on bone tissue, particularly its potential role as an adjunct in guided bone regeneration (GBR) procedures. To ensure an integrative approach, studies with different methodological designs were included, encompassing both preclinical and clinical research. The article search was performed in the digital databases PubMed/MEDLINE, Scopus, and Web of Science, using the following search terms: "Photobiomodulation therapy" AND "guided bone regeneration". The search was conducted from November 2024 to January 2025. A total of 85 articles were found using the presented terms; after checking the results, 11 articles were selected for this study. The remaining articles were excluded because they did not fit the proposed inclusion and exclusion criteria. Studies to date have shown preclinical models that demonstrated increased bone-volume fraction and accelerating healing. Although it has exciting potential in bone regeneration, offering a non-invasive and promising approach to promote healing and repair of damaged bone tissue, the clinical application of PBM faces challenges, such as the lack of consensus on the ideal treatment parameters. Calcium phosphate ceramics were one of the most used biomaterials in the studied associations. Further well-designed studies are necessary to clarify the effectiveness, optimal parameters, and clinical relevance of PBM in bone regeneration, in order to strengthen the current evidence base and guide its potential future use in clinical practice.

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1. Introduction

Insufficient bone volume is a significant clinical challenge affecting millions of patients worldwide, impacting procedures such as fracture repair, treatment of bone defects, osteoporosis management, and dental implant success [1–3]. The body's natural regenerative capacity can be compromised due to factors such as the location and severity of the injury, or systemic limitations, necessitating therapeutic interventions to promote effective bone healing [4,5].

Photobiomodulation (PBM), also known as low-level light therapy, has emerged as a promising adjunctive treatment that uses specific wavelengths of light to modulate biological processes and enhance tissue regeneration [4–8]. This technique involves delivering precise doses of light to target tissues, activating cellular pathways that stimulate proliferation, angiogenesis, and differentiation of osteogenic cells, thereby facilitating bone repair [3,9–15].

The integration of PBM with biomaterials—including bone grafts, biological membranes, and biodegradable scaffolds—has gained increasing attention in tissue engineering and guided bone regeneration (GBR) [2,8,16–19]. Biomaterials provide structural support and promote cellular migration while releasing bioactive molecules that facilitate new bone formation. When combined with PBM, these materials may enhance regenerative outcomes, as evidenced by preclinical studies demonstrating improved bone mineral density and graft integration [15,16,20–23]. Nevertheless, optimal treatment parameters and mechanistic understanding remain areas requiring further investigation to maximize clinical benefits.

PBM acts by delivering light energy absorbed by intracellular chromophores within bone cells and surrounding vasculature, triggering complex biochemical cascades that promote healing. These include stimulation of osteoblast proliferation, modulation of osteoclast activity, promotion of angiogenesis, and reduction of inflammation [24–29]. Animal studies have demonstrated accelerated bone formation and improved graft outcomes with PBM, while clinical reports suggest faster recovery and enhanced healing in dental and orthopedic patients [3,9–15,30,31].

Despite promising findings, challenges persist in standardizing PBM application for GBR, particularly regarding optimal dosimetry, treatment timing, and understanding its multifaceted mechanisms [32–34]. This integrative review aims to critically examine current evidence on the adjunctive use of PBM in guided bone regeneration, highlighting both therapeutic potential and existing knowledge gaps.

2. Methods

This integrative review aimed to analyze the current scientific literature regarding the use of photobiomodulation (PBM) and its effects on guided bone regeneration (GBR), with a focus on bone metabolism, bone formation, and bone resorption outcomes. A structured literature search was carried out in three electronic databases—PubMed/MEDLINE, Scopus, and Web of Science—between November 2024 and January 2025. The search strategy employed the Boolean operator "AND" with the following terms: "Photobiomodulation therapy" AND "guided bone regeneration". The same search string was applied uniformly across all databases to ensure consistency, using the following platforms: PubMed via NCBI, Scopus via Elsevier, and Web of Science via Clarivate. Related terms such as "low-level laser therapy" and "GBR" were considered during manual screening but were not part of

the automated search string. No date or study design filters were applied. The last search was carried out in January 2025 to ensure the inclusion of the most recent evidence.

Only studies published in English and in peer-reviewed journals were considered. Eligible studies included both preclinical (animal) and clinical (human) research that directly investigated the application of PBM in the context of guided bone regeneration, with or without the use of membranes and grafts. Articles were excluded if they were reviews, opinion pieces, editorials, case reports, abstracts, or if they were published in languages other than English. Studies focusing on therapeutic interventions other than PBM or bone regeneration procedures unrelated to GBR were also excluded, including those involving bone fixation devices, platelet-rich membranes, bone morphogenetic proteins (BMPs), miniplates, and combined orthodontic–surgical treatments.

All article screening was performed by a single independent researcher. Titles and abstracts were reviewed according to the predefined inclusion and exclusion criteria. Full texts of potentially relevant studies were retrieved for detailed evaluation. From each selected article, data were extracted regarding the authorship, year of publication, type of laser used, wavelength (nm), power output (mW), energy density (J.cm^{-2}), total energy delivered (J), irradiation site, treatment parameters, time of evaluation, and main reported outcomes related to bone regeneration.

Given the inclusion of both animal and human studies, ethical compliance was verified accordingly. All included preclinical studies explicitly stated having obtained approval from institutional animal care and use committees, in compliance with internationally accepted ethical standards for animal research. The single included clinical study reported approval from a human research ethics committee and informed consent procedures, ensuring adherence to the ethical conduct required for human experimentation.

