

Review Paper: Laser and Platelet-rich Fibrin: A Novel Approach for Tissue Healing in Dentistry - an Updated Review



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ABSTRACT



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Platelet-Rich Fibrin (PRF) is an autologous biomaterial that is increasingly used in regenerative dentistry due to its enrichment with growth factors and cytokines, which aid in tissue healing and regeneration. Its advantages over previous platelet concentrates, such as PRP, include its solid form, easier handling, and sustained release of bioactive molecules. Low-Level Laser Therapy (LLLT), which has biomodulatory effects, is also widely used in dentistry to enhance healing and reduce inflammation. While both PRF and LLLT have been separately explored for their regenerative effects, limited research has investigated their combined use across various dental specialties. This study aims to review the synergistic effects of PRF and LLLT, focusing on their potential for improving clinical outcomes in areas like bone regeneration, gingival depigmentation, and pulp capping. A review of experimental studies conducted between 2023 and February 2025 was carried out, using the PICO framework to ensure methodological precision. The results suggest that combining PRF and LLLT may lead to enhanced regenerative outcomes, such as improved bone formation, better sensory neural recovery, and more effective soft tissue healing compared to the use of each treatment alone. Despite promising findings, some studies showed inconsistencies, emphasizing the need for further research to better understand the combined effects and optimize treatment protocols. The study concludes that combining PRF and LLLT holds potential for improving clinical outcomes in various dental treatments, but more well-controlled trials are needed to confirm their synergistic efficacy and establish standardized guidelines for their application.

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1. Introduction

With the advancement of the Autologous Platelet Concentration method, PRF has been introduced as a novel therapeutic approach. Platelet-rich fibrin (PRF) is an autologous biomaterial prepared by centrifuging the patient's blood. It is enriched with growth factors, cytokines, and a fibrin network that acts as a natural scaffold. This structure not only retains bioactive molecules but also promotes healing at the surgical site (1-3). Compared to the previous generation (PRP), PRF offers several advantages, including easier handling due to its solid nature, long-term effects resulting from the sustained and gradual release of growth factors and cytokines, and the presence of leukocytes (3-5).

Numerous studies have demonstrated that PRF significantly enhances bone and soft tissue regeneration while also contributing to pain reduction following surgical procedures (6). The use of Low-Level Laser Therapy (LLLT) as a non-invasive approach has become increasingly common in various dental treatments (7). Additionally, its biomodulatory effects regulate the activity of healing elements at the treatment site (8). Nowadays, platelet-rich fibrin (PRF) and laser-assisted therapies are widely utilized in various fields of regenerative dentistry, including endodontics, oral surgery, and periodontics (9-12).

Despite numerous studies investigating and comparing the efficacy of these two methods (10, 11), limited research has reviewed their synergistic effects across various fields of dentistry. Furthermore, continuous advancements in PRF preparation protocols, as well as innovations in laser technologies with varying wavelengths and dosimetry parameters, emphasize the need for a comprehensive and up-to-date evaluation of their combined clinical applications. As both PRF and LLLT gain traction in modern regenerative dentistry, their integration into treatment protocols for periodontal regeneration, implantology, oral surgery, and endodontics warrants further investigation (13).

Regarding the importance of this issue, this study aims to evaluate the probable synergistic effects of PRF and LLLT on favourable clinical outcomes across different dental specialties. Additionally, it provides a concise, up-to-date, and quick overview of the latest research in this field.

2. Materials and Methods

To ensure methodological standardization, we tried to select and evaluate available research efficiently while maintaining scientific accuracy. In

this study, a structured PICO (Population, Intervention, Comparison, and Outcome) framework was used to clearly define the research question and guide the systematic review process.

The **Population (P)** includes individuals seeking regenerative therapy for dental applications, encompassing patients undergoing periodontal treatment, implant placement, oral surgery, and endodontic procedures.

The **Intervention (I)** in this study is the combined application of Low-Level Laser Therapy LLLT and PRF. LLLT is recognized for its biomodulatory effects, accelerating tissue repair and reducing inflammation, while PRF serves as an autologous biomaterial rich in growth factors that support wound healing and tissue regeneration.

