Tikrit Journal for Dental Sciences 13(2) (2025) 513-523
https://doi.org/10.25130/tjds.13.2.22

Tikrit Journal
for
Dental Sciences

https://tjds.tu.edu.iq
Print ISSN:2073-1213
Online ISSN:3105-9384

Role of Injectable Platelet-Rich Fibrin in Periodontal Wound Healing

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Keywords:
i-PRF, Platelet-rich fibrin, Regenerative periodontal therapy, Growth factors, Anti-inflammatory.

Article Info.:

Article History:
Received: 24/12/2024
Received in revised form: 28/1/2025.
Accepted: 16/2/2025
Final Proofreading: 16/2/2025
Available Online: 1/12/2025

Citation: Ali B Gh, Hasan TA. Role of Injectable Platelet-Rich Fibrin in Periodontal Wound Healing. Tikrit Journal for Dental Sciences 2025; 13(2):513-523.
https://doi.org/10.25130/tjds.13.2.22

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Abstract

Injectable Platelet-Rich Fibrin has emerged as a promising therapy for regenerative periodontal treatment. This liquid formulation offers several advantages over traditional Platelet-rich fibrin and platelet-rich plasma. It exhibits a higher concentration of growth factors, including platelet-derived growth factor , insulin-like growth factor, and transforming growth factor , which are crucial for tissue regeneration and bone augmentation. Current studies have demonstrated Injectable Platelet-Rich Fibrin's regenerative potential in encouraging fibroblast movement enhancing collagen production, growth and specialization of bone-forming cells. In Addition, to its ability to reduce inflammation by lowering inflammatory substances and boosting the production of anti-inflammatory agents. Its ability to fight bacteria is linked to blood cells and antimicrobial proteins, contributing to reducing bacterial load and preventing infections. Clinical studies have reported positive outcomes regarding surgical and non-surgical periodontal treatment, tissue regeneration, reduction in pocket depth, and improvement in clinical parameters. However, further research is needed to standardize protocols, determine optimal concentrations, and assess long-term outcomes. Despite these considerations, the current evidence suggests that Injectable Platelet-Rich Fibrin holds great potential and may become a widely used therapy in regenerative periodontal procedures.

Introduction:

Periodontal disease is a common and most prevalent inflammatory condition of multifactorial causes. Periodontitis is linked to many systemic illnesses such as diabetes, cardiovascular, obesity, and others (1, 2). Therefore, treating periodontal disease as early as possible is of great importance to restore the lost attached tissues. Various strategies have been proposed, including barrier membranes, the implementation of bone graft materials, and many biologic agents as blood concentrates. The first generation of platelet concentrate was the platelet-rich plasma (PRP). Since PRP utilized anticoagulant, this interfere with the angiogenic and regenerative ability of platelets ends with imped wound healing. And this gave rise to the introduction of a second generation of blood concentrates termed platelet-rich fibrin (PRF) (3). Platelet concentrates are categorized into types of PRF each possessing features and uses (4). The remarkable fibrin gel polymerization of PRF sets it apart from concentrates making it ideal, for orthopedic and sports medicine applications whether for topical or infiltrative purposes. The versatility of PRF in different medical fields highlights its potential as a valuable therapeutic agent for tissue repair and regeneration. The types of PRF, including Choukroun's PRF and L-PRF as shown in Figure(1) , show significant progress in platelet collection technology accompanying potential uses in current medicine and dentistry(5). The unique organic features of PRF, its dispassionate belongings on tissue curative, and indifferent healing fields underscore the importance of PRF as a valuable biomaterial (5, 6). While debates and discussions related to the standardization and productiveness, the potential of PRF in regenerative cures cannot be missed. Years ago, platelet concentrates were introduced for the treatment of intrabody defects (7).PRF plays a role, in periodontal treatment and dental surgeries. It is considered an option in invasive dental care to reduce inflammation and facilitate tissue healing as it is proven to be effective in minimizing tooth extraction complications, such as alveolar osteomyelitis. The distinctive three dimensional fibrin structure of PRF enhances its practicality (8). It comprises a dense interconnected network of fibrin providing a scaffold like framework.

PRF is a beneficial treatment for several types of periodontal abnormalities in the field of periodontal therapy as an adjunct to nonsurgical periodontal therapy, especially in the reduction of inflammation within the periodontal pocket and boosting some biomarkers as periostin level (9). Dental surgeons examine the effect of PRF on reducing the occurrence of alveolar osteitis following extraction of 3ed molars (10). Additionally applying PRF directly into the socket can be a successful method to notably lessen postoperative pain,jaw muscle stiffness, and swelling compared to a control group following surgery to remove mandibular third molars (11). The classification of PRF shown in Figure (1) takes into account factors like centrifugation speed and duration as the type of test tube used, which can impact the composition and efficacy of PRF preparations (12).Original PRF lack the fluidity with more dense fibrin constituents ,this give rise to a study looked into injectable-PRF (i-PRF), a liquid PRF formulation that doesn't require anticoagulants. While PRF has shown promising results in tissue healing and regeneration, there is a need for further research to establish standardized protocols and guidelines for its clinical use (3). The history of PRF dates back to the early 2000s when it was first brought in as an everyday biomaterial for fabric regeneration. by time, researchers have invented various formulations to enhance its clinical applicability, till the introduction of i-PRF that offers a more convenient and adaptable choice for clinicians compared to traditional PRF(4). There are indications that suggest the effectiveness of i-PRF, in therapy and dental surgery (5). In comparison to (PRF) and its liquid formulation, i-PRF has demonstrated promising potential in promoting tissue regeneration and enhancing cell proliferation. Inversely their potential applications in dentistry areas such as implantology and endodontics have not been thoroughly explored. Further exploration is needed to uncover how i-PRF contributes to tissue regeneration and promotes cell proliferation. Understanding the growth factors and signaling pathways involved is essential, for advancing our knowledge in this area (16). This knowledge will give researchers the ability to adjust the formulations potentially leading to the development of targeted treatments.

Physiologic characteristics of i-PRF aid in clinical dentistry

The preparation of i-PRF involves collecting the patient's blood without any anticoagulants and subjecting it to specific centrifugation protocols. The centrifugation speed and duration are critical factors that influence the concentration of platelets and the formation of the fibrin matrix. For instance, one method involves centrifuging the blood at 700 rpm (60 g) for 3 minutes in plastic tubes, resulting in a liquid PRF suitable for injection (17).