3. Results

3.1. Selected and Reviewed Studies

The initial search for articles that fit the objective of this study was conducted using the digital databases PubMed/MEDLINE, Scopus and Web of Science. By using the terms “Photobiomodulation therapy” AND “Guided bone regeneration”, after using the terms presented, a total of 85 articles were given as results. A total of 48 articles were obtained in a preliminary analysis. After an in-depth investigation, combined with checking the inclusion and exclusion criteria, 11 articles were selected for this integrative review, 23 articles were excluded because they included biomaterials or techniques other than those mentioned in the inclusion and exclusion criteria, such as bone fixation techniques, platelet-rich membranes, bone morphogenetic proteins (BMPs), miniplates, and combined orthodontic-surgical treatments, one article was excluded because it was in a language other than English, one article was excluded because it was impossible to access it, and 12 articles were excluded because they were literature reviews. The article selection scheme can be seen in Figure 1.

The findings related to the effects of using PBM on bone tissue from the articles selected and included in this study have been transcribed and organized in Tables 1 and 2. All the articles selected were published clinical studies and related to the topic in question, the effects on the process of guided bone regeneration, as well as bone tissue, caused by the joint use of PBM.

In addition to the preclinical animal studies summarized in Table 1, one clinical study conducted in humans met the inclusion criteria and is presented separately in Table 2. This separation was made to ensure clarity in reporting and to avoid conflating heterogeneous outcomes across distinct biological models. Whereas animal studies primarily assessed parameters such as bone volume fraction and histomorphometric changes, the clinical

trial focused on patient-centered outcomes, including clinical attachment levels and probing depth. Given the differences in methodology, context, and endpoint definition, the clinical data are synthesized independently to preserve the interpretive integrity of each evidence category.

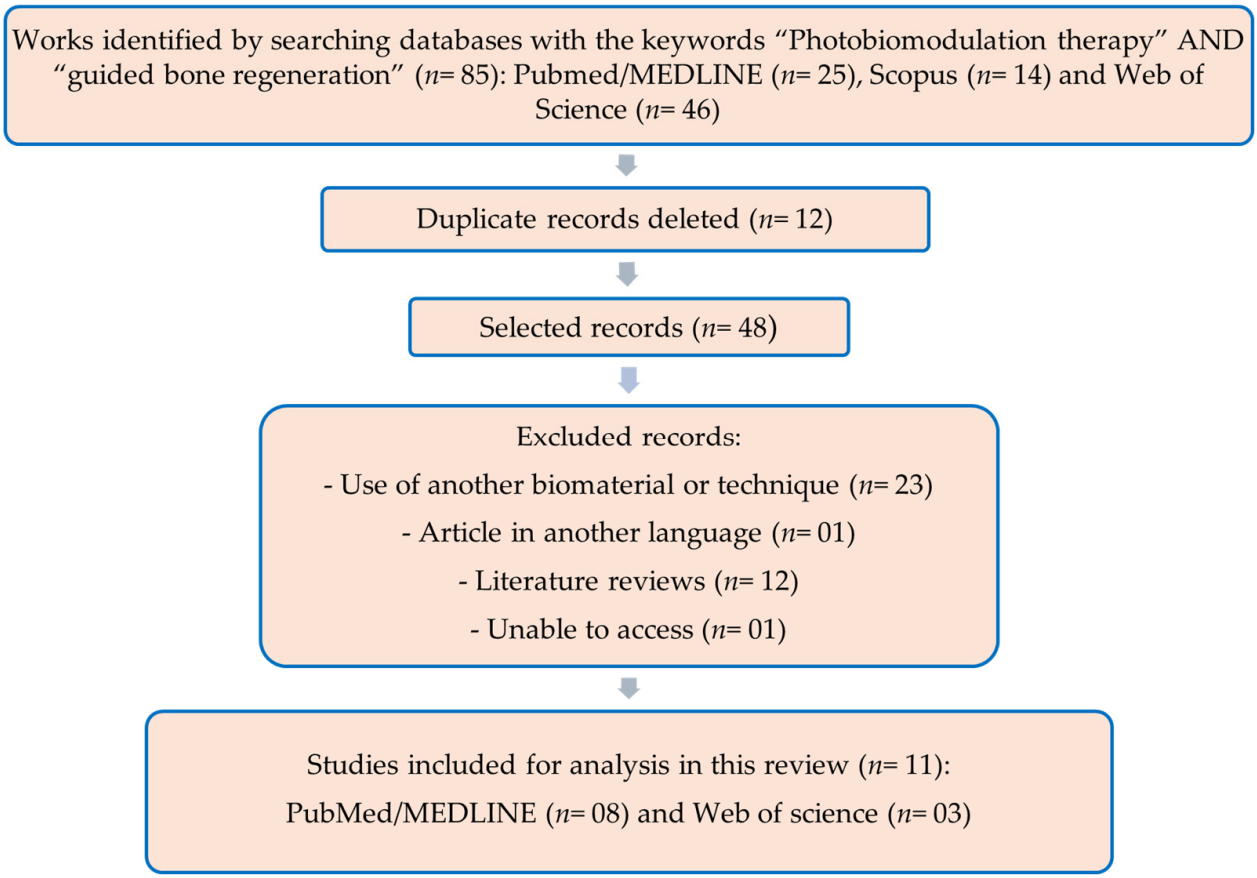

Figure 1. Diagram showing the selection process and the number of articles approved and subsequently reviewed.

Table 1. Selected and reviewed studies presenting the effects of using photobiomodulation in the process of guided bone regeneration and bone tissue on experimental animal studies.