The **Comparison (C)** involves evaluating the efficacy of PRF alone or LLLT alone. By comparing the combined approach to single-modality treatments, this study aims to determine whether the synergistic use of PRF and LLLT provides superior regenerative outcomes. This comparison is crucial for identifying whether their integration results in additional therapeutic advantages or merely replicates the effects of their independent application.

The **Outcome (O)** focuses on assessing the higher efficacy of the combined approach in terms of healing, recovery time, hard tissue formation, and depigmentation. Improved wound healing, faster recovery, enhanced bone regeneration, and effective management of oral pigmentation are key parameters that will be evaluated to determine the clinical significance of combining PRF and LLLT.

This study had the following focused question: Does the use of PRF and LLLT demonstrate a favourable synergistic effect in dentistry?

This study includes experimental studies that strictly adhere to the PICO framework, ensuring a systematic and relevant evaluation of the synergistic effects of PRF and LLLT in dentistry. The inclusion of these investigations enhances the reliability of findings by providing measurable clinical outcomes. However, some exclusion criteria were established to maintain methodological precision. Non-English studies were excluded to ensure accessibility and consistency in data interpretation, and non-experimental studies, such as case reports, reviews, and observational studies, were omitted to prioritize high-quality evidence. Additionally, studies in which the control group did not receive either LLLT or PRF as an intervention were excluded, as this would limit the ability to draw direct comparisons between their individual and

combined effects.

To conduct an electronic search that is specific and also covers PICO, this study followed the search strategy guidelines of the PRESS checklist (14). A comprehensive search from 2023 to February 2025 was conducted in PubMed using the following search strategy. Subsequently, a manual search was performed in Web of Science. Additionally, citation tracking was employed.

PubMed search syntax: ("platelet rich fibrin"[Title/Abstract] OR "PRF"[Title/Abstract] OR "autogenous platelet concentrates"[All Fields]) AND ("laser"[Title/Abstract] OR "photobiomodulation"[Title/Abstract]) AND 2023/01/01:3000/12/31[Date - Publication]

3. Results

As a result of the electronic, manual, and citation searches, a total of 67 articles were identified. After removing duplicates using Endnote software, 18 articles were deleted. A further review of 49 articles

based on their abstract and title resulted in the inclusion of seven articles that met the PICO criteria for this study. The remaining articles were excluded due to the reasons such as their incompatibility with the aim of study, study design and the lack of evaluation of the synergistic effects of these methods and only providing comparisons between two methods in their studies. Among the seven studies that met the inclusion criteria, one article which was identified through the citation search excluded due to its publication date (15). Ultimately, six articles were selected for full-text review (16-21) (Figure 1).

Among the included studies, there were four human studies (16-18, 20) and two laboratory studies (19, 21). The synergistic effect of PRF and LLLT was investigated in four studies on hard tissue regeneration (16, 17, 19, 21), one study on neurosensory recovery (18), and in one study on gingival depigmentation and wound healing (20) (Table 1).