Another approach uses horizontal centrifugation at 200 g for 8 minutes, producing a higher concentration of leukocytes and platelets(18). After centrifugation, i-PRF remains in a liquid state for a short period, typically around 15 to 20 minutes, before transitioning into a fibrin clot. This allows for immediate application in clinical settings, providing a more efficient and precise approach compared to traditional PRF preparations (19). It has presented promising prospects in an assortment of healing and dental processes, such as fascial reinvigoration and treatment of miscellaneous dermatologic issues (22-23). Most of the platelets, in PRP, come from blood, making up ninety-five percent of all platelets. These platelets play a role in regulating cell types like osteoblasts connective tissue cells, epithelial cells and periodontal ligament cells. While PRP is essential, for providing growth factors during stages of wound healing its primary function is to eliminate white blood cells from blood concentrates(4). Compared to (PRP) and (PRF), i-PRF has shown a remarkable increase in platelet count, surpassing PRP's increase. Additionally, i-PRF retains approximately 87% of its platelet wealth from whole blood, highlighting its efficacy in platelet concentration (25). The implications of i-PRF's superior platelet count and antimicrobial activity are substantial, highlighting its potential for enhancing tissue healing and combating infections. This makes i-PRF a valuable tool in various medical and dental procedures, offering improved therapeutic outcomes (26). Figure(2). Platelets are well known for their role in clotting. They also contain growth factors such as Platelet Derived Growth Factor (PDGF) , Transforming Growth Factor -beta (TGF β) and Vascular Endothelial Growth Factor (VEGF). These growth factors play a role, in healing wounds and tissue regeneration, reducing inflammation and inducing angiogenesis, eventually leading to improved clinical outcomes. Higher amounts of growth factors were released by i-PRF, which also increased fibroblast migration and collagenI TGF-β, and PDGF expression (5). Higher leukocyte content has been associated with enhanced antimicrobial properties and improved healing responses. The fibrin matrix formed during the coagulation of i-PRF serves as a scaffold that supports cell migration and proliferation, facilitating tissue regeneration (27,28). The studies have also studied the impacts of PRF and i-PRF, on the growth of gingival fibroblasts, showing that both agents enhance cell growth and that i-PRF appears more effective (29,30). In addition, the researchers investigated using two fractions derived from i-PRF for bone repair , red (contain RBCs ,that increase vascularization and can be created by blood centrifugation under low speed and short duration) and yellow i-PRF(contain few or no RBCs, and obtained by blood centrifugation at high speed and for long period), . Extracts from red i-PRF significantly affected cell migration and proliferation, whereas those from yellow i-PRF promoted osteoblast differentiation (31,32).

Role of i-PRF in Periodontal wound healing/Mechanism of Action:

Enhanced Tissue Regeneration:

The growth factors in i-PRF promote the proliferation and differentiation of periodontal ligament cells and osteoblasts, leading to improved regeneration of periodontal tissues (33).A study evaluated the growth factor release (VEGF, TGF-β1, and EGF) and platelet allocation pattern in three PRF forms (PRF, A-PRF, and A-PRF+) using variable centrifugation periods and relative centrifugation forces (RCF). The release was examined over ten days. These results addressed that growth factors release may improve leukocytes and platelets within the PRF matrix model by lowering RCF per the previously written LSCC (Low-Speed Centrifugation Concept) (34). Platelet-Derived-4 (PDEFG/PF-4), an anti-angiogenic factor found in (i-PRF), plays a significant role in regulating excessive blood vessel formation (angiogenesis). By doing so, it helps manage periodontal inflammation and disease progression.(35). Moreover the interplay between PDEFG/PF-4 and other growth factors like PDGF , IGF , and TGF aids in promoting fibroblast migration which essential for wound healing, collagen synthesis which is important for tissue strength and structure, and tissue remodeling which is critical for regeneration (36). Concentrated PRF (C-PRF), which contains a 10-fold increase in platelets and white blood cells (especially leukocytes), boosts the immune response and has anti-inflammatory properties, which are beneficial for managing periodontal diseases. It can aid in regenerating diseased gingival tissues by delivering a source of growth factors and bioactive substances. This contributes to enhancing the health and appearance of gingival tissues. Patients, with thin gingival phenotypes can benefit from using i-PRF to increase thickness and widen keratinized tissue areas (37,38). Platelet concentrates have displayed potential in assisting with root coverage procedures for treating gingival recession (39 ,40). Researchers have explored using them as a treatment to enhance the results of gold standard procedures (CTG+CAF). In a study involving grafts the application of i-PRF was observed to facilitate the healing process and improve the outcomes of root coverage. Incorporating i-PRF into the grafting process led to increased vascularization, decreased discomfort, and enhanced tissue integration (41). Likewise in another study utilizing tissue grafts, the presence of i-PRF was linked to results, in root coverage. Integrating i-PRF at the site helped accelerate wound healing boost tissue regeneration and enhance both stability and aesthetic outcomes ,further can play a role in improving root coverage outcomes (42). Miron et al., investigated the impact of i-PRF on fibroblast activity, which is crucial for tissue regeneration. They found that i-PRF significantly enhanced fibroblast migration and proliferation compared to PRP (43). Furthermore, i-PRF induced significantly higher levels of TGF-β, PDGF, and collagen type I expression compared to PRP, highlighting its superior ability to promote the production of key components involved in tissue repair. Using i-PRF for bone regeneration has demonstrated outcomes especially when utilized with bone grafting materials and in supporting bone regeneration as indicated by a variety of studies conducted in vitro and in vivo settings. Studies conducted in labs have revealed that i-PRF possesses properties when compared to other platelet concentrates such as PRP, A-PRF, L-PRF and freeze dried homologous PRP. These findings demonstrate proliferation and differentiation of osteoblasts along with increased production of nodules on surfaces like tissue culture plastic or titanium discs. Moreover the integration of i-PRF, into bone grafting materials has proven effective in enhancing human osteoblast characteristics and promoting increased bone formation (44).