Authors	Type of Laser (Manufacturer)	Wavelength (nm)/Spot Beam	Output Power (mW)	Energy Density (J.cm^{-2})	Total Delivered Energy (J, per Session)	Quantity of Radiation	Therapeutic Variables	Irradiation Site	Evaluation Time	Principal Results
Alves et al., 2020 [10]	GaAlAs (PhotonLase III, DMC Equipment, São Carlos, SP, Brazil)	808 nm	40 mW	4 J.cm^{-2} for group PBM-1 and 14 J.cm^{-2} for group PBM-2	0.48 J (PBM-1) and 1.6 J (PBM-2)	4 points for both groups, 3 s per point for the PBM-1 group and 10 s per point for the PBM-2 group	BioGide® (Geistlich Pharma AG, Wolhusen, Switzerland)	Rat calvaria	Immediately after the procedure, 48 h, and 96 h after the surgical procedure	The PBM-treated groups, especially PBM-1, had a significantly higher bone volume fraction and number of trabeculae compared to the control group. In addition, the thickness and separation values of the trabeculae and the structural model index were significantly lower in the PBM-treated groups. Connectivity density was also significantly higher in the membrane and PBM-treated groups compared to the control group.
AboElsaad et al., 2009 [9]	GaAlAs (Velopex Diode Laser, MeDivance Instruments Ltd., London, UK)	830 nm	40 mW	16 J.cm^{-2}	2.4 J	60 s directly on the defect area	PerioGlas® (NovaBone Products LLC, Alachua, FL, USA)	Rat jaw	At the beginning of the study and on days 3, 5, and 7 after surgery	At 3 months, there was a statistically significant difference between the sites with and without photobiomodulation. However, at 6 months, no difference was observed. According to the authors, it was possible to confirm the positive effect of the photobiomodulation in accelerating the healing of periodontal wounds.
Della Coletta et al., 2021 [3]	GaAlAs (Ibramed Laserpulse®, Amparo, São Paulo, Brazil)	830 nm	30 mW	6.2 J.cm^{-2}	2.88 J	Four spots around the surgical area, 24 s per spot	GenPhos XP® (Baumer S.A., Mogi Mirim, São Paulo, Brazil) and fibrin biopolymer developed by the Center for the Study of Venoms and Venomous Animals (CEVAP), São Paulo State University "Júlio de Mesquita Filho" (UNESP), Brazil	Rat calvaria	Immediately after surgery and three times a week until euthanasia	Bone growth was more evident in the BFMLG group at 42 days, limited to the edges of the defect and the permanence of the particles. Histomorphology tests showed an inflammatory infiltrate, with regression accompanied by the formation of mineralized bone tissue. All groups showed a progressive increase in new bone tissue, with BFMLG showing the greatest bone formation in both periods. Picrosirius-red staining revealed greater yellow-green birefringence of the collagen fibers in the BFMLG group, suggesting more advanced bone maturation.

Table 1. *Cont.*

Authors	Type of Laser (Manufacturer)	Wavelength (nm)/Spot Beam	Output Power (mW)	Energy Density (J.cm^{-2})	Total Delivered Energy (J, per Session)	Quantity of Radiation	Therapeutic Variables	Irradiation Site	Evaluation Time	Principal Results
de Oliveira et al., 2018 [35]	GaAlAs (Therapy XT, CW, DMC Equipment, São Carlos, SP, Brazil)	808 nm	100 mW	354 J.cm^{-2}	4.0 J	Photobiomodulation was conducted transcutaneously, with the laser tip in contact with the skin for 10 s per point, totaling 40 s per session. There were 7 sessions, applied every 48 h for 13 days, starting immediately after the suture.	Deproteinized bovine bone (DBB; Bio-Oss®, Geistlich AG, Wolhusen, Switzerland) and biphasic ceramic comprising hydroxyapatite and β-tricalcium phosphate (HA/βTCP; Straumann® Bone Ceramic, Straumann AG, Basel, Switzerland)	Lateral region of the rat's mandible	There were 7 sessions, applied every 48 h for 13 days, starting immediately after the suture.	The author could see an increase in the formation of mineralized tissue and bone, especially after 90 days, an increase in the expression of BMP2, OCN, and ALP proteins, greater expression of ALP, BMP2, and Jagged1 mRNA. There was also an improvement in the osteoconductive potential of deproteinized bovine bone and HA/βTCP grafts and bone formation in areas without grafts.
Freitas et al., 2023 [12]	GaAlAs (TheraLase DMC®, São Carlos, São Paulo, Brazil)	730 nm	100 mW	210 J.cm^{-2}	24.0 J	60 s, at four points on the edges of the surgical defect created (12 h, 3 h, 6 h and 9 h), as well as a central point on the bone graft	Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland) and BioGide® (Geistlich Pharma AG, Wolhusen, Switzerland)	Rat calvaria	A single application during the transoperative period	The group that received photobiomodulation in conjunction with deproteinized bovine bone showed statistically significant differences in all the variables analyzed compared to the group treated only with deproteinized bovine bone. The application of photobiomodulation in guided bone regeneration resulted in a reduction in the residual particle area compared to the group treated only with guided bone regeneration, and this difference was statistically significant. However, no significant results were observed in relation to the area of newly formed bone and the linear extension of the bone.