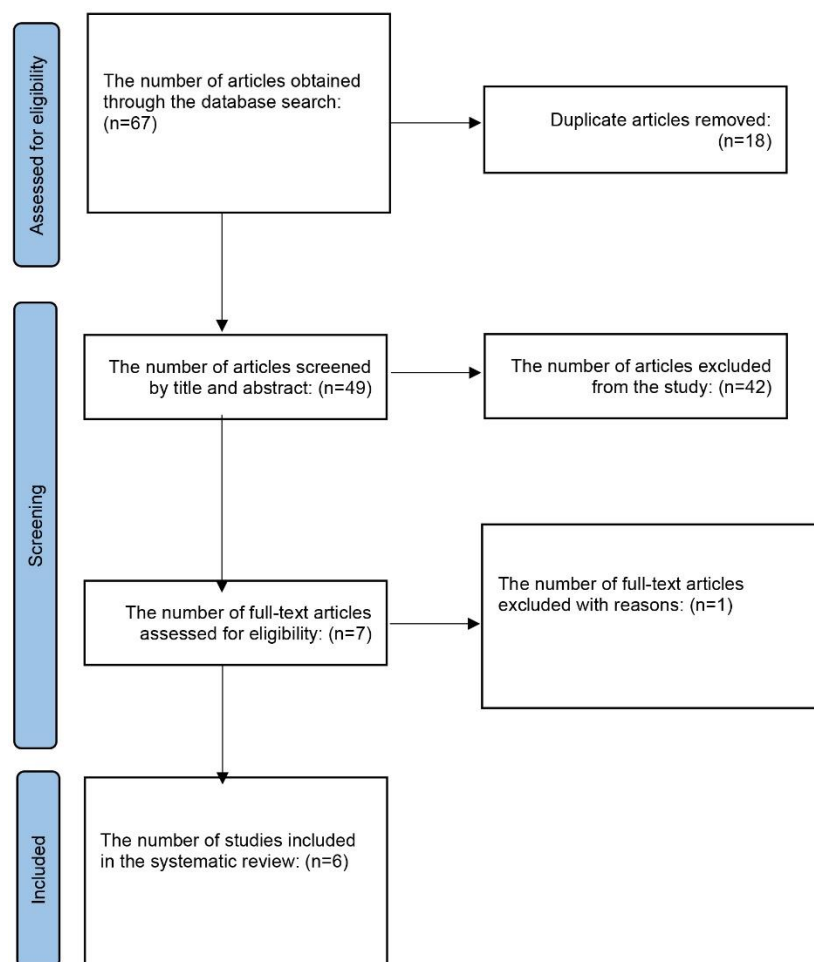


Figure 1. PRISMA Flow Diagram of Study Selection

Table 1. The characteristics of included study

Author (Year)	Type of Study	Sample Size	Subject of Assessment	Parameters Measured	Follow-ups	Centrifugation
Agrawal A (2024)	Human Study (clinical and Radiological assessment)	120	Formation of dentin bridge following direct pulp capping	- clinical examinations (cold, heat, and electric pulp tests) - radiographic assessment of dentin bridge thickness	7 (days) 1, 6, 12 (months)	Choukroun's technique
Akkaya S (2023)	Human Study (clinical assessment)	40(socket)	- Gingival blood perfusion - bone healing	- Gingival blood perfusion - Fractal dimension - visual analog scale (VAS) - 2-point discrimination, directional discrimination, pain discrimination, and thermal discrimination tests	0, 1, 3, 7, 30 (days)	-
Behnia P (2024)	Human Study (clinical assessment)	40 quadrant	- general sensitivity - neurosensory recovery		1, 3, 7, 14, 21, 28 (days) 2 (months)	-
Chou LH (2025)	Animal Study (Histological assessment using culture medium)	Not Applicable	- Tissue engineering in bone repair	cell viability, migration, and calcium deposition	1, 3, 7, 14 (days)	Not Reported (NR)
Ibrahim SSA (2024)	Human Study (clinical and histological assessment)	10 patient (20 site)	- Wound healing - Gingival Pigmentation - patient satisfaction	- Wound Healing Score (WHS), Histological assessment - Dummet oral pigmentation index (DOPI), - patient satisfaction score, - bone nodule formation, expression of bone morphogenetic proteins (BMP)	1 (week), 1, 3 (months)	700 rpm, 3 min
Ramírez DG (2024)	In Vitro (Histological assessment using culture medium)	Not Applicable	- Osteogenic differentiation		1, 3 (weeks)	3200 rpm, 12 min

4. Discussion

Recent studies have explored the combined use of PRF and LLLT in various dental applications, aiming to optimize regenerative treatments. Both therapies have proven regenerative properties: PRF, derived from the patient's blood, is rich in growth factors that promote tissue healing, while LLLT uses specific wavelengths of light to enhance cellular functions like proliferation and migration, alongside reducing inflammation. The combination of these two modalities is being investigated to determine if their synergistic effects can lead to more effective tissue repair and regeneration in areas like bone regeneration, pulp capping, neural healing, gingival depigmentation, and osteogenic differentiation.

