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REVIEW ARTICLE

Novel approaches to the use of platelet-rich fibrin: A literature review

Atalay Elver *, **Mehmet Gagari Caymaz**

Cyprus Health and Social Sciences University, Department of Oral and Maxillofacial Surgery, Güzelyurt, TRNC (Turkish Republic of North Cyprus), Mersin 10, Turkey

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Contents

1. Introduction

Tissue engineering has been used to develop new biomaterials that improve wound healing and biocompatibility after surgery. Platelet-rich materials are cost-effective, easy-to-manufacture, and highly applicable (Ghanaati et al., 2014). They are preferred because of their biocompatibility, reliability, low cost, and rapid recovery.(See Table 1 and Table 2)

A comparison of platelet-rich fibrin (PRF) and a control has often been made in research studies. However, to date, a standard PRF protocol is still unavailable, but all the protocols applied show great promise in maxillofacial surgery.

Platelet-rich plasma (PRP) is the initial platelet concentration method used in regenerative dentistry. However, it has limitations, such as a lengthy application period and the use of anticoagulants, which may affect tissue healing. PRF was developed as an alternative; it provides a more concentrated and natural healing environment, promoting rapid and effective tissue healing while avoiding some of the limitations of PRP (Miron et al., 2020a, 2020b).

According to the application protocol, 10–100 cc of venous blood was collected from each patient. For this procedure, plastic, glass, or titanium tubes are preferred (Tunalı et al., 2020). Blood was centrifuged as soon as it was collected. Transport times > 60 s can result in clotting. After centrifugation, the upper coagulated layer was removed. A buffy coat was present in the middle. Solid PRF can be cut and pressed according to the defect; however, injectable-PRF must be injected immediately after coagulation occurs.

In PRF, platelets, leukocytes, and fibrin increase the wound healing ability at high physiological levels. In addition, PDGF and TGF-B contained in PRF increase the number of defence

* Corresponding author.
E-mail addresses: atalayelver1@gmail.com, atalay.elver@kstu.edu.tr (A. Elver), m.gagari.caymaz@gmail.com (M.G. Caymaz).

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Table 1 Developmental History of PRF.

1954	The term "PRP" was first used.
1997	The term "Platelet Gel" was first used (Agrawal, 2017)
2000	Choukroun et al. developed PRF and branded it as a "second generation" platelet concentrate (3000 RPM 10 min) (Xu et al., 2021).
2006	Concentrated Growth Factors (CGF) were introduced (Stanca et al., 2021).
2010	Sticky bone (fibrin and bone graft mixture) was introduced (Rupawala et al., 2020).
2013	Titanium-PRF (T-PRF) was introduced (Tunalı et al., 2014).
2014	Advanced-PRF (A-PRF) was introduced (Ghanaati et al., 2014).
2015	Mourão et al. described the preparation of injectable PRF (i-PRF) in detail (Mourão et al., 2015).
2017	A-PRF + was introduced (Choukroun and Ghanaati, 2018).
2020	Horizontal-PRF (H-PRF) based on horizontal centrifugation was introduced (Feng et al., 2020).
2020	Concentrated-PRF (C-PRF) was introduced (Miron et al., 2020a, 2020b).
2021	Albumin Gel Platelet-rich Fibrin mixture (Alb-PRF) was introduced (Gheno et al.,2021).

Table 2 Current General Platelet Concentrate Protocols.

