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Review

Effects of Photobiomodulation Using Low-Level Laser Therapy on Alveolar Bone Repair

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Abstract: Alveolar bone repair is a complex and extremely important process, so that functions such as the mastication, occlusion and osseointegration of implants can be properly reestablished. Therefore, in order to optimize this process, many procedures have been used, such as grafting with biomaterials and the application of platelet-rich fibrin (PRF). Another method that has been studied is the use of photobiomodulation (PBM) with the use of low-level laser therapy (LLLT), which, through the absorption of photons by the tissue, triggers photochemical mechanisms in the cells so that they start to act in the search for homeostasis of the affected region. Therefore, the objective of this review was to analyze the use of LLLT as a possible auxiliary tool in the alveolar bone repair process. A search was carried out in scientific databases (PubMed/MEDLINE, Web of Science, Scopus and Cochrane) regarding the following descriptors: "low-level laser therapy AND alveolar bone repair" and "photobiomodulation AND alveolar bone repair". Eighteen studies were selected for detailed analysis, after excluding duplicates and articles that did not meet predetermined inclusion or non-inclusion criteria. According to the studies, it has been seen that LLLT promotes the acceleration of alveolar repair due to the stimulation of ATP production, activation of transcription and growth factors, attenuation of the inflammatory process and induction of angiogenesis. These factors depend on the laser application protocol, and the Gallium Aluminum Arsenide—GaAlAs laser, with a wavelength of 830 nm, was the most used and, when applications of different energy densities were compared, the highest dosages showed themselves to be more efficient. Thus, it was possible to conclude that PBM with LLLT has beneficial effects on the alveolar bone repair process due to its ability to reduce pain, the inflammatory process, induce vascular sprouting and, consequently, accelerate the formation of a new bone matrix, favoring the maintenance or increase in height and/or thickness of the alveolar bone ridge.

Keywords: alveolar bone loss; bone regeneration; low-level laser therapy; photobiomodulation therapy; alveolar bone atrophy; low-power laser therapy

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1. Introduction

Loss of alveolar bone can occur for several reasons, such as resorption due to periodontal diseases which can be caused by excessive smoking, with consequent gingival recession and loss of alveolar bone due to vasoconstriction of periodontal tissues [1,2]. In addition, alveolar losses occur due to oral surgeries involving tumors in the maxilla and mandible [3] and due to factors linked to advancing age, which leads to an imbalance between the processes of osteogenesis and bone resorption [4,5]. The alveolar bone tissue is also influenced by hormonal imbalances, such as estrogenic decline, which leads to increased activity of osteoclasts [6] or inflammatory processes, which interfere with bone homeostasis and accelerate the reabsorption of bone tissue. However, the main cause of bone loss or atrophy of the alveolar ridge is tooth extractions [7].

Alveolar bone repair after tooth extraction, under normal conditions, occurs following a four-stage physiological process: cell proliferation, connective tissue development, maturation of the formed connective tissue and bone differentiation or mineralization [8]. Initially, there is the formation of a clot in the alveolar cavity, which is gradually reabsorbed as endothelial cells and fibroblasts migrate to the site, forming an immature connective tissue filled with inflammatory cells resulting from clot formation. Subsequently, the differentiation of osteoprogenitor cells into osteoblasts occurs through bone-modulating protein molecules (BMP) [9].

Thus, there is the production of more BMP molecules so that there is a proliferation of osteoblasts in the tissue, in which the development of connective tissue occurs through the synthesis of the organic matrix composed of collagen, proteoglycans and glycoproteins. After the formation of the organic matrix, the osteoblasts produce Alp (Alkaline Phosphatase) vesicles, which receive calcium and phosphate from the blood vessels, enabling the synthesis of hydroxyapatite crystals—a compound that promotes the mineralization of bone tissue [10,11]. This process of alveolar repair is important, as problems related to loss or damage to alveolar bone can lead to several negative consequences, such as difficulty in dental occlusion, masticatory function, maintenance of prosthetic function and aesthetic impairment [12].

In order to optimize this process, procedures have been used, such as bone grafting with biomaterials [13], the application of platelet-rich fibrin (PRF) [14], and the application of plasma rich in growth factors (PRGF) [15]. The most commonly used bone grafts are natural or synthetic polymers, which have osteogenic, osteoinductive and osteoconductive characteristics, widely used in bone regeneration applications [16]. The use of PRF and PRGF is due to the secretion of growth factors by platelets and leukocytes, which stimulate the process of bone regeneration [17].

Another method for optimizing alveolar bone repair that has been studied and used in clinical dental practice is local low-level laser therapy (LLLT). The use of LLLT, or currently called photobiomodulation therapy (PBM), consists of applying light from a low-energy laser (with a wavelength spectrum of 600–1110 nm) [18], which is absorbed by the irradiated tissue. This promotes chemical changes (photobiostimulation), resulting in the production of a series of growth factors which act on the proliferation of molecules and cells necessary for bone repair, such as collagen, fibroblasts, molecules involved in angiogenesis and osteoblasts [19].

The restorative tissue effects promoted by the use of LLLT were initially investigated in 1967 by the researcher Endre Mester, who described the biostimulatory action of lasers in the tissue repair process [20]. From the year 1980, after advances in scientific experimentation, there was a gradual expansion of the use of LLLT in several cases, such as in repair processes of nervous tissue, bone tissue, respiratory tract tissues and tissues affected by burns, among others [21]. This biostimulatory effect is due to the induction of cell proliferation and growth factors essential to the tissue repair process, in addition to promoting a decrease in the density of inflammatory cells and stimulating collagen synthesis [22,23].

Physical stimulation is considered as the most popular among non-conventional techniques that can improve bone formation mechanisms. Technologies include photonic, magnetic, electrical and mechanical stimulatory techniques, with photonics being the most popular and promising technique in the mechanisms of new bone formation, with mitochondrial stimulation through a biochemical effect. Photonics include static laser therapy, pulsed laser therapy techniques and LLLT [24–26].

In dentistry, LLLT can be used for both soft and hard tissue [27]. Studies use complementary or adjuvant techniques in order to favor the rehabilitation or prevention of diseases that affect structures of the stomatognathic system—for example, the use of ozone therapy alone or in association with LLLT [28,29], medication-related osteonecrosis of the jaw (MRONJ) [30], antimicrobial therapies (photodynamic therapy, PDT) [31], acute and chronic pain [32], acceleration of the orthodontic tooth movement [33] and other things [34].