Accelerating Periodontal Wound Healing

i-PRF facilitates vascularization, improving blood supply to the affected area and aid in the generation of new connective tissue in various dental procedures, particularly in periodontal surgery .It will accelerate wound healing and contribute , both for the recovery of gingival tissues and improved patient comfort and quality of life (45,46). Torumtay Cin et al. (47). discovered that incorporating i-PRF with scaling and root planing (SRP) markedly enhanced the effectiveness of treatment resulting in decreases in pocket depth.and gains in clinical attachment level (CAL) compared to SRP alone. This enhanced healing was associated with increased levels of VEGF and IL-10, an anti-inflammatory cytokine, suggesting i-PRF's role in creating a more favorable healing environment. Several studies have highlighted i-PRF's positive effects in various surgical procedures. Sousa et al. (48) showed that A-PRF, an advanced form of PRF, significantly decreased postoperative pain and discomfort following the harvesting of free gingival graft (FGG). Similarly, Albatal et al.(49) found that i-PRF significantly accelerated healing and increased tissue thickness in palatal wounds after subepithelial connective tissue graft (SCTG) harvesting. Moreover, Bahar et al. (50) reported that i-PRF significantly improved wound healing and reduced complications following gingivectomy and gingivoplasty procedures. In a comparative study, Kiziltoprak and Uslu (51) found that both i-PRF and autologous fibrin glue (AFG) accelerated wound healing and reduced morbidity, with AFG demonstrating slightly superior properties. However, i-PRF remains a valuable alternative, especially considering its ease of preparation and cost-effectiveness.

Reduction of Inflammation:

The anti-inflammatory properties of i-PRF contribute to decreased postoperative discomfort and swelling, enhancing patient comfort and quality of life (52).

The wound healing benefits of i-PRF are not solely attributed to its growth factor content. i-PRF's inherent anti-inflammatory properties, due to the presence of anti-inflammatory cytokines(IL-4 and IL-10) and leukocytes, help modulate the inflammatory response and create a more favorable environment for healing. Additionally, i-PRF possesses antibacterial properties due to the presence of leukocytes and antimicrobial peptides, further aiding in wound healing by reducing bacterial load and preventing infections and thus i-PRF has shown effectiveness in expediting the recovery of wounds in different periodontal treatments (53).

Improved Clinical Outcomes:

Clinical studies have demonstrated that the application of i-PRF in periodontal therapy leads to significant improvements in clinical parameters, such as reduced pocket depth and increased attachment levels. In addition to increased healing of intrabony defects after treatment with advanced forms of PRF, demonstrating significant clinical improvements (54). Animal studies have further corroborated i-PRF's positive impact on bone formation. For instance, research has shown that i-PRF promotes maxillary bone regeneration during sinus augmentation in rabbit models (55). Another study found that gelatin nanoparticles combined with i-PRF enhanced blood clot formation and osteogenesis at an early stage, generating favorable cortical bone at the alveolar ridge crest 8 weeks post-implantation in a beagle dog extraction site, suggesting its potential as a candidate treatment for ridge preservation. Research has also explored the synergistic effects of combining i-PRF with other biomaterials. For instance, studies have demonstrated that combining i-PRF with sticky bone significantly increases solidification rate and resistance to degradation compared to PRF fragments or i-PRF alone, suggesting improved stability and longevity of the bone graft (56). This combination also exhibited superior mechanical properties and enhanced osteoblast migration and differentiation, further supporting its potential in bone regeneration. Clinical trials have revealed outcomes from incorporating i-PRF with bone graft materials, for procedures. According to a research study by Chenchev et al. (57) the use of both bone graft material and i-PRF, in maxillary ridge augmentation resulted in bone formation and successful implant placement within four months post surgery. Similarly combining i-PRF with PRF and bone grafts has shown results in improving bone augmentation. Furthermore, i-PRF has been associated with positive outcomes in sinus grafting procedures using a collagen plug and bovine bone graft (58). Comparatively, combining i-PRF with allograft, compared to autogenous block grafting, has been shown to improve outcomes in guided bone regeneration (GBR) with simultaneous implant placement (59). Managing furcation involvement, a complication that arises in cases of periodontal disease poses a significant challenge, during treatment. Various methods have been employed to address this issue, including debridement, surgical interventions like flap surgery and regenerative techniques such as guided tissue regeneration and bone regeneration. Additionally treatments involving platelet concentration, hemisection, root resection and even tooth extraction may be necessary in instances (60). Regenerative periodontal surgery, particularly when using enamel matrix derivative (EMD) either on its own or combined with bone grafts has demonstrated a promising results, in the management of furcation defects (61). Research indicates that combining biomaterials as PRF (61) with bone graft substitutes is an effective strategy for addressing infrabony defects and Grade II furcation defects, enhancing clinical parameters and bone regeneration. However, there is no universally accepted optimal regenerative material for Grade II furcation defects. Few studies have shown that when bone grafts are paired with concentrates, like PRP, PRF and bone grafts with PRF membranes lead to better regeneration in intra bony defects compared to bone grafts alone. Particularly the utilization of PRF alongside hydroxyapatite (HA) and beta tricalcium phosphate (β TCP) has demonstrated improvements in CAL gain, reduction in probing depth (PD), compared to HA and β TCP on their own (8,61,62). In addition a randomized trial was conducted to evaluate the effectiveness of combining i-PRF with a bone graft for treating Grade II furcation defects. The research revealed enhancements in both clinical and radiographic parameters(63). i-PRF may boost the regenerative capabilities of bone grafts, in furcation defects and in both lip and palatal clefts (64). These findings suggest that i- PRF, which is rich in blood cells and growth factors can be effectively utilized for treating defect related mandibular and implant sites (65,66). Additionally, combining the VISTA(Vestibular Incision Subperiosteal Tunnel Access) technique with a collagen membrane and i-PRF has shown effectiveness in addressing isolated gingival recessions falling under Millers Class I and II defects (67). Moreover a split mouth randomized controlled trial comparing the effects of hyaluronic acid and i-PRF injections on patients with gingival phenotypes revealed improvements in gingival thickness and keratinized tissue width , for both treatments (68). A new study investigated the advantages of pairing i-PRF with xenograft, for treating intra osseous defects. The findings revealed an impact on reducing pocket depth and enhancing attachment levels in the group that received both i-PRF and xenograft as opposed to the group that solely received xenograft. This suggests that incorporating i-PRF with xenograft could enhance the healing process, for bone defects (63). Adding i-PRF to SCTG in the treatment of deep gingival recession further improves the reduction of gingival recession and keratinized tissue height at 6 month follow-up (69). It's important to highlight that much of the research on i-PRF has been carried out in laboratory settings or with animal models. Although these studies offer insights, further research involving participants is essential to confirm the results and ensure their relevance in real clinical settings . Clinical trials and studies with subjects are crucial to validate the efficacy and safety of these treatments. By addressing these knowledge gaps, a comprehensive understanding of i-PRF can be attained, especially regarding their applications in regenerative dentistry (70).