However, the results of studies investigating the combination of PRF and LLLT have been

inconsistent. While some studies suggest that their combined use improves tissue regeneration, others report conflicting results, which may be attributed to variations in experimental protocols, patient factors, and the specific conditions treated. Disparities in PRF preparation, laser parameters, and treatment duration could also contribute to these discrepancies. These inconsistencies highlight the need for more standardized methodologies and further research to better understand the mechanisms behind their combined effects and establish optimal protocols for clinical practice.

In the most recent study published up to the time of writing this article, Chou et al (19). investigated the efficacy of combination of PRF and LLLT on bone regeneration, specifically focusing on preosteoblasts, which are key cells involved in bone formation. The study found that PRF alone had a beneficial effect on bone regeneration, promoting

cellular processes such as migration and proliferation, which are essential for tissue repair and regeneration. However, when PRF was combined with LLLT, the effects were significantly enhanced. The combination treatment not only improved cell migration and proliferation but also contributed to increased calcium deposition, a critical factor for bone mineralization and strength. This dual approach led to much more substantial bone regeneration outcomes compared to PRF alone. Furthermore, the study demonstrated that the regenerative effects were dose-dependent, with a notable increase in bone regeneration as the concentration of PRF rose from 50% to 100%. These findings suggest that the synergistic use of PRF and LLLT could offer an optimized strategy for enhancing bone healing, with potential applications in a range of dental and orthopedic regenerative therapies. However, the dose-dependent nature of the effects raises the question of whether such a protocol would be feasible and effective in clinical settings, where the concentration of PRF may vary between patients.

In a study published in 2024 by Agrawal A et al. (16), evaluated the impact of LLLT and PRF on direct pulp capping outcomes in patients with minor pulp exposure. Patients were divided into two groups based on whether they received laser therapy, and each group was further subdivided into three treatment subgroups: MTA (Mineral Trioxide Aggregate) alone, MTA + PRF, and calcium hydroxide. The results showed that the subgroup receiving laser therapy, PRF, and MTA achieved a 100% success rate in dentin bridge formation, while the subgroup treated with laser and MTA but without PRF demonstrated a slightly lower success rate of 95%, suggesting a potential additional benefit of PRF in promoting dentin regeneration. However, the study did not conduct statistical significance testing among subgroups, which raises concerns about possible reporting bias and limits the strength of its conclusions. Despite this limitation, the findings highlight a statistically significant advantage of laser-treated groups over non-laser-treated groups, reinforcing the potential role of LLLT and PRF in improving pulp capping outcomes. Further well-controlled studies with rigorous statistical analysis are needed to validate these findings and establish standardized protocols

for optimizing pulp regeneration therapies. However, the lack of statistical testing between subgroups means that this result could be due to random variation.

In 2024, Behnia et al. (18) conducted a study to evaluate the effect of combining PBM with PRF on sensory neural healing following mental nerve injury. This split-mouth study applied PRF alone on one side as the control and PRF combined with LLLT on the other side. Sensory recovery was assessed using the brush test and two-point discrimination test, which measure tactile perception and nerve function. The results demonstrated that the combination of PRF and LLLT significantly enhanced sensory neural recovery compared to PRF alone, suggesting that photobiomodulation may accelerate nerve fiber repair, increase vascularization, and stimulate cellular activity. These findings highlight the potential of integrating biological scaffolds like PRF with light-based therapies for nerve regeneration, particularly in dental and maxillofacial applications. However, further large-scale clinical studies with extended follow-ups are necessary to validate these findings and optimize treatment protocols. However, the study's small sample size and lack of long-term follow-up raise questions about the durability and sustainability of these positive outcomes. Larger, multi-center studies with longer follow-up periods are needed to fully validate the clinical relevance of combining PRF with LLLT for nerve regeneration.