Laser irradiation is effective when applied to healing sites such as fractures or bone defects and tooth extraction sites. In this way, osteoblasts can be recruited along the bone borders of undifferentiated precursor cells, and LLLT can potentially stimulate osteoblast recruitment and/or maturation [35,36]. There is also stimulation of collagen synthesis, with type I collagen mRNA being increased by LLLT during healing. Because type I collagen is the major bone matrix protein, laser PBM stimulation of the collagen level supports a stimulatory effect on bone formation [37]. Another event in repair is the sprouting of new blood vessels, which provides important elements for this process [38].

Considering the importance of the osteogenic, anti-inflammatory and biostimulating capacity of photobiomodulation, with low-level laser therapy, and in order to compare scientific studies in the area, the objective of this review was to analyze the use of PBM as a possible therapy that improves the alveolar repair process in the maxilla and mandible.

2. Materials and Methods

We accessed and selected manuscripts from 4 databases, PubMed/MEDLINE, Web of Science, Scopus (Elsevier) and Cochrane, without a search period limit relative to the year of publication and using the keywords: "low-level laser therapy AND alveolar bone repair" and "photobiomodulation AND alveolar bone repair". With the intersection of keywords, a detailed analysis of the results was carried out, with the title of the scientific paper and its abstract being important criteria for selection. Subsequently, the manuscripts were separated into included and non-included according to the eligibility criteria we stipulated. When selecting studies for detailed analysis, two independent reviewers scanned the manuscripts, considering the selection criteria, with the aim of minimizing bias.

The criteria used for inclusion were studies carried out in both humans and animals, in vivo studies, publications in English that allowed access to the full text and sufficient data for the understanding of the photobiomodulation protocol. The following were not included: duplicate articles, when the manuscript was not directly related to the purpose of this review; cases in which photobiomodulation with a low-level laser was not used or a high-intensity laser was used; languages other than English; when we did not have access to the full text; articles such as letters to the editor, reviews, commentaries, conference abstracts or dissertations and theses from repositories.

The studies that presented a title and abstract related to the chosen topic were initially selected based on the focus of this review: low-level laser therapy and photobiomodulation, as used in the alveolar bone repair process. The next step used was to exclude duplicated articles in the databases consulted and also to remove studies that did not follow the eligibility criteria through careful reading of the texts. This step was carried out paying special attention to the methodology used in the study, ensuring that the procedures used were, in fact, related to the theme proposed here.

The article selection scheme is shown in Figure 1.

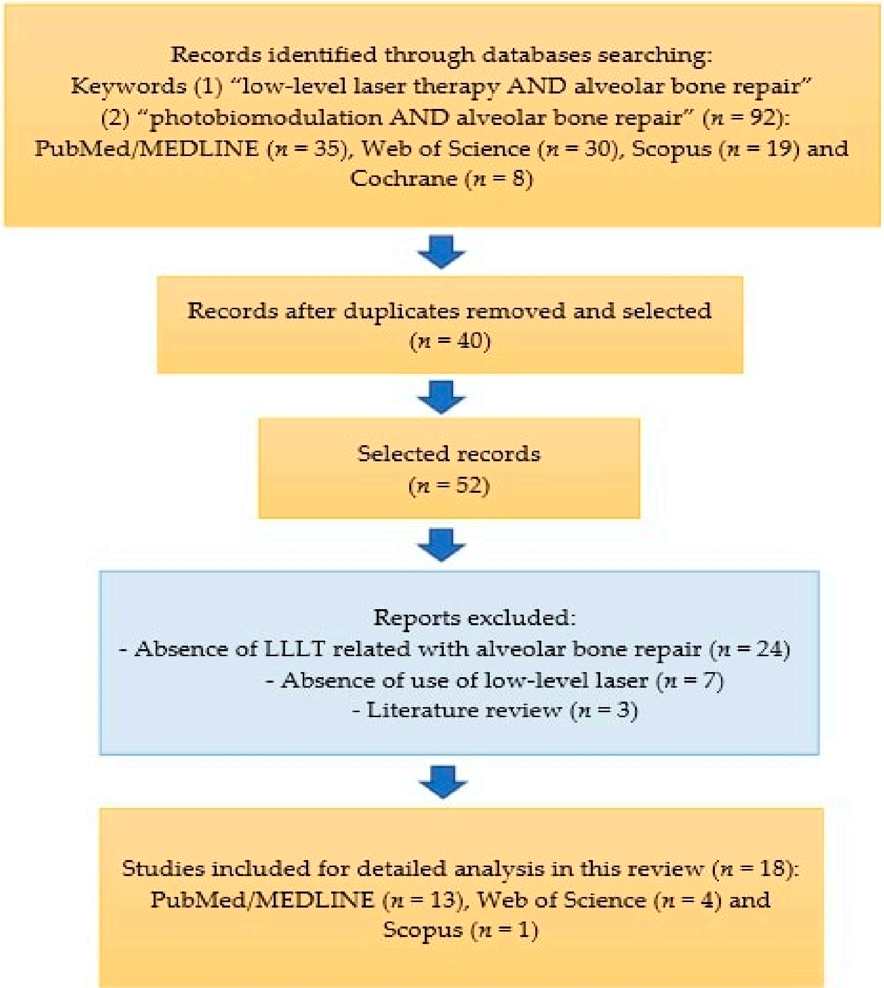

Figure 1. Diagram showing the selection of review articles.

3. Results

In the search and scanning carried out in the bibliographic databases, we found 35 articles in PubMed/MEDLINE, of which 22 were excluded because they were duplicates or due to the inclusion/exclusion criteria. We also found thirty articles on Web of Science and selected four articles, nineteen articles on Scopus and one article was selected and eight articles on Cochrane and no articles were selected, totaling eighteen articles for qualitative and detailed analysis.

From the studies selected for detailed, we can see that eleven studies used a gallium–aluminum–arsenide laser (GaAlAs), two used helium–neon (He-Ne), one used indium gallium aluminum phosphorus (InGaAlP); one used a twin laser, one used a Wiser wireless diode laser, one used a CO_2 laser and one used neodymium-doped yttrium aluminum garnet (Nd;YAG) (Figure 2).