Table 1. *Cont.*

Authors	Type of Laser (Manufacturer)	Wavelength (nm)/Spot Beam	Output Power (mW)	Energy Density (J.cm^{-2})	Total Delivered Energy (J, per Session)	Quantity of Radiation	Therapeutic Variables	Irradiation Site	Evaluation Time	Principal Results
Freitas et al., 2018 [13]	GaAlAs (TheraLase DMC®, São Carlos, São Paulo, Brazil)	808 nm	100 mW	30 J.cm^{-2}	30.0 J	60 s per point, applied at five points: four on the surface of the surgically created defect, according to clockwise positions (12 h, 3 h, 6 h, 9 h), plus a central point	BioGide® (Geistlich Pharma AG, Wolhusen, Switzerland) and TheraLase DMC® (DMC Equipamentos Ltd.a., São Carlos, SP, Brazil)	Rat calvaria	Only one application was conducted during the trans operative period	All the groups showed a greater area of newly formed bone compared to the control group. The PBMT + M group achieved the greatest amount of new bone, followed by the PBMT, M, AB + PBMT and AB + PBMT + M groups. The groups treated with PBMT (PBMT and PBMT + M) showed a greater amount of new bone compared to the groups treated with autogenous material (AB and AB + M). There was no statistically significant difference in the area of remaining particles between the AB + M and AB + PBMT + M groups.
Luca et al., 2020 [14]	GaAlAs (IRRADIA Mid-Laser®, Stockholm, Sweden)	808 nm	450 mW	24.075 J.cm^{-2}	30.6 J	Four opposite peripheral points and a central point of the defect using a plastic surgical guide for 17 s each point	NuOss® (natural cancellous and cortical bone matrix, ACE Surgical Supply, Brockton, MA, USA) and ACE RCM6® (resorbable collagen membrane, ACE Surgical Supply, Brockton, MA, USA)	Rat calvaria	Day of the surgery and every 48 h, for 14 days, 21 days and 30 days, respectively	The results obtained by the authors indicate that photobiomodulation had a superior healing effect compared to the support provided by the biomaterial alone, especially during the first 14 days after surgery.
Pinheiro et al., 2009 [15]	GaAlAs (Thera Lase®, DMC Equipamentos, São Carlos, SP, Brazil)	830 nm	40 mW	4 J.cm^{-2}	-	Transcutaneous application at four points around the surgical site	Gen-Phos® and Gen-Derm® (Baumer S.A., Mogi Mirim, São Paulo, Brazil)	Rat femur	After placing the sutures and repeated every other day for 15 days	According to the author, the data may suggest that photobiomodulation can have a positive effect on the early healing of bone defects treated with a combination of biomaterial and guided bone regeneration.

Table 1. *Cont.*

Authors	Type of Laser (Manufacturer)	Wavelength (nm)/Spot Beam	Output Power (mW)	Energy Density (J.cm^{-2})	Total Delivered Energy (J, per Session)	Quantity of Radiation	Therapeutic Variables	Irradiation Site	Evaluation Time	Principal Results
Rufato et al., 2022 [36]	GaAlAs (Twin Laser, Mm Optics, São Carlos, SP, Brazil)	780 nm	40 mW	30 J.cm^{-2}	4.8 J	The laser was applied in contact with and perpendicular to the edges of the bone defect. Irradiation took place at four points (positions 3 h, 6 h, 9 h and 12 h), with 30 s per point, totaling 120 s per session. The protocol consisted of 12 sessions in total.	Textured membranes of poly (vinylidene fluoride–trifluoroethylene)/barium titanate [P(VDF-TrFE)/BT] (developed by UNIFEI, Itajubá, Brazil) and Surgitime PTFE (Bionnovation®, Bauru, São Paulo, Brazil)	Calvaria of ovariectomized rats	The first application was conducted 24 h after surgery and repeated every 2 days, totaling 12 sessions.	The P(VDF-TrFE)/BT membrane favored bone repair, regardless of photobiomodulation. The combination of PBM and polytetrafluoroethylene (PTFE) increased the expression of *Runx2*, *Alp*, *Bsp*, *Bglap*, *Sp7* and *Rankl* genes.
Valiati et al., 2012 [37]	GaAlAs (Thera Lase®, DMC Equipamentos, São Carlos, SP, Brazil)	830 nm	-	16 J.cm^{-2}	-	The laser was applied at four points on the calvaria, with eight sessions in total	Allograft blocks harvested from two rabbits and processed by deep freezing	Rabbit calvaria	The laser was applied immediately after the surgical procedure and repeated every 48 h, totaling eight sessions	Photobiomodulation improved graft incorporation, reduced initial inflammation and increased collagen deposition. Microscopy confirmed that the allograft treated with deep freezing and PBM is a viable alternative for bone repair.

Table 2. Selected and reviewed studies presenting the effects of using photobiomodulation in the process of guided bone regeneration and bone tissue on human clinical trial.

Authors	Type of Laser (Manufacturer)	Wavelength (nm)/Spot Beam	Output Power (mW)	Energy Density ($J.cm^{-2}$)	Total Delivered Energy (J, per Session)	Quantity of Radiation	Therapeutic Variables	Irradiation Site	Evaluation Time	Principal Results
Emrem Doğan et al., 2014 [11]	Nd:YAG (Smarty A10; DEKA, Firenze, Italy)	1064 nm	100 mW	4 $J.cm^{-2}$	-	The beam was emitted through a phototherapeutic probe at a distance of 1 cm from the soft tissue target area covering the bone defect. The exposure time was 300 s per tooth, i.e., 60 s for each application to a defect	Bio-gen® (BGM-O5; Bioteck S.p.A., Riva Presso Chieri, Italy) and Biocollagen® (BCG-O1; Bioteck S.p.A., Riva Presso Chieri, Italy)	Bilateral intraosseous periodontal defects in humans	It was applied for 5 min at the time of surgery and on postoperative days 1, 3, 5 and 7	The study demonstrated that RTG is an effective treatment for periodontal regeneration and that TLBP can improve the effects of RTG in the treatment of periodontal defects.

3.2. Results of the Literature Review

Lasers (Light Amplification by Stimulated Emission of Radiation) are devices that emit electromagnetic radiation with specific wavelength, phase, and polarization characteristics. They can be classified into high-power lasers (HLLT), with surgical applications, and low-intensity lasers (LLLT), used mainly for therapeutic purposes. LLLT acts through the absorption of photons by tissues, triggering photobiological mechanisms and promoting beneficial effects in the biological system, such as inflammatory modulation, analgesia, and stimulation of tissue regeneration [38,39]. The light radiation is absorbed by intracellular chromophores, such as cytochrome c oxidase in the mitochondria so that these benefits can be observed [40]. In recent years, studies involving the therapeutic properties of lasers have grown significantly, revealing positive effects in different areas of regenerative medicine, including the regeneration of nerve, muscle, bone, and other tissues [3,9–11,13–15].