In 2024, Ibrahim et al. (20) conducted a split-mouth study on 10 patients with gingival hyperpigmentation to evaluate the combined effect of PRF and LLLT on gingival depigmentation. All participants initially underwent LLLT, and half of the arch sites were randomly assigned to receive additional PRF treatment. The results showed that while LLLT alone significantly reduced gingival pigmentation, the addition of PRF did not lead to a statistically significant enhancement in depigmentation. However, the combined approach demonstrated several other benefits, including increased epithelial thickness, improved wound healing, enhanced vascularization, and reduced inflammatory cell infiltration. These findings suggest that while PRF may not directly impact pigmentation reduction, it contributes to soft tissue

healing and regeneration, making it a valuable adjunct in periodontal therapies. Further studies with larger sample sizes and longer follow-up periods are necessary to confirm these effects and explore the broader clinical implications of combining PRF with LLLT in aesthetic and regenerative dentistry. It should be noted, however, that these results may vary depending on the specific clinical conditions of patients and the treatment protocols used.

Ramires et al. (21) conducted a study to evaluate the osteogenic differentiation potential of combining LLLT and PRF by assessing bone nodule formation and the gene expression levels of bone morphogenetic proteins BMP2 and BMP4. The study was performed on stem cells isolated from the apical papilla, a critical source of multipotent cells involved in dental and craniofacial bone regeneration. The findings revealed that while both LLLT and PRF individually enhanced osteogenic differentiation by promoting bone nodule formation and increasing the expression of BMP2 and BMP4, their combination produced a synergistic effect, amplifying these regenerative processes beyond the effects of either treatment alone. This suggests that the concurrent application of LLLT and PRF may offer a more effective approach to stimulating bone formation and accelerating tissue repair in dental and orthopedic applications. While these results are promising, there is still a need to investigate the exact mechanisms by which LLLT and PRF interact at the cellular level. Further research is required to understand the molecular pathways involved in this synergistic effect and whether these findings can be translated to clinical practice.

In another study conducted in 2023, Akkaya et al. (17) investigated the effects of PRF and LLLT on bone regeneration and gingival perfusion to assess their potential in regenerative dentistry. The findings indicated that neither PRF nor LLLT alone had a statistically significant impact on gingival perfusion at the 30-day follow-up, suggesting that these methods may not independently influence blood flow dynamics within gingival tissues in the short term. Similarly, when applied separately, neither PRF nor LLLT significantly enhanced bone regeneration, highlighting their potential limitations as standalone treatments. However, when both methods were combined, a significant increase in

bone formation was observed, suggesting a synergistic effect that enhanced osteogenesis beyond what either intervention could achieve alone. These results underscore the importance of integrating multiple regenerative approaches for improved clinical outcomes in bone healing and tissue repair, emphasizing the need for further research to elucidate the mechanisms underlying their combined effects and optimize their application in dentistry. These results contrast with other studies that observed more substantial effects, indicating that the interaction between PRF and LLLT may depend on the specific experimental conditions, such as the type of tissue treated or the timing of application.

5. Conclusion

This study, through a review of the most recent literature, concludes that combining PRF and LLLT may have a synergistic effect in areas such as hard tissue regeneration, gingival depigmentation, and direct pulp capping. The combination of PRF's growth factor-rich matrix and LLLT's ability to promote cellular proliferation and reduce inflammation shows promise in enhancing healing and regenerative outcomes. However, the existing body of research is not without discrepancies, and the results of the included studies vary depending on treatment protocols, sample sizes, and specific clinical contexts. Therefore, further well-designed and large-scale studies are essential to confirm the clinical benefits of this combination and to determine the most effective treatment protocols. Given the novelty of laser applications in dentistry and the limited number of studies investigating the synergistic effects of these two methods, this study highlights the need for further research to confirm their combined efficacy. If proven effective, this combination could be a valuable therapeutic approach in various dental fields, improving treatment outcomes and expanding options for regenerative dental therapies.

Ethical Considerations

Compliance with ethical guidelines

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Authors' Contributions

Pedram Hajibagheri: Conceptualization, Investigation, Methodology, Project administration, Writing-Original draft, Writing-review & editing.

Conflict of Interests

None

Availability of data and material

Not applicable

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