In the photobiomodulation protocols of the selected studies, when the wavelengths were analyzed the most used was 830 nm in four studies. Then, the next most was 980 nm in three studies; 808 nm in two studies; and 660 nm, 632.8 nm, 780 nm, 810 nm, 904 nm, 1064 nm and 1780 nm with one study each (Figure 3).

Table 1 shows the selected studies that were carried out in animal models and, in Table 2, the studies in humans. In the layout of the columns in Tables 1 and 2 of this integrative review, the references, elements of the PBM protocol and PICO strategy (P: patient or problem; I: intervention; C: control or comparison; O: outcome) were inserted [39].

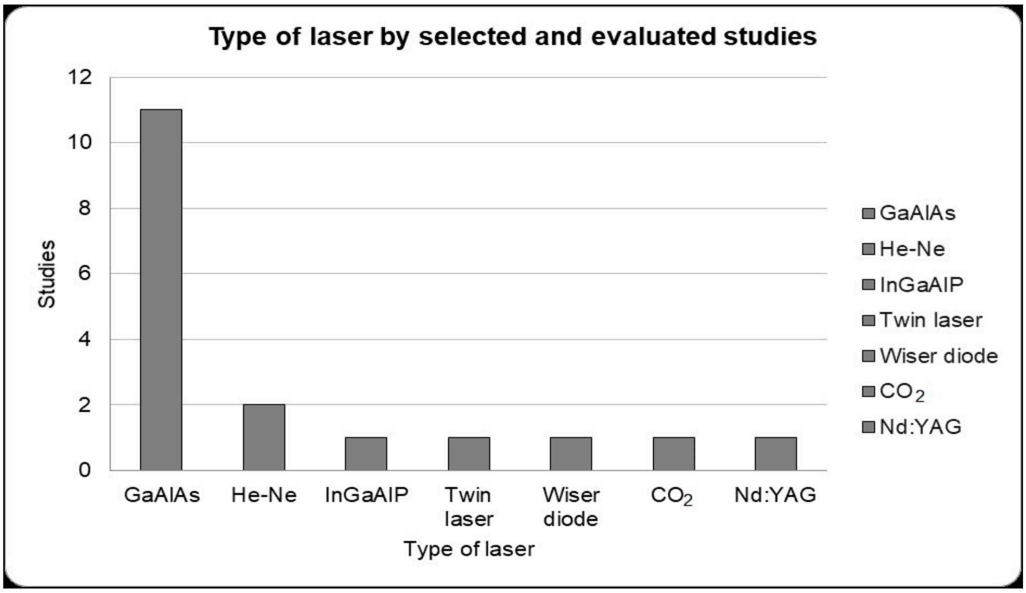

Figure 2. Type of laser used for photobiomodulation therapy presented by the selected studies for detailed analysis. Gallium–aluminum–arsenide (GaAlAs) laser that presented greater use in the selected studies in alveolar bone repair (11 studies).

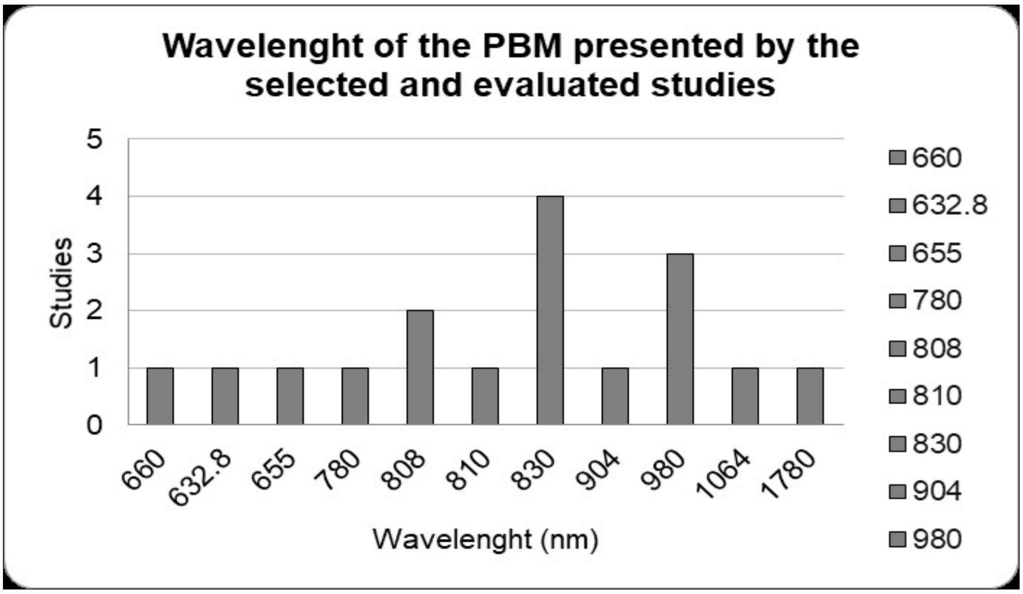

Figure 3. Photobiomodulation protocols. Wavelength (nm) used by the studies included. The 830 nm wavelength was the most used in studies with alveolar bone repair (four studies). Studies that used different wavelengths were considered separately in the data shown in the figure.

Table 1. Articles that were selected for detailed analysis—animal studies.