PBM has been widely investigated as a non-invasive therapeutic approach capable of modulating biological processes in different tissues. In the dental field, for example, alveolar bone defects are important considerations when planning implant treatments for the proper oral rehabilitation of patients. To improve local conditions and achieve successful implant treatments, various methods are used to increase bone volume, with guided bone regeneration being one of the most effective and versatile [41–43].

The application requires light in the near-infrared or red spectrum range in order to activate cellular chromophores, triggering a series of biochemical and biophysical events that favor healing. This includes the promotion of cell proliferation, extracellular matrix synthesis by osteoblasts, and angiogenesis, resulting in a favorable balance between bone formation and resorption [44–47]. Pre-clinical and clinical studies have provided convincing evidence of the benefits of PBM in bone regeneration, including an increase in bone mineral density, accelerated bone formation, better integration of bone grafts, and a faster and less painful recovery in patients undergoing orthopedic and dental surgical procedures [3,9–15]. Figure 2 shows some of the positive effects obtained through the association of PBM.

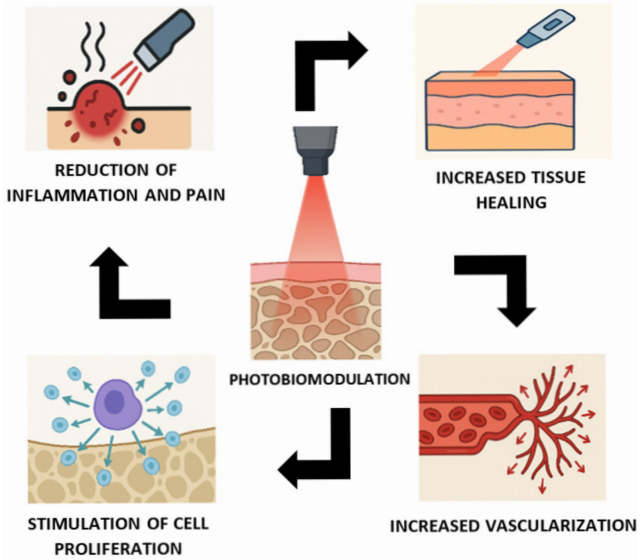

Figure 2. The illustration highlights the effects of photobiomodulation on bone regeneration, including cell proliferation, increased vascularization, reduced inflammation, accelerated bone matrix deposition, and improved collagen organization.

In addition to its beneficial effects on bone tissue, PBM has also been shown to have a positive impact on other structures in the body. Studies have reported its effectiveness in regenerating soft tissues such as muscles, skin, and cartilage, as well as reducing pain and inflammation in a variety of conditions, including musculoskeletal injuries, skin wounds,

arthritis, and neuropathy. These combined effects make PBM a versatile and promising therapeutic option for a variety of clinical conditions, contributing to improving patients' quality of life and enhancing treatment outcomes [48–52].

The association of PBM with various types of biomaterials has been explored as a promising strategy for tissue regeneration in a variety of clinical applications. Among the most commonly used biomaterials are bone grafts, such as those derived from bovine, synthetic or autogenous origin, which provide structural support for the formation of new bone tissue. Biological membranes also play a fundamental role, acting as physical barriers that protect the injury site and promote cell migration [11,12,14,53]. In addition, biodegradable materials such as polylactic acid (PLA) and polyglycolic acid (PGA) have been used to release bioactive agents in a controlled manner, stimulating tissue regeneration [54,55]. Other options include hydroxyapatite, tricalcium phosphate, and polymeric materials, each with unique properties that can be exploited in combination with PBM to enhance therapeutic effects. Pre-clinical studies have demonstrated the effectiveness of these combinations in promoting bone, cartilage, and soft tissue regeneration, providing valuable insights for the development of more effective clinical approaches [56–59]. Some of the observed effects of the association between PBM and biomaterials can be seen in Figure 3.

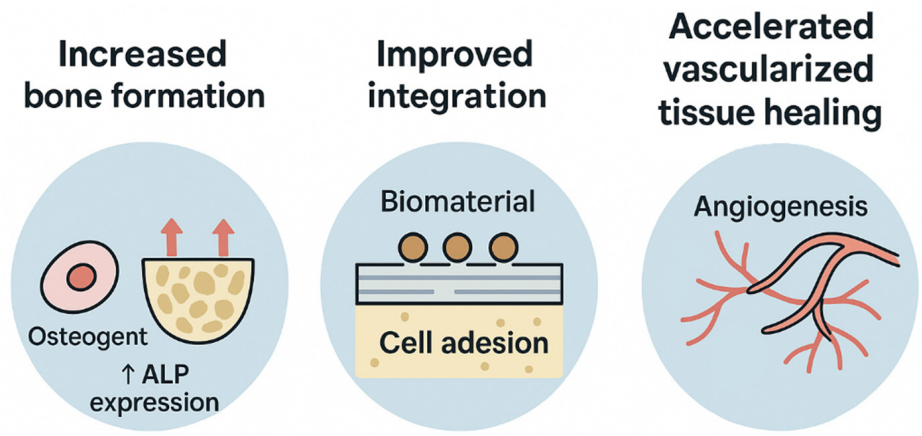

Figure 3. Illustration of key regenerative effects from the combination of photobiomodulation and biomaterials: enhanced bone formation (via osteoblast activity), improved cell adhesion to biomaterials, and accelerated vascularized tissue healing through angiogenesis stimulation.

The effects of bone repair induced by PBM vary according to the specific characteristics of the different types of lasers used. Various parameters, such as wavelength, power, fluence, and mode of application, can influence the therapeutic results obtained [32–34,60,61]. With regard to the studies selected for this integrative review, Figure 4 shows the energy density used by the authors to conduct their experiment and Figure 5 illustrates the wavelengths chosen by them.