P-PRP	It is difficult and expensive, platelet yield is low, and the platelets are damaged. Therefore, calcium chloride is used for coagulation. However, there is a problem with the repeatability of the procedure (Matos et al.,2017).
L-PRP	Leukocyte-PRP contains leukocytes and a low-density fibrin network (Collins et al., 2021)
P-PRF	Pure-PRF (Leucosyte-Poor PRF) is a more stable fibrin matrix despite lower leukocyte counts (Dohan et al., 2009).
L-PRF	Leucosyte_PRF is the second generation of platelet concentrates. It does not require the addition of anticoagulants. It is prepared by using 9 mL glass-lined plastic tube at 2700 rpm for 12 min at room temperature (Chandra et al., 2019).
CGF	Includes several growth factors such as Vascular endothelial growth factor, Platelet-derived growth factor, Insulin-like growth factor 1, and Transforming growth factor beta 1. This enables the gradual release of growth factors, which helps in the healing of wounds (Mijiritsky et al., 2021).
Sticky Bone	A combination of bone graft granules with i-PRF. A barrier membrane is often used to provide additional support to the grafted bone (Soni et al.,2019).
T-PRF	The utilisation of titanium tubes in lieu of glass tubes for sample collection and subsequent centrifugation at 2800 rpm for 12 min was implemented (Tunalı et al., 2014).
A-PRF	Achieved by decreasing the centrifugation speed and increasing the waiting time. The enhanced porosity of the matrix promotes a faster release of the contents, facilitating angiogenesis and cytokine release, while also promoting faster vascularisation and soft tissue growth (Kobayashi et al., 2016).
A-PRF+	Several studies have demonstrated that the fibrin matrix of A-PRF + exhibits greater platelet and leukocyte concentrations, as well as a more porous structure than that of L-PRF (Pitzurra et al.,2020).
i-PRF	"Injectable PRF" was obtained by shortening the centrifugation times with minor tube modifications. Cellular activities and growth factor contents were higher than those of PRP due to slow centrifugation and lack of anticoagulants (Shashank and Bhushan, 2021).
H-PRF	The distribution of cells within H-PRF is reliant on the tube position instead of the centrifugation protocol. Horizontal-angle centrifugation devices possess a more inclusive and angled design than fixed-angle devices. In fixed-angle centrifugation procedures, a significant proportion of cells accumulate on the back wall of the tubes, whereas in H-PRF applications, cells demonstrate a more uniform distribution pattern (Fujioka-Kobayashi et al., 2021).Furthermore, investigations have reported that H-PRF preparations exhibit greater antibacterial properties than those of L-PRF (Feng et al., 2020).
C-PRF	Higher platelet masses were obtained from the area 0.5 mm higher from the buffy coat layer (+1 zone) (Miron et al., 2020a, 2020b).
Alb-PRF	Platelet-poor plasma (particularly albumin protein) layer is combined with liquid L-PRF to support the content of growth factors with loss of growth factors by heat treatment. Alb-PRF is defined as a solid, opaque, and stable structure. The L-PRF liquid phase was obtained using the same protocol as for H-PRF applications. Subsequently, an average of 2 mL of plasma sample from the upper layer was subjected to denaturation by heating at 75 °C for 10 min. The denatured plasma was then combined with L-PRF and homogenised. After 5 min, the mixture was processed into a membrane that was deemed suitable for use (Gheno et al.,2021).

cells in the region by supporting mitogenesis and chemotaxis. Thus, the bone density in this area increases significantly (Mohan et al., 2019).

The fundamental principle underlying all PRF materials is the centrifugation of a patient's venous blood at different revolutions per minute (RPM) and relative centrifugal force (RCF) or g force values for varying durations. The centrifugation time and speed can be adjusted according to the desired application, resulting in PRF with greater liquid consistency or denser texture.

2. Materials and methods

A literature search was conducted using PubMed and ResearchGate databases, and the search period was extended until August 2022. The search was performed using various keywords related to PRF, including history, desquamative lesions, sinus lifting, augmentation procedures, orthodontic tooth movements, furcation defects, wisdom tooth management, treatment for gingival recession, osteomyelitis, and regenerative endodontics.

The PRF protocols used in maxillofacial surgery and other areas of dentistry and medicine are summarised in Table 3.

3. Current PRF application areas

In a study by Youssef et al., two different study groups in which regenerative endodontics with blood clots and PRF were performed were followed up for 6 and 12 months. After 12 months, periradicular improvement and increased tooth sensitivity were observed in both groups (Youssef et al., 2022).

Considering the studies on gingival recession, PRF was found to be more successful than the coronal shift flap. When PRF + coronal shift was applied, better covering and keratinised mucosa were obtained, but no difference was found in the attachment level and probing. In addition, PRF was more effective in terms of postoperative comfort and pain (Miron et al., 2020a, 2020b).

PRF accelerates the formation of new vessels and wound healing by affecting angiogenesis during bone osteonecrosis (Ding et al., 2021). First, Steller et al. applied zoledronic acid to osteoblasts and observed decreased proliferation and differ-

Table 3 PRF Protocols (Summary).

L-PRF	2700 rpm for 12 min (Chandra et al., 2019)
i-PRF	700 rpm for 3 min (Miron et al., 2017)
A-PRF	1500 rpm for 14 min (Ghanaati et al., 2014)
A-PRF+	1500 rpm for 8 min (Simões-Pedro et al., 2022)
T-PRF	Inside titanium tubes, 2800 rpm for 12 min (Tunalı et al., 2014)
H-PRF	2200 rpm, maximum 700 RCF for 8 min on horizontal centrifugation (Fujioka-Kobayashi et al., 2021).
C-PRF	2700 rpm for 10 min with a particular harvesting method (Miron et al., 2020a, 2020b)

Table 4 Current PRF Application Areas.