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Özyurt et al., 2018 [40]	Investigate the effect of GaAlAs diode laser used in LLLT with the application of Mecsina herbal hemostopper on mandibular alveolar bone healing	GaAlAs Diode Laser (BLT®, Brno, Czech Republic)	830	50	-/-	10	Mecsina	Defects were created on the left mandibular diastema sites of 32 rats that were allocated to four groups: CG (A), Laser Group (B), Mecsina Group (C) and Laser–Mecsina Group (D)	Once every 24 h for 7 days	There were more osteoblastic cells in the laser and laser-Mecsina groups then the others. Moreover, the laser–Mecsina combination group showed more bone tissue formed	Laser treatment, Mecsina application and the combination of both were more effective treatments on alveolar bone healing than the others
Ribeiro et al., 2020 [41]	Evaluate osteoclastogenesis in tooth treated with LLLT and exposure to cigarette smoke, after tooth extraction in rats, at different times of healing	GaAlAs Diode Laser (Photon Laser®, DMC Equipaments, São Carlos, Brazil)	830	30	-/-	54	-/-	Four groups of 15 Wistar rats were divided in CG (with right maxillary extraction-ME); Exp I (with ME and LLLT); Exp II (with ME and cigarette smoke) and Exp III (with ME, LLLT and cigarette smoke)	Immediately after extraction and once per day for 3 days	Exp III group expression of RANK, RANKL and OPG genes was higher than Exp II, but lower than CG and Exp I groups. Moreover, Exp I showed up regulation of these genes over all time compared to the CG	The results concluded that LLLT had positive effect, whereas cigarette smoke had negative effect on RANK, RANKL and OPG gene expression in bone remodelling process
Ribeiro et al., 2022 [42]	Evaluate the effect of LLLT in enhancing bone healing in irradiation alveolus post-tooth extraction	GaAlAs Diode Laser (Photon Laser®, DMC Equipaments, São Carlos, Brazil)	830	30	-/-	54	-/-	Two groups of 30 Wistar rats were divided into CG (with left maxillary molar extraction) and EG (with tooth extraction and LLLT). These groups were subdivided in six groups according to the observation time point: 1, 2, 3, 5, 7 and 10 days post-extraction	Immediately after extraction and once per day for 3 days	Histomorphometric analysis revealed an increase of osteoblast (RUNX-2) and osteoclast (TRAP) activity in the area percentage of cancellous bone in the EG compared to CG	The experiment concluded that the application of LLLT enhanced healing and mineralization on alveolar region

Table 1. *Cont.*

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Çırak et al., 2018 [43]	To evaluate the effects of He-Ne and GaAlAs lasers with various doses on bone healing following tooth extraction	He-Ne laser (LABpen MED 30; Therapilaser, Graz, Austria) and GaAlAs laser (BTL Laser 2000; BTL Industries Ltd., Hertfordshire, UK)	Group B: 655 Group C: 830	Group B: 30 Group C: 100	-/-	B1(6); B2 (10); C1 (6); C2 (10)	-/-	Five groups were divided: four groups with He-Ne (B), GaAlAs (C) lasers and CG (A).	Once per day for 7 days; 6 J/cm^2 (B1/C1) and 10 J/cm^2 (B2/C2)	Both laser groups showed faster bone healing and the GaAlAs laser increased vascular immunoreactivity. The most increasing in bone formation was observed in the B2	LLLT was effective on alveolar bone healing and that energy dose of 10 J/cm^2 did not have inhibition effect on bone regeneration
Park et al., 2012 [44]	To evaluate the effect of LLLT on the healing of extraction sockets in diabetic and healthy rats	GaAlAs diode laser (Diobeauty-30®, Diotech, Busan, Korea)	980	10	-/-	13.95	-/-	A total of 48 rats were divided into normal (n = 24) and diabetic (n = 24) rats. Then, after a tooth extraction, these were subdivided in groups submitted to LLLT and not irradiated	Every day after tooth extraction for 3, 5, 7 or 14 days	Both groups that were submitted to LLLT showed faster initial healing and more new alveolar bone formation than the groups without laser therapy	LLLT is beneficial for the initial stages of alveolar bone healing and for further calcification
Oliveira et al., 2008 [45]	To evaluate the effect of LLLT associated to mineral trioxide aggregate (MTA) on the alveolar bone repair process	Twin Laser (MMOptics®, São Carlos, Brazil)	1780	40	-/-	16	Mineral trioxide aggregate (Angelus®; Londrina, Brazil)	Forty Wistar rats were divided into four groups after tooth extraction: G1 (control group); G2 (MTA); G3 (LLLT) and G4 (LLLT and MTA)	Four sessions every 48 h after extraction	In G2, was observed intense vascular hyperemia and chronic inflammation while in G4 it was quite distinguishable and there was intense deposition of thin bone trabeculae	It was observed that LLLT was the most successful treatment to improve alveolar bone repair

Table 1. *Cont.*

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Pretel et al., 2007 [46]	To evaluate the bone repair in defects created in rat lower jaws after stimulation with infrared LLLT directly on the injured tissue	GaAlAs diode laser (Laser Beam Multi Laser DR 500 device®; Laser Beam Ind. Tecn. Ltd., Niterói, Brazil)	780	50	-/-	178	-/-	Thirty Holtzman rats that had defects prepared in their mandibles were divide in two groups: Control Group, CG and Laser group, LG (n = 15), which were subdivided in three evaluation period (15, 45 and 60 days)	A single application after tooth extraction	The LG exhibited an advanced tissue response compared to the CG, decreasing the initial inflammatory reaction and promoting rapid new bone matrix formation	LLLT showed to be a good method by stimulating the modulation of inflammatory response and anticipating the resolution to normal conditions
Park et al., 2015 [47]	To investigate the effects of irradiation time on the healing of extraction sockets by evaluating the expressions of genes and proteins related to bone healing	GaAlAs diode laser (Diobeauty-30®; Diotech, Busan, Korea)	980	10	-/-	13.95	-	Twenty-four rats were submitted to a tooth extraction and then were divided into four groups according to the time that the wound received LLLT	For 0, 1, 2 or 5 min each day for 3 or 7 days	LLLT increased the expressions of all tested genes related to bone healing and vascular endothelial growth factor. The highest levels of gene expressions were in the 5 min group after 7 days	LLLT had positive effects on the early stages of bone healing of extraction sockets in rats, which were irradiation time-dependent
Abdel Hamid et al., 2021 [48]	To evaluate the effect of PBM on socket healing in the maxilla and mandible	Wiser wireless diode laser (Doctor Smile—LAMBDA Spa Vicenza, Italy)	980	600	770 mW/cm^2	46	-/-	It was a split-mouth experimental where six dogs had the 3rd premolar tooth extracted from both sides of maxilla and mandible, then the right side was treated with laser and the left side was kept as control	Immediately after tooth extraction and at 48 h interval for 14 days	Maxillary sockets in the PBM group had higher bone density compared to control one at 3, 4 and 5 weeks	The experiment concluded that PBM using a flat-top hand-piece of 980 nm improved the bone density of extraction sockets