Conclusion

i-PRF represents a promising advancement in periodontal therapy, offering enhanced healing of periodontal wounds through its regenerative properties. Recent studies support its efficacy in improving clinical outcomes, making it a valuable adjunct in the management of periodontal defects. It offers advantages over PRF and PRP) due to its levels of growth factors essential for tissue regeneration and bone enhancement. Clinical studies have demonstrated results with i-PRF showing improvements in tissue regeneration reduced pocket depth and enhanced clinical parameters. . . It underscores the increased concentration of growth factors in i-PRF and its ability to support cell migration ,collagen production as well as osteoblast differentiation and proliferation in addition to the anti- inflammatory and antibacterial properties .Additional studies needed for further research to standardize protocols ,evaluate long term effects, understand mechanisms of action, explore broader applications and validate the effectiveness of i-PRF, in real world clinical scenarios.

Author Contributions:
Conceptualization, B.G.A. and T.A.H.; Validation, B.G.A. and T.A.H, B.G.A.; Writing – original manuscript preparation, B.G.A. and T.A.H.; Writing – review and editing, B.G.A. and T.A.H.; Visualization, B.G.A.; Monitoring, T.A.H. All authors read and approved the published version of the manuscript.

Acknowledgments: A big thank to the Department of Periodontics, at Baghdad College of Dentistry for their support and resources.