Endodontics	Pulp floor perforations (Jayadevan et al., 2021)Traumatised immature teeth (Arshad et al.,2021)Regenerative endodontics (Youssef et al., 2022)
Sinus Lifting	PRF can be used as a graft or a membrane (Ortega-Mejia et al., 2020; Aoki et al., 2016)
Orthodontic Tooth Movements	Rapid movement using i-PRF in canine distalisation (Erdur et al., 2021)
Extractions	Less pain, trismus, and swelling after third molar extraction following PRF application (Gupta and Agarwal, 2021) Decreases the rate of osteomyelitis (Arshad et al., 2021).A-PRF reduces postoperative pain after wisdom tooth extraction (Caymaz and Uyanik, 2019).PRF combined with piezosurgery significantly reduces postoperative pain after third molar extraction (Bilginaylar et al., 2016)
Gingival Recessions	PRF + coronal shift has a high success rate in gingival recession (Miron et al., 2020a, 2020b)A-PRF might benefit gingival regeneration from blood vessel formation and growth factors around the gingiva from the first day (Liu et al., 2022).
Congenital Defects	Accelerates wound healing in alveolar defects (Al-Mahdi et al., 2021)
Vestibuloplasty	It can be preferred as a soft tissue graft to reduce secondary healing areas (Amiri et al., 2021).
Osteonecrosis	Affecting angiogenesis (Ding et al., 2021)Increases the viability of osteoblasts (Steller et al., 2022).
Cysts of Tumours of the Jaw	It can be successfully used for bone repair in cavities formed after enucleation and curettage of cysts in the jaw (Dar et al., 2016)Successful results were obtained in treating paradental cysts, and treatment of traumatic bone cysts is reported in the literature (Bernabeu-Mira et al., 2021).
Oroantral Relations	PRF can be used in oroantral openings smaller than 5 mm (Bilginaylar, 2018; Manuel et al., 2021; Salgado-Peralvo et al., 2022)Clinical reports show that PRF can be used in larger openings (Barbu et al., 2021; Bilginaylar, 2019)
Antibacterial and Anti-inflammatory Activity	Have anti-inflammatory properties by supporting M1-M2 conversion in murine macrophages (Nasirzade et al., 2020).İ-PRF has more antibacterial effects (Kour et al., 2018).
TMJ Problems	When injected into the upper joint space, it decreased pain, and increase function oral opening were observed (Herrera et al., 2021).
Bone Defects	The amount of bone in the region increased when applied to intraosseous defects (Miron et al., 2021)PRF, alongside the graft, increased the regenerative capacity (Caymaz et al., 2020; Ustaoğlu et al., 2020)
Desquamative Lesions	A decrease in pain and the size of lesion was observed (Sağlam et al., 2021)
Wound Healing and Cell Migration	Occurs faster in PRF groups, especially in A-PRF+ (Pitzurra et al., 2020).

entiation. Using PRF and PRP in the medium, cell viability increased. This indicates that PRF and PRP may be therapeutically beneficial for bisphosphonate-associated osteonecrosis (Steller et al., 2022).

Studies support that higher success can be achieved by applying PRF and the "sticky bone" concept together as the graft material to accelerate bone regeneration. Therefore, new tools are being developed to produce "sticky bones" (Miron et al., 2021).

In recent years, the concept of "sticky bone" has been introduced and has led to the development of the "sticky tooth" concept. Socket preservation based on the combination of an autogenous dentin graft and i-PRF has been investigated; van Orten et al. have reported successful outcomes (van Orten et al., 2022).

In a study on dogs, PRF was applied to one side after bilateral extraction. When the dry replanted teeth were replanted after 60 min and examined after 8 weeks, no difference was found other than decreased inflammatory root resorption in the sockets, which made their use in replantation questionable (Behnaz et al., 2021).

In a study by Liu et al., Advanced-PRF (A-PRF) was applied to the appropriate area following bilateral premolar extraction in the upper and lower jaws of dogs. The effects of A-PRF on gingival regeneration were evaluated using immunohistochemical and Laser Doppler analyses. These findings indicate that A-PRF may promote gingival regeneration through the development of blood vessels and the presence of growth factors around the gingival tissue from the initial days of treatment. These results suggest that A-PRF has the potential to serve as an effective therapy to promote gingival regeneration after tooth extraction (Liu et al., 2022).

In a split-mouth study by Sağlam et al., 24 patients diagnosed with bilateral erosive lichen planus were treated with either injectable PRF (i-PRF) or methylprednisolone acetate to one of the bilateral lesions. Their findings suggest that i-PRF can be effective for reducing the symptoms associated with erosive lichen planus (Saglam et al., 2021).

Studies show that the Alb-PRF (21 days) group showed less resorption than that in the L-PRF and H-PRF groups (14 days). Therefore, Alb-PRF can also be applied as a more stable membrane in YDR. (Gheno et al.,2021).

The broad application areas of PRF materials are shown in Table 4.

4. Conclusion

Tissue engineering continues to evolve with the emergence of new protocols and biomaterials aimed at improving postoperative wound healing and biocompatibility. One such material is PRF, which contains growth factors that support tissue healing and leukocytes involved in defence, imparting antibacterial and angiogenic effects. PRF is valued for its biocompatibility, reliability, low cost, and potential for rapid recovery, making it the preferred choice in various fields of medicine and dentistry. PRF is utilised across a wide range of dental specialties, including endodontics, periodontology, orthodontics, and maxillofacial surgery.

The simplicity of the application of PRF makes it accessible to a wide range of healthcare professionals, including surgeons and general practitioners. Its regenerative properties have piqued interest in the dental and medical communities. As a fully autologous material, PRF can be used instead of allografts or costly membranes to achieve postoperative targeted tissue regeneration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2023.07.008.

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