Table 1. *Cont.*

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Fukuoka et al., 2010 [49]	To clarify the healing promoting effects of carbon dioxide laser irradiation in high and low reactive-level laser therapies (HLLT and LLLT, respectively) on extraction sockets	CO_2 laser (Panalas $CO_5\sum$; Panasonic Shikoku Electronics Co., Ltd., Osaka, Japan)	-/-	LLLT and HLLT: 1000	-/-	LLLT- 40 J/cm^2 HLLT- 152 J/cm^2	HLLT	Forty-two Wistar rats were divided into two groups: Laser group (LG), which underwent HLLT immediately after tooth extraction and LLLT 1 day post-extraction. Tissue was excised 6 h, 3, 7 or 21 days after extraction	A single application one day after tooth extraction	On day 3, almost no α-SMA-positive myofibroblasts were present in the irradiation group while many of these were present in the CG. On day 21, the alveolar bone height was significantly higher in the irradiation group	The ppearance of fewer α-SMA-positive myofibroblasts and the higher alveolar bone formed in the LG suggest that laser therapy improves the healing of alveolar bone
Rochkind et al., 2004 [50]	To investigate the therapeutic efficiency of laser irradiation and Bio-Oss® on the post-traumatic regeneration of bone tissue in rats	He-Ne laser	632.8	35	-/-	-/-	Bio-Oss®	Twenty-nine Wistar rats were submitted to a bone defect in the right alveolar process, then were divided into four groups: G1 (n = 5, control); G2 (n = 8, filled with Bio-Oss), G3 (n = 8, treated by laser), G4 (n = 8, Bio-Oss + laser)	For 20 min daily for the following 14 consecutive days	The G3 showed the process of absorption of inorganic component increased compared to the CG. The groups G3 and G4 showed the mineralization index significantly increased	The results suggest that the use of LLLT irradiation for the repair of bone defect can significantly improve the quality and velocity of recovery

Table 1. *Cont.*

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Luca et al., 2020 [51]	Evaluation of the effect of PBM on the bone regeneration process, using rat calvarial defects of filled with xenograft	GaAlAs laser (IRRADIA Mid-Laser® Stockholm, Sweden)	808	450	450 mW/cm^2	24.075	Bovine bone graft (NuOss® natural cancellous and cortical bone matrix, ACE Surgical Supply, Brockton, MA, USA) and collagen membrane (ACE RCM6® Resorbable Collagen Membrane, ACE Surgical Supply, Brockton, MA, USA)	Twenty-four Wistar rats had a circular defect created in the calvaria, then were divided into three groups: NC group (spontaneous healing), PC group (filled with bone graft and covered with collagen membrane) and +LLLT group (bone graft + membrane + laser)	Surgery day and every 48 h for 14, 21 and 30 days	The +LLLT group on the 14-day fragments revealed well-represented fibrous (young) connective tissue and low inflammatory infiltration compared to other groups. Moreover, the thickness of newly-formed bone on the defect borders is higher in the +LLLT group than in the PC group from the same period	The results concluded that PBM is significantly effective in short periods as it increases the bone volume with respect to the exclusive use of the xenograft
Forte et al., 2020 [52]	To evaluate the influence of photo-biomodulation therapy (PBMT) application during bone healing post exodontia in rats	GaAlAs active-mode diode infrared laser (Therapy EC®; DMC Equipments, São Carlos, Brazil)	810	100	-/-	70	-/-	Eighty-four Wistar rats were submitted to tooth extraction and then were divided into two groups: control group (CG) and test group (TG) with LLLT	Immediately after extraction and every 72 h (day 1, 3, 6, 9, 12, 15, 18, 21, 24 and 27 after extraction	There was no difference in body variation and bone neoformation between the groups, but TG presented inflammatory decrease and higher blood vessels count throughout the repair process	PBMT attenuated the inflammatory process after exodontia without interfering with bone neoformation

Table 1. *Cont.*

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Statkievicz et al., 2018 [53]	To evaluate effects of PBM on the alveolar repair process of rats with major risk factors for medication-related osteonecrosis of the jaws (MRONJ)	InGaAlP laser device (Thera Lase®, DMC Equipaments Ltd., São Carlos, Brazil)	660	35	1.23 W/cm^2	74.2	-/-	Twenty-eight Wistar rats were divided into four groups: VEH (*n* = 7, treated with vehicle); VEH-PMB (*n* = 7, vehicle and PBM); ZOL (*n* = 7, treated with zoledronate); and ZOL-PBM (*n* = 7, zoledronate and PBM)	For 0, 2 and 4 days after extraction	ZOL-PBM showed significant improvement compared to ZOL, such as greater amount of mature collagen fibres, positive repair tissue and decrease of inflammatory molecules	PBM in multiple sessions can improve the alveolar repair process, constituting a promising preventive therapy to avoid the onset
Mergoni et al., 2016 [54]	To investigate the action of laser therapy on extraction socket healing in rats in conditions at risk for MRONJ	Nd:YAG laser therapy (Fidelis®, Fotona, Slovenia)	1064	1250	268.8 W/cm^2	14.37	Zoledonate and dexam-ethasone	Thirty Sprague-Dawley rats were divided into four groups: control group (CG); laser group (L); treatment group (T) and laser + treatment group (T+L).	After tooth extraction and the following 2, 4 and 6 days	The groups L and T+L revealed significant higher expression of neoformation bone (OCN) than groups CG and T. However, the expression of OPN did not present significant differences among the groups	The results demonstrated that laser therapy after tooth extraction can promote increase in bone healing, even in conditions at risk for MRONJ

Table 2. Articles that were selected for detailed analysis—human studies.

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Romão et al., 2015 [55]	To evaluate the human alveolar bone repair 40 days after molar extraction in patients submitted to LPT (Laser phototherapy)	GaAlAs diode laser device (Twin Flex®; MMOptics Ltd., São Carlos, Brazil)	808	100	-/-	75	-/-	Twenty patients were divided into Control Group, CG (n = 10) and Laser Group, LG (n = 10) that were submitted to LPT; then 40 days later, samples of the tissue formed were analysed	During the surgical procedure, immediately after the procedure, and at 24 h, 48 h, 72 h, 96 h, 7 days and 14 days after the procedure	The analysis showed that the LG presented higher relative bone volume than the CG. Moreover, the LG showed a significant negative correlation between the thickness and separation of trabeculae, while the CG showed positive correlation between these parameters	LPT is able to accelerate alveolar bone repair after molar extraction, leading to a more homogeneous trabecular configuration represented by large number of trabeculae with a small thickness
Mozzati et al., 2012 [56]	To study the effect of laser therapy on alveolar healing process in patients waiting for liver transplantation	GaAlAs laser (Fisioline s.n.c., Verduno, Cuneo, Italy)	904–910	200	200 mW/cm^2	180	-/-	Twelve patients waiting for liver transplantation were submitted to a split-mouth study where, after bilateral tooth extraction, one post-extractive defect was treated with laser while the other was left without treatment	Immediately after molar extraction and at days 3 and 5 after the procedure	IL-1β increase and induced IL-6, IL-10, and collagen III was observed in the laser-treated side; in the other side, the parameters were unmodified. Epithelial regeneration evidenced a positive result of laser therapy. Patients reported less pain in the site treated with laser	The results concluded that laser therapy appears to be the treatment of choice for patients due to its clinical efficacy, safety, good tolerance and its ability to prevent inflammation