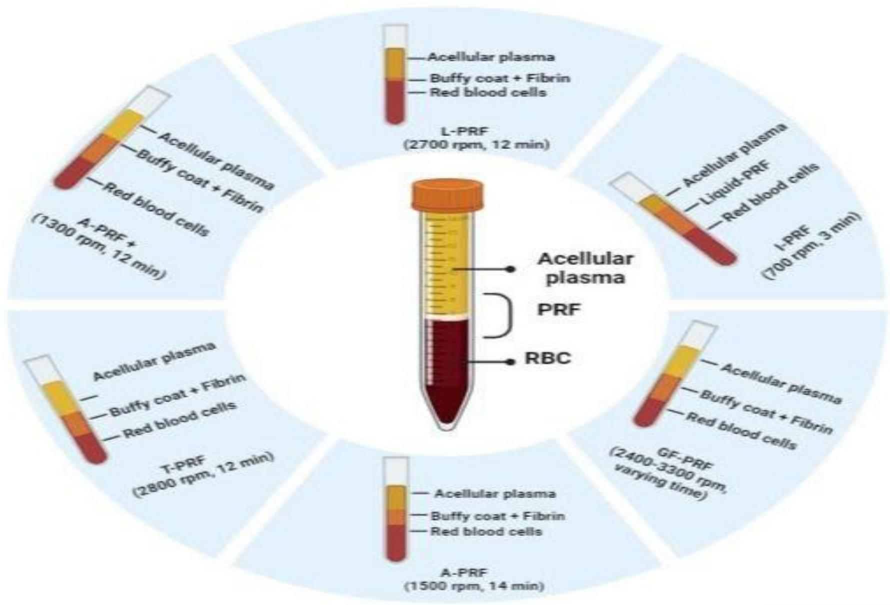

Figure 1: Types of platelet-rich fibrin with protocols for preparation method

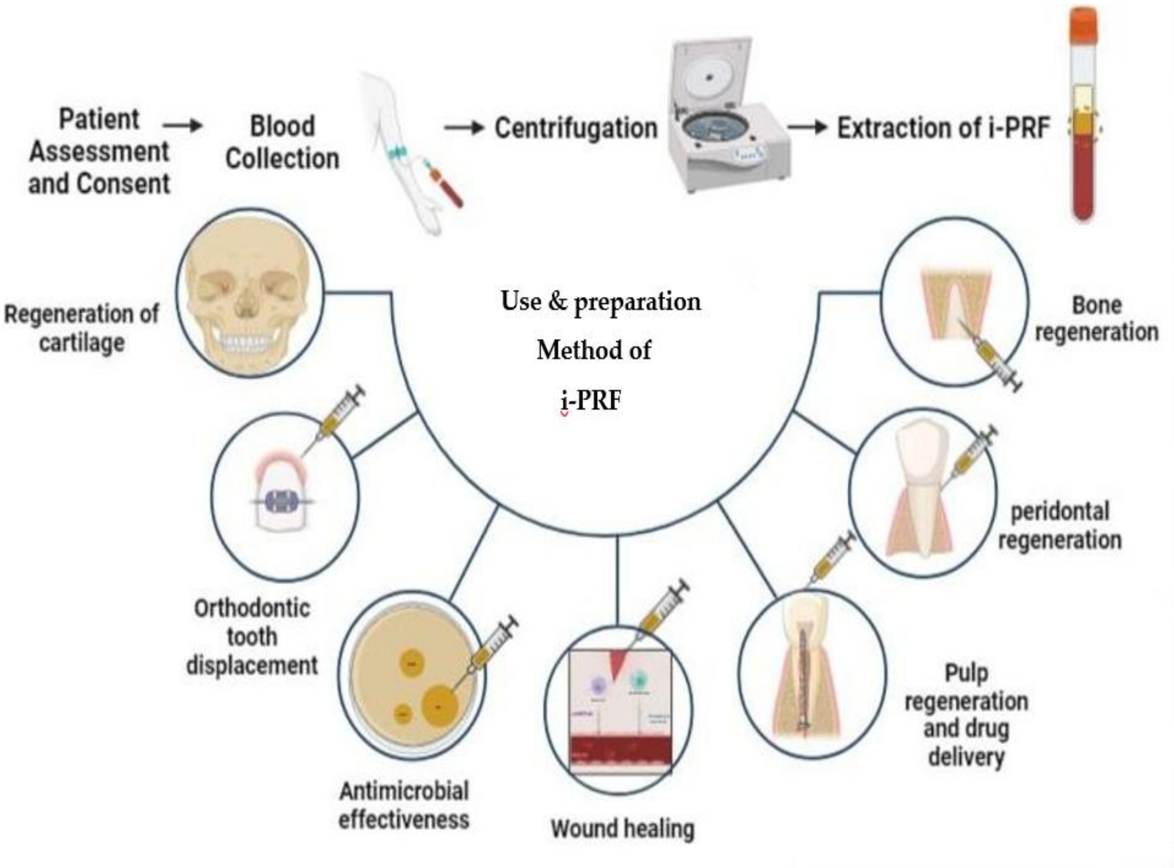

Figure 2: A diagram illustrating the use of i-PRF for the regeneration of soft and hard tissues in the context of oral and maxillofacial structures, including its preparation method

References

1. Ghazi FM, Ahmed MAA. Prevalence of Periodontal Disease Among Undergraduate Students In AL-Qadisiyah Governorate, Iraq: A Cross-Sectional Study. Tikrit J Dent Sci. 2024;12(1):179-87. doi: https://doi.org/10.25130/tjds.12.1.20.
2. Ali OH. The Influence of Fixed Orthodontic Appliances on Periodontal Health Status. Tikrit J Dent Sci. 2019;7(2):83-9. doi:10.25130/tjds.7.2.6.
3. Miron RJ, Fujioka-Kobayashi M, Bishara M, Zhang Y, Hernandez M, Choukroun J. Platelet-rich fibrin and soft tissue wound healing: a systematic review. Tissue Eng Part B Rev. 2017;23(1):83-99. doi: 10.1089/ten.TEB.2016.0233.
4. Choukroun J, Diss A, Simonpieri A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:56-60. DOI: 10.1016/j.tripleo.2005.07.011.
5. Narayanaswamy R, Patro BP, Jeyaraman N, Gangadaran P, Rajendran RL, Nallakumarasamy A, et al. Evolution and Clinical Advances of Platelet-Rich Fibrin in Musculoskeletal Regeneration. Bioengineering. 2023;10(1):58. doi: 10.3390/bioengineering10010058.
6. Shashank B, Bhushan M. Injectable Platelet-Rich Fibrin (PRF): The newest biomaterial and its use in various dermatological conditions in our practice: A case series. J Cosmet Dermatol. 2021;20(5):1421-6. DOI: 10.1111/jocd.13742.
7. Miron RJ, Moraschini V, Fujioka-Kobayashi M, Zhang Y, Kawase T, Cosgarea R, et al. Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis. Clin Oral Investig. 2021;25:2461-78. DOI: 10.1007/s00784-021-03825-8.
8. Al-Rihaymee S, Mahmood MS. Platelet-rich fibrin potential role in periodontal regeneration: A review study. Med J Babylon. 2023;20:1-6. doi:10.4103/MJBL.MJBL_237_22
9. Rihaymee S, Mahmood SM. The efficacy of non-surgical platelet-rich fibrin application on clinical periodontal parameters and periostin level in periodontitis: Clinical trial. J Cell Mol Med. 2023;27:529-37. doi: 10.1111/jcmm.17675.
10. Kareem ASA, Al HAH. Effect of platelet-rich fibrin on alveolar osteitis incidence following surgical removal of impacted mandibular third molars: a comparative study. J Baghdad Coll Dent. 2019;31(4):68-9. Doi:10.26477/jbcd.v31i4.2723.
11. Al-Saadi TS, Al-Quisi AF. The Influence of the Hyaluronic Acid Gel on the Postoperative Sequelae following Surgical Removal of the Impacted Mandibular Third Molar in Comparison with the A-PRF: A Randomized Controlled Trial. Int J Biomater. 2023 Apr 29;2023:1883460. doi: 10.1155/2023/1883460. PMID: 37159615; PMCID: PMC10163971.