Another important consideration concerns the timing of PBM application. The literature shows that early application, in the first 24 to 72 h after extraction or surgical intervention, is more effective in influencing the initial stages of bone repair. Synchronizing the application with the natural biological events of bone repair can enhance the desired effects, such as greater bone deposition and remodeling, indicating that the chronobiology of bone tissue should be considered when designing therapeutic protocols [12,33].

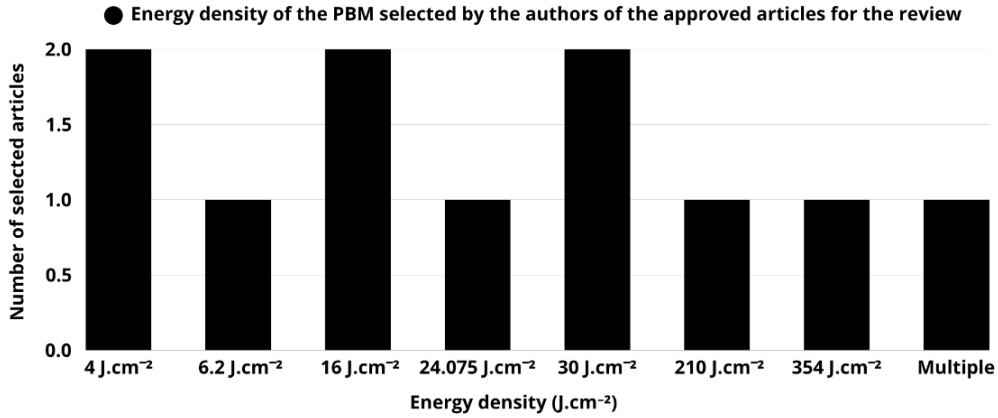

Figure 4. Frequency distribution of energy density (J.cm^{-2}) values used in the included studies applying photobiomodulation for guided bone regeneration. The most frequently used energy densities were 4, 16, and 30 J.cm^{-2} (each reported in two studies), while higher values such as 210 and 354 J.cm^{-2} appeared less consistently. This variability underscores the lack of standardized dosimetric parameters across studies, which may hinder reproducibility and the ability to draw robust comparisons between protocols.

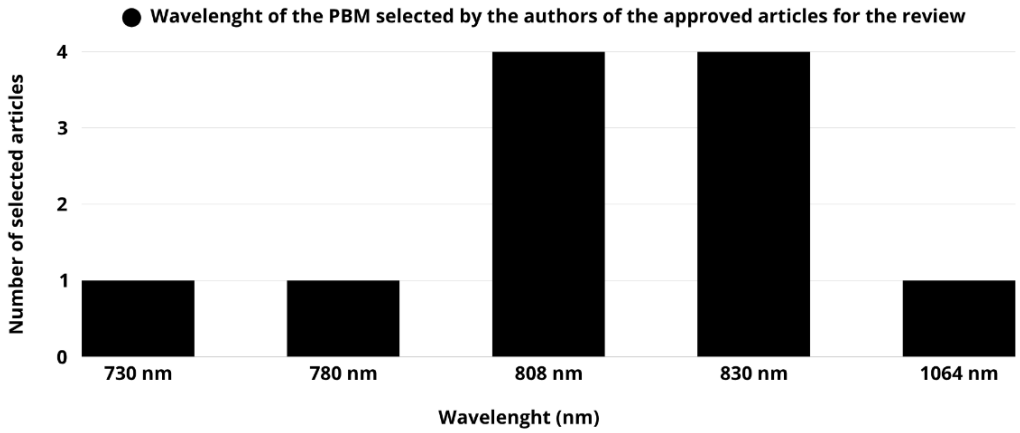

Figure 5. Distribution of wavelengths used in photobiomodulation across the included studies. The wavelengths 808 nm and 830 nm were the most frequently applied (each in four studies), reflecting their widespread use in PBM due to favorable tissue penetration and mitochondrial interaction. Less frequent choices, such as 730 nm, 780 nm, and 1064 nm, highlight the lack of standardization in PBM protocols for guided bone regeneration, which complicates comparisons across studies and may affect clinical translatability.

It is also important to select the type of laser to be used for the study or treatment. Low-power lasers, such as diode lasers, have been widely studied due to their ability to penetrate biological tissues safely and effectively, stimulating beneficial cellular processes [60–64]. On the other hand, high-power lasers, such as carbon dioxide (CO_2) or erbium-doped yttrium aluminum garnet (Er:YAG) lasers, can be more effective in removing bone tissue and preparing surgical beds, although they can also induce adverse thermal effects if not used properly [65–69]. In addition, lasers with specific wavelengths, such as the near-infrared (NIR), have been associated with greater absorption by chromophores in bone tissue, which can potentiate the therapeutic effects of PBM [70–73]. Therefore, the selection of the ideal laser for PBM applications in bone repair must take into account a number of factors, including the type of lesion, the depth of the target tissue, and the individual characteristics of the patient, in order to optimize therapeutic results and minimize the risk of adverse effects. Figure 6 shows the types of lasers chosen by the authors of the studies selected for this study.