Table 2. *Cont.*

Reference	Objective	Type of Laser (Manufacturer)	Wavelength (nm)	Output Power (mW)	Power Density	Energy Density (J/cm^2)	Therapeutic Variables	Intervention	Laser Application	Outcome/ Results	Conclusions
Rosero et al., 2020 [11]	Aimed to evaluate the effects of PBM therapy on alveolar bone repair	GaAIAs diode laser (Photon III®, DMC, São Carlos, Brazil)	808	100	3.6 W/cm^2	89	-/-	Twenty patients were enrolled in a split-mouth clinical trial where were submitted to bilateral extraction of lower molars. Then one side was treated by the laser, and the other was the control side	Immediate postoperative and after 1, 2, 3, 4, 7 and 15 days	Samples from the PBMT group exhibited a higher number of spatially organized and connected bone trabeculae, as well the higher density of blood vessels when compared with the control group	The results indicated that the PBM therapy improved the new bone trabeculae formation and their connectivity which increased bone surface

4. Discussion

In view of the increase in research on methods that improve and accelerate alveolar bone repair after tooth extraction, and also the findings on the beneficial effects of low-level laser therapy (LLLT) on tissue repair, this integrative review aimed to evaluate, based on the scientific literature, the effects of LLLT or photobiostimulation in the repair of maxillary or mandibular alveolar bone. It was possible to describe that there is scientific evidence attesting to the fact that treatment with LLLT collaborates in reducing repair time and improves the quality of the process of neoformation of alveolar bone.

The biological bases of the alveolar repair process were first described by Euler who, after histological and radiographic analysis, was able to discriminate the alterations that occurred in dental sockets of dogs after extraction [57,58]. Subsequently, the repair process of bone alveolar tissue was defined by Carvalho et al. (1997) who, using histometric analysis in rats, were able to determine the set of reactions triggered within the alveolus after tooth extraction [59].

Experiments to analyze alveolar repair have already been conducted in several animal species, such as rats [60,61], dogs [62], rabbits [63,64], guinea pigs [65] and humans [66], since the repair stages are the same in all these beings, however, the duration of the process varies according to the specimen studied. In our study, it was possible to observe that the rat was the animal model most used to carry out experiments on the dental alveolar repair process because these animals, like rabbits, are good models due to their ease of use, creation, maintenance and ethical aspects. However, unlike experiments carried out in dogs, which have greater bone compatibility with humans, it is not possible to fully transfer the results obtained in rats and rabbits to clinical situations in humans [63,67].

The chronology of events involving bone tissue repair after tooth extraction in rats has already been widely studied and can be summarized as follows: 24 h postoperatively: the site is filled with blood clots and fibrin bundles; 3–5 days: the proliferation of fibroblasts, blood capillaries and the beginning of the replacement of the clot by granulation tissue with an increase in inflammatory cells is observed; 6–7 days: an increase in the amount of osteoblasts in the periphery of the socket and the formation of bone trabeculae in the apical and middle thirds; 9–10 days: the presence of more organized connective tissue, vascularized and rich in fibroblasts, in addition to thickening of bone trabeculae; 13–21 days: there is an intensification of osteoblast activity with the formation of osteoid tissue while the central portion remains filled with granulation tissue; 24–28 days: the occupation of all thirds and central portion of the alveolus by thickened bone trabeculae and gradual decrease of the intertrabecular spaces, determining the beginning of bone remodeling; over 28 days: bone remodeling of the socket and alveolar process [68–70].

Comparatively, alveolar tissue repair in humans follows the same steps as that presented by rats, but the chronology differs so that only between 12 and 16 weeks postoperatively does the complete filling of the dental alveolus by bone tissue occur, and only after the 17th week are the bone remodeling of the socket and alveolar process verified [71] (Figure 4).

Lasers (light amplification by stimulated emission of radiation) are devices that emit a type of electromagnetic radiation, characterized by being relatively uniform in parameters related to wavelength, phase and polarization. Theodore Maiman initially studied these factors in 1960, when he carried out his research using ruby laser [72]. Lasers can be divided into two main classifications: high-power lasers (HLLT), which are indicated for surgical procedures, such as cuts and cauterization, and have an ablation effect [73]; and low-level lasers (LLLT), which are more used for therapeutic purposes and biostimulators [74]. Low-level laser is a type of laser whose action does not take the form of heat but through the absorption of photons by the tissue, which triggers photochemical mechanisms at the cellular level, promoting various effects in the biological system and resulting in the biomodulation of the cell so that it works in search of the normalization state of the affected region [75].