12. Choukroun J, Adda F, Schoeffler C, Vervelle A. An opportunity in perio-implantology: the PRF. Implantodontie. 2001;42:55-62.
13. El Bagdadi K, Kubesch A, Yu X, Al-Maawi S, Orlowska A, Dias A, et al. Reduction of relative centrifugal forces increases growth factor release within solid platelet-rich-fibrin (PRF)-based matrices: a proof of concept of LSCC (low speed centrifugation concept). Eur J Trauma Emerg Surg. 2019;45(3):467-79. doi: 10.1007/s00068-017-0785-7.
14. Farshidfar N, Amiri MA, Jafarpour D, Hamedani S, Niknezhad SV, Tayebi L. The feasibility of injectable PRF (i-PRF) for bone tissue engineering and its application in oral and maxillofacial reconstruction: From bench to chairside. Mater Sci Eng C Mater Biol Appl. 2021;128:112557. doi: 10.1016/j.msec.2021.112557.
15. Pakhare VV, Bajaj PP, Bhongade ML, Shilpa BS. Gingival depigmentation by free gingival autograft: a case series. Dent Update. 2017;44:158-62. DOI:10.12968/denu.2017.44.2.158.
16. Dambhare A, Bhongade PV, Dhadse B, Sehdev KK, Ganji K, Thakare Z. A randomized controlled clinical study of autologous platelet-rich fibrin (PRF) in combination with HA and beta-TCP or HA and beta-TCP alone for treatment of furcation defects. J Hard Tissue Biol. 2019;28:185-90. doi:10.2485/jhtb.28.185.
17. Choukroun J, Ghanaati S. Reduction of relative centrifugation force within injectable platelet-rich-fibrin (PRF) concentrates advances patients' own inflammatory cells, platelets and growth factors: the first introduction to the low speed centrifugation concept. Eur J Trauma Emerg Surg. 2018;44:87-95. doi: 10.1007/s00068-017-0767-9.
18. Thanasrisuebwong P, Kiattavorncharoen S, Surarit R, Phruksaniyom C, Ruangsawasdi N. Red and Yellow Injectable Platelet-Rich Fibrin Demonstrated Differential Effects on Periodontal Ligament Stem Cell Proliferation, Migration, and Osteogenic Differentiation. Int J Mol Sci. 2020;21(14):5153. doi: 10.3390/ijms21145153.
19. Danastri AA, Suryono S, Murdiastuti K. The influence between injectable platelet-rich fibrin and platelet-rich plasma towards gingival fibroblast cell proliferation. ODONTO : Dent J. 2021;8(2):25. doi: 10.30659/odj.8.2.25-31.
20. Pullishery F, Hussein Alattas M, Roshdy Abdelrasoul M, Fouad Hassan A, Abdelhamid Ahmed Derbala D, Hashir S. Effectiveness of i-PRF in periodontal regeneration - A systematic review and meta-analysis. Saudi Dent J. 2024 Feb;36(2):214-21. doi: 10.1016/j.sdentj.2023.10.017. Epub 2023 Oct 31. PMID: 38419983; PMCID: PMC10897594.
21. Gollapudi M, Bajaj P, Oza RR. Injectable Platelet-Rich Fibrin - A Revolution in Periodontal Regeneration. Cureus. 2022;14(8):e28647. doi: 10.7759/cureus.28647.
22. Hassan H, Quinlan DJ, Ghanem A. Injectable platelet-rich fibrin for facial rejuvenation: A prospective, single-center study. J Cosmet Dermatol. 2020;19(12):3213-21. DOI: 10.1111/jocd.13692.
23. Varela HA, Souza JC, Nascimento RM, Araújo RF, Vasconcelos RC, Cavalcante RS, et al. Injectable platelet rich fibrin: cell content, morphological, and protein characterization. Clin Oral Investig. 2019;23:1309-18. DOI: 10.1007/s00784-018-2555-2.
24. Farshidfar N, Amiri MA, Jafarpour D, Hamedani S, Niknezhad SV, Tayebi L. The feasibility of injectable PRF (i-PRF) for bone tissue engineering and its application in oral and maxillofacial reconstruction: From bench to chairside. Biomater Adv. 2022 Mar;134:112557. doi: 10.1016/j.msec.2021.112557. Epub 2021 Nov 24. PMID: 35527147; PMCID: PMC9295636.
25. Karde PA, Sethi KS, Mahale SA, Khedkar SU, Patil AG, Joshi CP. Comparative evaluation of platelet count and antimicrobial efficacy of injectable platelet-rich fibrin with other platelet concentrates: An in vitro study. J Indian Soc Periodontol. 2017;21(2):97. DOI: 10.4103/jisp.jisp_201_17.
26. Miron RJ, Chai J, Zhang P, Li Y, Wang Y, Mourão CFDA, et al. A novel method for harvesting concentrated platelet-rich fibrin (C-PRF) with a 10-fold increase in platelet and leukocyte yields. Clin Oral Investig. 2020;24:2819-28. DOI: 10.1007/s00784-019-03147-w.
27. Miron RJ, Fujioka-Kobayashi M, Hernandez M, Kandalam U, Zhang Y, Ghanaati S, et al. Injectable platelet rich fibrin (i-PRF): opportunities in regenerative dentistry? Clin Oral Investig. 2017;21(8):2619-27. doi: 10.1007/s00784-017-2063-9.
28. Kökdere NN, Baykul T, Findik Y. The use of platelet-rich fibrin (PRF) and PRF-mixed particulated autogenous bone graft in the treatment of bone defects: An experimental and histomorphometrical study. Dent Res J (Isfahan). 2015 Sep-Oct;12(5):418-24. doi: 10.4103/1735-3327.166188. PMID: 26604954; PMCID: PMC4630704.
29. Sağsöz A, Kaya FA. Use of platelet-rich fibrin (PRF) in the periodontology: A review. J Med Dent Invest. 2023;4:e230317-e230317. doi:10.5577/jomdi.e230317
30. Wang J, Li W, He X, Li S, Pan H, Yin L. Injectable platelet-rich fibrin positively regulates osteogenic differentiation of stem cells from implant hole via the ERK1/2 pathway. Platelets. 2023;34(1):1-10. doi: 10.1080/09537104.2022.2159020.
31. Thanasrisuebwong P, Kiattavorncharoen S, Surarit R, Phruksaniyom C, Ruangsawasdi N. Red and Yellow Injectable Platelet-Rich Fibrin Demonstrated Differential Effects on Periodontal Ligament Stem Cell Proliferation, Migration, and Osteogenic Differentiation. Int J Mol Sci. 2020;21(14):5153. doi: 10.3390/ijms21145153.
32. Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells. J Oral Implantol. 2014;40:679–89. doi: 10.1563/aaid-joi-D-14-00138.
33. Pullishery F, Hussein Alattas M, Roshdy Abdelrasoul M, Fouad Hassan A, Abdelhamid Ahmed Derbala D, Hashir S. Effectiveness of i-PRF in periodontal regeneration - A systematic review and meta-analysis. Saudi Dent J. 2024 Feb;36(2):214-21. doi: 10.1016/j.sdentj.2023.10.017. Epub 2023 Oct 31. PMID: 38419983; PMCID: PMC10897594.
34. Alsabri, G. A., van der Horst, F., Alkaabi, S. A., Alavi, S. A., Forouzanfar, T., & Helder, M. N. Evaluating growth-factor release in leukocyte- and platelet-rich fibrin, advanced platelet-rich fibrin, and injectable platelet-rich fibrin protocols: a narrative review. Growth Factors.(2024);42(4),216–228. https://doi.org/10.1080/08977194.2024.2432951
35. Everts PA, Lana JF, Onishi K, Buford D, Peng J, Mahmood A, et al. Angiogenesis and Tissue Repair Depend on Platelet Dosing and Bioformulation Strategies Following Or-thobiological Platelet-Rich Plasma Procedures: A Narrative Review. Biomedicines. 2023;11(7):1922. doi: 10.3390/biomedicines11071922. PMID: 37509560; PMCID: PMC10377284.