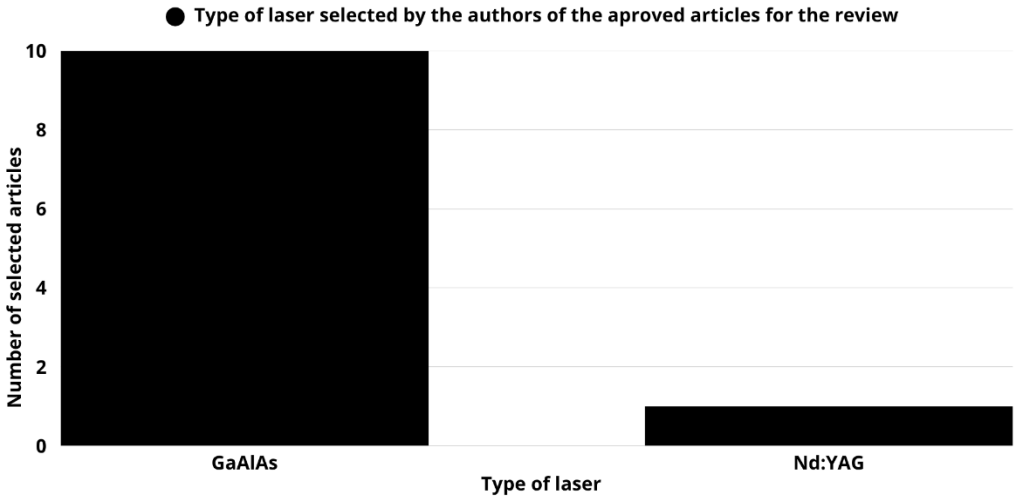

Figure 6. Distribution of laser types used in the articles approved for this review. It is observed that the vast majority of the selected studies employed the gallium aluminum arsenide (GaAlAs) laser, with a total of 10 articles. Only one study used the neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, indicating a predominant preference for GaAlAs among the authors of the reviewed papers.

The Table 3 below summarizes the findings from preclinical studies conducted in animal models evaluating the effect of PBM in the context of guided bone regeneration. The outcome types are categorized by the analytical methods employed, and the direction of effect indicates whether PBM showed beneficial outcomes (↑) or no significant difference (=) when compared to control groups.

Table 4 presents the results from the single clinical study included in this review. Given the methodological differences and direct relevance to clinical practice, this human trial is shown separately from the animal studies. The direction of effect was positive (↑), suggesting a clinical benefit of PBM in periodontal regeneration.

Table 3. Effects of PBM in animal models (preclinical studies).

Study	Laser (λ)	Outcome Type	Direction	Interpretation
Della Coletta et al., 2021 [3]	GaAlAs (830 nm)	Histology	↑	Greater bone formation and maturation in PBM group.
AboElsaad et al., 2009 [9]	GaAlAs (830 nm)	Clinical/Histologic	↑	Accelerated healing at 3 months; no difference at 6 months.
Alves et al., 2020 [10]	GaAlAs (808 nm)	Micro-CT	↑	Increased bone volume fraction, trabecular number, and connectivity; reduced trabecular separation.
Freitas et al., 2023 [12]	GaAlAs (730 nm)	Histomorphometry	=	Significant reduction in residual graft particles; no difference in new bone area.
Freitas et al., 2018 [13]	GaAlAs (808 nm)	Histomorphometry	↑	More new bone in PBM groups compared to autogenous graft groups.
Luca et al., 2020 [14]	GaAlAs (808 nm)	Histology	↑	Superior healing during early postoperative period (first 14 days).

Table 3. *Cont.*

Study	Laser (λ)	Outcome Type	Direction	Interpretation
Pinheiro et al., 2009 [15]	GaAlAs (830 nm)	Histology	↑	Suggests early positive effect of PBM in GBR context.
de Oliveira et al., 2018 [35]	GaAlAs (808 nm)	Histology/Molecular	↑	Increased mineralized tissue and gene expression (BMP2, ALP, OCN).
Rufato et al., 2022 [36]	GaAlAs (780 nm)	Molecular	↑	Upregulation of osteogenic genes with PBM + PTFE.
Valiati et al., 2012 [37]	GaAlAs (830 nm)	Histology	↑	Improved graft incorporation, reduced inflammation, enhanced collagen.

Table 4. Effect of PBM in human study (clinical evidence).

Study	Laser (λ)	Outcome Type	Direction	Interpretation
Emrem Doğan et al., 2014 [11]	Nd:YAG (1064 nm)	Clinical	↑	PBM improved clinical outcomes in periodontal defects.

4. Discussion

Within the context of guided bone regeneration, different therapeutic strategies have been evaluated with the aim of improving the biological response in bone defects, especially through the association between biomaterials and PBM. Luca et al. [14] demonstrated an innovative analysis protocol to evaluate the effect of PBM on the bone regeneration process, using 5 mm diameter calvaria defects in rats, filled with xenotransplant and covered with a collagen membrane, followed by exposure to laser radiation. The animals were sacrificed at different times (14, 21, and 30 days post-operatively), and samples of identical dimensions were taken to compare the results. The analysis combined information obtained by histology and synchrotron-based high-resolution tomography on the same samples, comparing them with a negative control group (NC—bone defect left to heal spontaneously) and a positive control group (PC—bone defects filled with xenotransplants and collagen membrane without PBM). The results showed that PBM was associated with more effective healing than biomaterial support alone, especially during the first 14 days after surgery.

The use of PBM in association with membranes and biomaterials has shown favorable outcomes in the regeneration of critical defects. One of the studies selected for the present review evaluated 80 rats subjected to calvaria defects, distributed into eight experimental groups, considering different materials and the presence or absence of PBM. The results indicated that PBM, especially when combined with collagen membrane, was associated with a significant increase in bone neoformation. The group treated with both resources (PBMT + M) achieved the highest percentage of newly formed bone (64.09 ± 7.62%), standing out from the other groups in a statistically significant way ($p < 0.05$) [13]. These data support the hypothesis that the combination of PBM and physical barrier may favor the environment for tissue regeneration.

In addition, the isolated action of PBM on bone tissue has also been explored with encouraging findings. In an experimental model with mandibular defects filled with bioactive glass, the application of the laser (GaAlAs, 830 nm) promoted more accelerated bone healing at weeks 4 and 8, compared to the group that received only the biomaterial. Although the effects were not significantly different in week 12, these findings suggest that PBM could play an important role in the early stages of regeneration [9].

Other authors have also reported potential benefits of PBM in bone repair, such as Pinheiro et al. [15] who observed increased bone formation in irradiated femoral defects. Valiati et al. [37] highlighted improvements in the incorporation of allografts treated with PBM, as evidenced by bone remodeling and collagen deposition. De Oliveira et al. [35] reported increased expression of osteogenic proteins (BMP2, OCN, ALP) and relevant genes following PBM application in combination with different biomaterials.