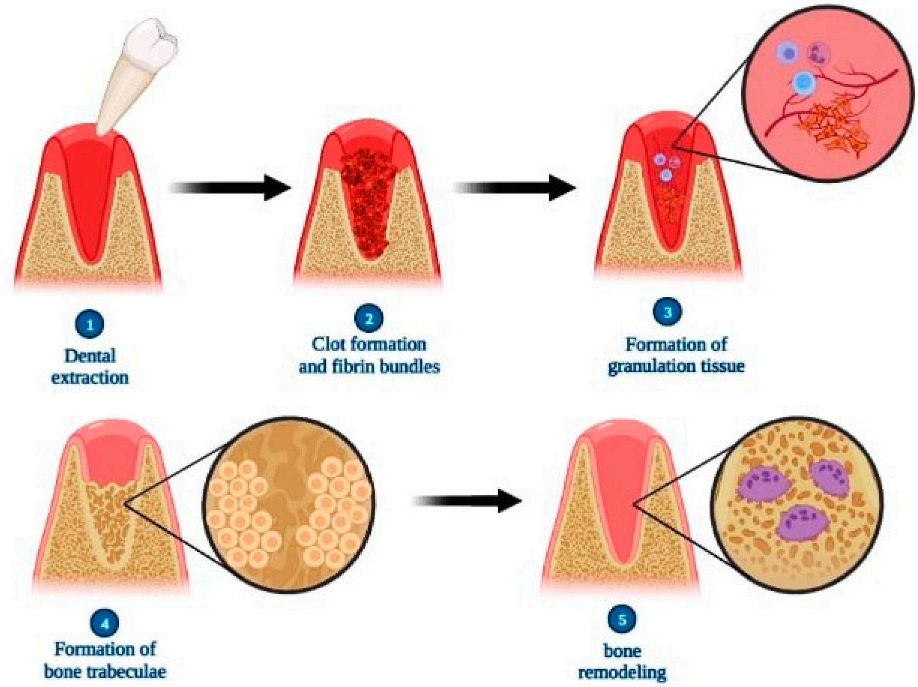

Figure 4. Scheme illustrating the steps of alveolar bone repair after tooth extraction. Briefly, the repair process is characterized initially by the formation of the clot and fibrin bundles, followed by the proliferation of fibroblasts, blood capillaries and inflammatory cells resulting in granulation tissue. In sequence, there is an increase in the amount of osteoblasts at the site, producing bone trabeculae that replace the granulation tissue. Finally, there is a gradual decrease in intertrabecular spaces in the process of bone remodeling, resulting in repaired bone tissue. Created with BioRender.com (accessed on 6 April 2023).

Since the last decade, studies involving the therapeutic properties of low-level laser have been increasing in such a way that many beneficial effects related to the application of this device in the field of dentistry have already been discovered. We can highlight properties such as the reduction of pain, inflammation and edema, assisting in the healing process and accelerating the tissue repair process [76,77]. Regarding this last property, studies have already demonstrated that LLLT is already widely used in the area of rehabilitation and regenerative medicine to accelerate the regeneration of different types of tissue in the human body, such as nervous tissue [78–81]; muscles [82]; bone tissue [83–86]; respiratory tract tissue [87]; tissues affected by burns [88] and other body tissue types [89]. Metin et al. (2018) obtained positive results when using LLLT in soft and hard tissues after endodontic surgery, such that the laser group presented better results in relation to tissue repair, increase in bone volume and density and decrease in postoperative pain [90].

This property on tissue repair is due to factors such as the stimulation of ATP production, the activation of transcription factors, the activation of genes responsible for the synthesis of growth factors, the inhibition of factors responsible for cell death, the attenuation of the inflammatory process resulting from the extraction and the promotion of greater blood supply to the site to be repaired [91,92] (Figure 5).

According to our study, it was possible to analyze that the use of low-level lasers in the dental socket generated a significant increase in the expression of genes related to the neoformation of bone tissue, such as genes responsible for the synthesis of the receptor activator of nuclear factor kappa (RANK), the receptor activator of nuclear factor kappa B ligand (RANKL), osteoprotegerin (OPG), runt-related transcription factor 2 (RUNX-2), type 1 collagen and osteocalcin (OCN) and essential factors for the bone tissue deposition process [40–42,47,93].

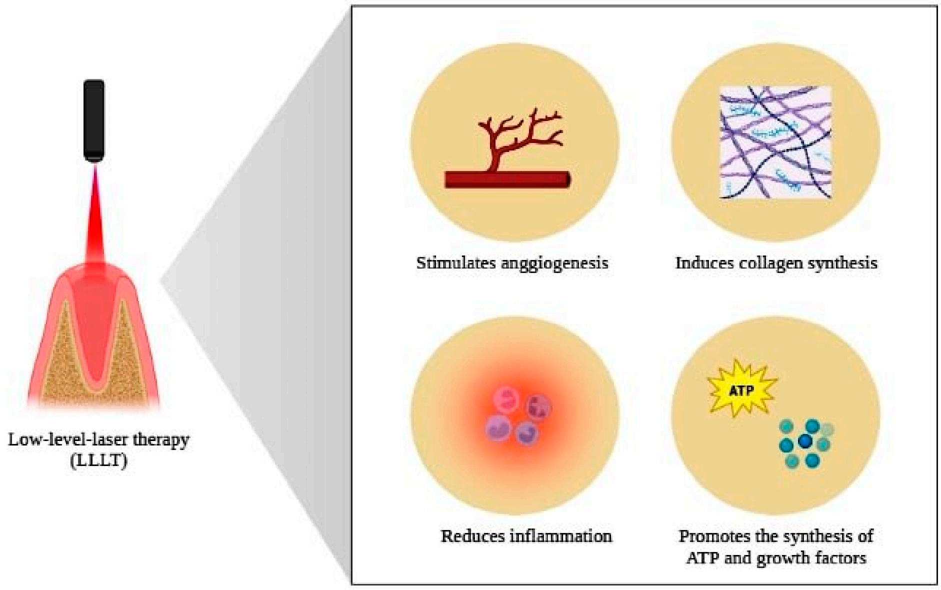

Figure 5. Scheme illustrating the beneficial properties of low-level laser therapy on body tissues. Photobiomodulation, through the application of LLLT, stimulates angiogenesis, induces collagen synthesis, promotes the attenuation of the inflammatory process and stimulates the synthesis of ATP, as well as growth factors, properties that determine the accelerating potential of tissue repair provided for the use of this therapy. Created with BioRender.com (accessed on 6 April 2023).

It was also possible to observe a significant reduction in the inflammatory process after tooth extraction and an increase in vascularization in the region, which benefits new bone formation due to the greater contribution of minerals to the region [11,43,45,46,52,53,94]. Given these facts, LLLT accelerated the production of bone trabeculae and promoted an increase in the density of the formed bone [49,95].

These entire laser properties depend on the application protocol, which includes factors such as the wavelength used, energy density, irradiated area, time and frequency of laser application, in addition to the type of laser used [75,96]. Low-level lasers can be obtained from various sources such as GaAlAs (gallium–aluminum–arsenide); He-Ne (helium–neon); twin laser; Wiser wireless; CO_2; InGaAlP (indium gallium aluminum phosphorus); Nd;YAG (neodymium-doped yttrium aluminum garnet), but it was possible to observe that the most used in dentistry in alveolar repair were the GaAlAs laser and the He-Ne laser (Figure 2). When comparing these two types of laser, the He-Ne laser and GaAlAs laser, GaAlAs proved to be more efficient due to its greater ability to penetrate tissue [43].