36. Lynch SE, Williams RC, Polson AM, Howell TH, Reddy MS, Zappa UE, et al. A combina-tion of platelet-derived and insulin-like growth factors enhances periodontal regeneration. J Clin Perio-dontol. 1989 Sep;16(8):545-8. doi: 10.1111/j.1600-051x.1989.tb02334.x. PMID: 2778088
37. Shaker SA, Salman SA. Efficacy of Concentrated Platelets-Rich Fibrin versus Injectable Platelets Rich Fibrin on Gingival Thickness and Keratinized Tissue Width in Subjects with Thin Gingival Phenotype: Split-Mouth Randomized Clinical Trial. Al-Rafidain J Med Sci. 2023;5:14–19. doi: 10.54133/ajms.v5i.130
38. Faour NH, Dayoub S, Hajeer MY. Evaluation of the Hyaluronic Acid Versus the Injectable Platelet-Rich Fibrin in the Management of the Thin Gingival Phenotype: A Split-Mouth Randomized Controlled Clinical Trial. Cureus. 2022;14(5):e25104. doi: 10.7759/cureus.25104. PMID: 35607316; PMCID: PMC9123359.
39. Li T, Wang YY, Liu C. The effectiveness of using platelet-rich concentrate with iliac bone graft in the repair of alveolar cleft: a meta-analysis of randomized controlled trials. Int J Oral Maxillofac Surg. 2023 Oct;52(10):1049-56. doi: 10.1016/j.ijom.2023.01.021. Epub 2023 Mar 14. PMID: 36925370.
40. Rodas MAR, Paula BL, Pazmiño VFC, Lot Vieira FFDS, Junior JFS, Silveira EMV. Platelet-Rich Fibrin in Coverage of Gingival Recession: A Systematic Review and Meta-Analysis. Eur J Dent. 2020 Mar;14(2):315-26. doi: 10.1055/s-0040-1701907. Epub 2020 Mar 27. PMID: 32221958; PMCID: PMC7296445.
41. Izol BS, Uner DD. A new approach for root surface biomodification using injectable platelet-rich fibrin (i-PRF). Med Sci Monit. 2019;25:4744-50. DOI: 10.12659/MSM.915142.
42. Jamjoom AG. From Healing to Regeneration: A Comprehensive Review of the Efficacy of Plate-let-Rich Fibrin in Periodontal Plastic Surgery Procedures. Cureus. 2024 Sep 12;16(9):e69287. doi: 10.7759/cureus.69287. PMID: 39268023; PMCID: PMC11392565.
43. Farshidfar N, Amiri MA, Jafarpour D, Hamedani S, Niknezhad SV, Tayebi L. The feasibility of inject-able PRF (I-PRF) for bone tissue engineering and its application in oral and maxillofacial reconstruction: From bench to chairside. Biomater Adv. 2022 Mar;134:112557. doi: 10.1016/j.msec.2021.112557. Epub 2021 Nov 24. PMID: 35527147; PMCID: PMC9295636.
44. Liu M, Liu Y, Luo F. The role and mechanism of platelet-rich fibrin in alveolar bone regenera-tion. Biomed Pharmacother. 2023;168:115795. doi: 10.1016/j.biopha.2023.115795
45. Bahar ŞÇ, Karakan NC, Vurmaz A. The effects of injectable platelet-rich fibrin application on wound healing following gingivectomy and gingivoplasty operations: single-blind, randomized controlled, pro-spective clinical study. Clin Oral Investig. 2024 Jan 10;28(1):85. doi: 10.1007/s00784-023-05477-2. PMID: 38196007; PMCID: PMC10776463.
46. Gollapudi M, Bajaj P, Oza RR. Injectable Platelet-Rich Fibrin - A Revolution in Periodontal Regenera-tion. Cureus. 2022 Aug 31;14(8):e28647. doi: 10.7759/cureus.28647. PMID: 36196318; PMCID: PMC9525133.
47. Torumtay Cin G, Lektemur Alpan A, Çevik Ö. Efficacy of injectable platelet-rich fibrin on clinical and biochemical parameters in non-surgical periodontal treatment: a split-mouth randomized controlled trial. Clin Oral Investig. 2023 Aug;28(8):3649-59. doi: 10.1007/s00784-023-05447-8. Epub 2023 Jul 12. PMID: 37438036.
48. Sousa F, Machado V, Botelho J, Proença L, Mendes JJ, Alves R. Effect of A-PRF Application on Palatal Wound Healing after Free Gingival Graft Harvesting: A Prospective Randomized Study. Eur J Dent. 2020 Feb;14(1):63-9. doi: 10.1055/s-0040-1702259. Epub 2020 Mar 13. PMID: 32168533; PMCID: PMC7069756.
49. Albatal W, Qasem T, Tolibah YA. Evaluation of the Effect of Injectable Platelet-rich Fibrin on Palatal Wound Healing: A Two-arm Randomized Controlled Clinical Trial. J Contemp Dent Pract. 2023 Apr 1;24(4):214-20. doi: 10.5005/jp-journals-10024-2942. PMID: 37057021; PMCID: PMC1008102343.
50. Bahar ŞÇ, Karakan NC, Vurmaz A. The effects of injectable platelet-rich fibrin application on wound healing following gingivectomy and gingivoplasty operations: single-blind, randomized controlled, prospective clinical study. Clin Oral Investig. 2024 Jan 10;28(1):85. doi: 10.1007/s00784-023-05477-2. PMID: 38196007; PMCID: PMC10776463.
51. Kiziltoprak M, Uslu MO. Comparison of the effects of injectable platelet-rich fibrin and autologous fibrin glue applications on palatal wound healing: a randomized controlled clinical trial. Clin Oral Investig. 2020 Dec;24(12):4549-61. doi: 10.1007/s00784-020-03431-y. Epub 2020 Jun 20. PMID: 32564257.
52. Laforgia A, Inchingolo AD, Riccaldo L, Avantario P, Buongiorno S, Malcangi G, et al. The Use of Platelet-Rich Fibrin (PRF) in the Management of Dry Socket: A Systematic Review. Int J Mol Sci. 2024 Sep 19;25(18):10069. doi: 10.3390/ijms251810069. PMID: 39337554; PMCID: PMC11432458.
53. Nasirzade J, Kargarpour Z, Hasannia S, Strauss FJ, Gruber R. Platelet-rich fibrin elicits an an-ti-inflammatory response in macrophages in vitro. J Periodontol. 2020 Feb;91(2):244-52. doi: 10.1002/JPER.19-0216. Epub 2019 Sep 14. PMID: 31376159; PMCID: PMC7065136.
54. Csifó-Nagy BK, Sólyom E, Bognár VL, Nevelits A, Dőri F. Efficacy of a new-generation platelet-rich fibrin in the treatment of periodontal intrabony defects: a randomized clinical trial. BMC Oral Health. 2021 Nov 15;21(1):580. doi: 10.1186/s12903-021-01925-1. PMID: 34781955; PMCID: PMC8591936.