Furthermore, the influence of PBM on the quality of regenerated tissue was also investigated in a study using calvaria defects filled with biphasic calcium phosphate and fibrin biopolymer. Laser-irradiated animals showed greater bone formation and collagen maturation, as revealed by Picrosirius-red staining. A reduction in inflammatory infiltrate was also observed, which may suggest a role for PBM in modulating the local inflammatory process and influencing tissue quality; however, such conclusions are limited by the descriptive nature of histological analysis and the absence of confirmatory in vivo functional data [3].

Although PBM shows promising results in bone regeneration, it is important to recognize several limitations and challenges associated with this therapy. One of the main challenges is the lack of consensus regarding optimal treatment parameters, including wavelength, laser power, fluence, and treatment duration, as evidenced by the variability in the studies reviewed. This heterogeneity contributes to inconsistent outcomes and complicates comparative analyses and protocol standardization. The absence of a complete understanding of PBM's mechanisms of action on bone tissue further limits the ability to optimize clinical applications and may obscure potential risks or limitations. Thus, additional research is needed to clarify the benefits and limitations of PBM in the context of bone regeneration [32–34,74,75].

The wide variability in experimental protocols—such as differences in wavelength, power output, and energy density—makes it difficult to establish evidence-based therapeutic guidelines [32,33,74,76]. In addition, interactions between light and certain biomaterials can reduce PBM's therapeutic efficacy. For example, Varela et al. [77] demonstrated that collagen membranes can attenuate laser transmission, potentially diminishing the biological effects of PBM.

Supporting these concerns, a systematic review by Hanna et al. [78] evaluated 38 in vivo studies involving bone defects treated with or without biomaterials and noted generally positive outcomes for bone healing. However, the authors emphasized the lack of standardization in PBM parameters, which prevented robust meta-analysis and limited the generalizability of findings. This reinforces the need for studies with well-defined and replicable protocols to validate the effects of PBM, particularly when used in conjunction with grafting materials.

Similarly, Brassolati et al. [79] reviewed 147 articles on PBM in critical calvaria defects in rats, ultimately including only 14 studies due to strict inclusion criteria. Most of these reported increased bone neoformation, collagen synthesis, and vascular reorganization following PBM. Nonetheless, considerable variation in key laser parameters, including power, fluence, and total energy delivered, limited comparative interpretation. While infrared wavelengths appeared more effective, the authors stressed that further work is needed to define optimal protocols.

Moreover, studies like Rufato et al. [36] have shown that although PBM may not always enhance the performance of specific biomaterials—such as textured P(VDF-TrFE)/BT membranes—it may still contribute to biological improvements in bone tissue, including increased gene expression related to osteogenesis. These mixed results further highlight the need to contextualize PBM's effects based on material type, application protocol, and biological model.

Taken together, the reviewed data indicate that PBM has the potential to support bone regeneration, particularly through mechanisms involving angiogenesis, collagen deposition, and modulation of local inflammatory activity. Nevertheless, the inability to compare diverse PBM protocols remains a significant limitation in the field, hindering standardization efforts and slowing clinical translation. The predominance of animal studies with few clinical trials also underscores the need for more robust human research to confirm preclinical findings and refine PBM's therapeutic potential in guided bone regeneration.

Therefore, future studies should aim to define standardized PBM protocols—specifying wavelength, output power, application technique, and duration—as well as increase the volume of randomized controlled clinical trials. These steps are essential to improve the reliability and clinical utility of PBM in bone regenerative therapies.

5. Conclusions

Photobiomodulation (PBM) shows promising potential in bone regeneration, offering a non-invasive approach to supporting the healing and repair of damaged bone tissue. Preclinical and limited clinical studies to date have reported encouraging results, highlighting beneficial effects on bone formation, healing acceleration, and improved clinical outcomes. However, several limitations remain, including the predominance of animal-based evidence, the lack of high-quality randomized controlled trials in humans, the absence of consensus on optimal treatment parameters, the heterogeneity of study designs, and an incomplete understanding of the underlying biological mechanisms.

To advance the field and improve the quality of evidence, future research should prioritize well-designed, multicenter randomized controlled trials with standardized dosimetry protocols and harmonized outcome measures. Additionally, head-to-head comparisons with established regenerative adjuvants are recommended. These steps will be essential to determine the true clinical applicability and effectiveness of PBM in bone regeneration, ensuring safe and evidence-based integration into clinical practice.

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Abbreviations

The following abbreviations are used in this manuscript:

CO_2	Carbon dioxide
Er:YAG	Erbium-doped yttrium aluminum garnet
PBMT	Photobiomodulation therapy
PBM	Photobiomodulation
NC	Negative control
PC	Positive control
M	Collagen membrane

Laser	Light amplification by stimulated emission of radiation
LLT	Low-intensity lasers
HLLT	High-power lasers
HA/βTCP	Biphasic ceramic comprising hydroxyapatite and β-tricalcium phosphate
GaAIAs	Aluminum gallium arsenide diode
PLA	Polylactic acid
PGA	Polyglycolic acid
PTFE	Polytetrafluoroethylene
BMP2	Bone morphogenetic protein 2
OCN	Osteocalcin
Runx2	Runt-related transcription factor 2
Bsp	Bone sialoprotein
Bglap	Bone gamma-carboxyglutamate protein
Sp7	Osterix
Rankl	Receptor activator of nuclear factor kappa-B ligand
Alp	Alkaline phosphatase
P(VDF-TrFE)/BT	Poly (vinylidene fluoride-trifluoroethylene)/barium titanate
NIR	Near infrared
Nd:YAG	Neodymium-doped yttrium aluminum garnet

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