Regarding the laser energy density, it can be seen that the studies warn about care so that its intensity is not so low in such a way that it does not promote beneficial effects, nor so high that it can result in tissue damage that worsens the bone tissue regeneration [97]. The parameters are still not standardized, varying a lot between experiments, from 6 J/cm^2 to 180 J/cm^2 [43,56]. Furthermore, it was observed that when comparing two values of energy density of the same type of laser (6 J/cm^2 or 10 J/cm^2), the higher dosage of 10 J/cm^2 proved to be more efficient in stimulating the tissue repair [43].

LLLT is not only used alone in an attempt to accelerate alveolar bone repair but is also used as a possible adjuvant in the action of other repair methods, such as mineral trioxide aggregate (MTA), bovine bone graft, collagen membrane and Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland). Mineral trioxide aggregate is a biomaterial that has the ability to induce osteogenesis by stimulating calcium deposition in the connective tissue [45]. According to the experiment, it was observed that the association of MTA with LLLT is more effective than the use of MTA alone, as a greater intensity of trabecular bone deposition was obtained. However, even though this association promotes good results, it was observed that the use of LLLT alone obtained better results, since a greater intensification of trabecular bone deposition was observed [45,98].

Bovine bone graft is widely used as an osteoconductor in the repair of bone alveolar tissue after tooth extraction and is often associated with the application of a collagen membrane to surround the graft (guided tissue regeneration—GTR). According to the experiment, grafting associated with the LLLT protocol proved more efficient in relation to the use of the isolated graft, as together the presence of greater bone volume was detected during tissue regeneration [31].

Bio-Oss® collagen is a bone substitute widely used in reconstructive dentistry due to its osteoconductive properties, in addition to being recommended for the reconstruction of alveolar bone after tooth extraction. According to the experiment, it was observed that the association of bone substitute with LLLT proved to be more efficient than the use of Bio-Oss alone, since both the association and the use of LLLT alone presented a higher mineralization index in relation to the use of Bio-Oss® alone [50]. However, the mechanism of the effect of the combination of LLLT and Bio-Oss® is not yet clear and needs to be further studied.

Visible light has wavelengths in the range of approximately 400 nm to 780 nm. When the wavelength is above this range we have infrared radiation, and when it is below we have ultraviolet radiation (UV) [99]. The wavelengths most used in dentistry are included in the red and infrared range, close to the electromagnetic spectrum, and this range of non-ionizing energy is safer for clinical application [100]. We can mention the use of UV irradiation, the management of polymicrobial biofilms in periodontal and peri-implant microbiomes, or endodontic infections and inflammation in root canals, contributing to the destruction of microorganisms and the release of cytokines, chemokines and biomarkers in tissues [101]. Longer wavelengths (>1110 nm), such as erbium lasers (2780 nm and 2940 nm) and carbon dioxide (CO_2) lasers (9300 nm and 10,600 nm), are high-power lasers that, in dentistry, the erbium is used for caries prevention, cavity preparations, surface treatment of ceramics and the CO_2 laser indicated for soft tissues [102].

LLLT uses low-power lasers with wavelengths from 660 nm to 1110 nm, a range that is more indicated to have good effects in the initial stages of bone repair [18]. In this review, it was observed that the most used wavelength was 830 nm, which demonstrated satisfactory results [18]. In addition, regarding the laser application protocol, different application intervals during and after tooth extraction were analyzed; however, it was observed that the laser has more visible and efficient results in the initial period of the alveolar bone repair process, and after this period the action of the laser is not as noticeable when compared to the natural repair process [51,103].

Most of the laser systems studied in this review are continuous-wave (CW) lasers. CW lasers are light sources that continuously pump and emit light [104]. Ultrashort pulse lasers offer innovative opportunities for material processing. The most common forms of laser technology are the nanosecond, picosecond and femtosecond lasers [105]. Picosecond and femtosecond lasers with reduced pulse durations have significant advantages in the higher-precision ultra-fast laser ablation industry [106]. Femtosecond lasers can be used in dental surgery and minimally invasive treatments of carious tissue. Femtosecond laser ablation offers a tool for generating cavities without cracking tooth tissue [107].

For brief context, it is possible to state that low-level laser therapy is beneficial to the alveolar bone repair process due to its biostimulatory effects, which are angiogenesis and collagen matrix synthesis inducers, inflammation, pain and edema inhibitors [108,109]. The difficulty in comparing the different protocols for the use of LLLT for alveolar bone repair can be considered a limitation of this review, in view of the use of very different protocols between one study and another.

Still, another difficulty to be reported, after consulting the PubMed/Medline, Web of Science, Scopus and Cochrane databases with the crossing of the keywords determined by us, was the existence of few articles with a randomized clinical trial, so that the findings regarding the benefits of LLLT in alveolar bone repair are not, in fact, much used in clinical research for this purpose. In this way, the expectation is created that more studies should be carried out in order to seek the standardization of the LLLT protocols and that more clinical experiments should be carried out so that LLLT has its use in the repair of alveolar bone consolidated and used in a way routine in dentistry. In addition, we can describe as future objectives, new studies on other materials or techniques that contribute to improving bone regeneration, such as the use of ozone or other methods of physical stimulation [110–112].

5. Conclusions

This integrative review was designed with the objective of analyzing studies that used low-level laser therapy associated with alveolar bone repair. The use of LLLT is mainly due to the fact that it is considered an auxiliary therapy in the tissue repair process, since studies show its biostimulating effects such as stimulation of collagen synthesis, growth factors and ATP; decreased inflammation, pain, and swelling; and induction of angiogenesis among other factors that help in the process of tissue repair. We also observed that these factors depend on the laser application protocol, with the GaAlAs (gallium–aluminum–arsenide)-type laser with a wavelength of 830 nm being the most prevalent, and when comparing applications of different energy densities, higher dosages proved to be more efficient.

However, there is difficulty in standardizing the application protocols due to the diversity of equipment and their forms of use after tooth extraction. Future studies that evaluate other complementary therapies and that aim to improve bone formation, such as ozone therapy and physical stimulation, should be carried out to contribute to clinical practice in dentistry and other areas of health.

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