55. Wang J, Li W, He X, Li S, Pan H, Yin L. Injectable platelet-rich fibrin positively regulates osteogenic differentiation of stem cells from implant hole via the ERK1/2 pathway. Platelets. 2023;34(1):1-10. DOI: 10.1080/09537104.2022.2159020.
56. Ibrahim SM, Al-Hmedat SJA, Alsunboli MH. Histological Study to Evaluate the Effect of Local Application of Myrtus Communis Oil on Alveolar Bone Healing in Rats. Open Dent J. 2024;18(1). DOI: 10.2174/0118742106299510240405O4391.

57. Chenchev IL, Ivanova VV, Neychev DZ, Cholakova RB. Application of Platelet-Rich Fibrin and Injectable Platelet-Rich Fibrin in Combination of Bone Substitute Material for Alveolar Ridge Augmentation - a Case Report. Folia Med (Plovdiv). 2017 Sep 1;59(3):362-6. doi: 10.1515/folmed-2017-0044. PMID: 28976904.
58. Gülsen U, Dereci Ö. Evaluation of new bone formation in sinus floor augmentation with injectable platelet-rich fibrin–soaked collagen plug: a pilot study.

Implant Dent. 2019;28:220-5. DOI: 10.1097/ID.0000000000000883.
59. Işık G, Özden Yüce M, Koçak-Topbaş N, Günbay T. Guided bone regeneration simultaneous with implant placement using bovine-derived xenograft with and without liquid platelet-rich fibrin: a randomized controlled clinical trial. Clin Oral Investig. 2021;25:5563-75. DOI: 10.1007/s00784-021-03987-5.
60. Jepsen K, Sculean A, Jepsen S. Complications and treatment errors related to regenerative periodontal surgery. Periodontol 2000. 2023 Jun;92(1):120-34. doi: 10.1111/prd.12504. Epub 2023 Jul 12. PMID: 37435999.
61. Dambhare ML, Bhongade PV, Dhadse B, Sehdev KK, Ganji KS, Thakare Z, et al. A Randomized Controlled Clinical Study of Autologous Platelet Rich Fibrin (PRF) in Combination with HA and Beta-TCP or HA and Beta-TCP Alone for Treatment of Furcation Defects. J Hard Tissue Biol. 2019 28(2):185-190 .DOI:10.2485/jhtb.28.185
62. Nair UP, Shivamurthy R, Nagate RR, Chaturvedi S, Al-Qahtani SM, Magbol MA, et al. Effect of Injectable Platelet-Rich Fibrin with a Nano-Hydroxyapatite Bone Graft on the Treatment of a Grade II Furcation Defect. Bioengineering. 2022;9(11):602. doi: 10.3390/bioengineering9110602.
63. Elbarbary A, Reda A, Abd ELaziz A. Evaluation of the Addition of Injectable Platelet Rich Fibrin to Xenograft in Management of Periodontal Intraosseous Defects. Al Azhar Dent J Girls. 2022;9(2):321-30. DOI: https://doi.org/10.21608/adjg.2022.111166.1461.
64. Dayashankara Rao JK, Bhatnagar A, Pandey R, Arya V, Arora G, Kumar J, et al. A comparative evaluation of iliac crest bone graft with and without injectable and advanced platelet rich fibrin in secondary alveolar bone grafting for cleft alveolus in unilateral cleft lip and palate patients: A randomized prospective study. J Stomatol Oral Maxillofac Surg. 2021;122(3):241-7. doi: 10.1016/j.jormas.2020.07.007. Epub 2020 Aug 8 PMID: 32781256.
65. Majeed SS, Hassan TAL. Opportunity of the Effect of Injectable Platelet Rich Fibrin (I-PRF) Mixed with Bone Graft on the Corre-lation Between Dental Implant Stability and Alveolar Ridge Width. A Clinical Comparative Study. Tikrit J Dent Sci. 2024;12(1):155-64. doi:10.25130/tjds.12.1.17
66. Naser AI, Hamed RS, Taqa GAA. The impact of silver/beta-tricalcium phosphate nanocomposite combined with injectable platelet-rich fibrin on the healing of mandibular bone defects: An experimental study in Dogs. Iraqi J Vet Sci. 2024;38(3):501-7. doi:10.33899/ijvs.2024.145856.3400.
67. Patra L, Raj SC, Katti N, Mohanty D, Pradhan SS, Tabassum S, et al. Comparative evaluation of effect of injectable platelet-rich fibrin with collagen membrane compared with collagen membrane alone for gingival recession coverage. World J Exp Med. 2022 Jul 20;12(4):68-91. doi: 10.5493/wjem.v12.i4.68. PMID: 36157336; PMCID: PMC9350719.
68. Ozsagir ZB, Saglam E, Sen Yilmaz B, Choukroun J, Tunali M. Injectable platelet-rich fibrin and microneedling for gingival augmentation in thin periodontal phenotype: A randomized controlled clinical trial. J Clin Periodontol. 2020;47(4):489-99. doi: 10.1111/jcpe.13247. Epub 2020 Feb 11 PMID: 31912532
69. Ucak Turer O, Ozcan M, Alkaya B, Surmeli S, Seydaoglu G, Haytac MC. Clinical evaluation of injectable platelet-rich fibrin with connective tissue graft for the treatment of deep gingival recession defects: A controlled randomized clinical trial. J Clin Periodontol. 2020;47:72-80. DOI: 10.1111/jcpe.13193.
70. Fujioka-Kobayashi M, Schaller B, Mourão CFDA, Zhang Y, Sculean A, Miron RJ. Biological characterization of an injectable platelet-rich fibrin mixture consisting of autologous albumin gel and liquid platelet-rich fibrin (Alb-PRF). Platelets. 2021;32:74-81. DOI: 10.1080/09537104.2020.1717455.

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