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Review Article

Use of Platelet-Rich Fibrin (PRF) in Periodontology: Current Approaches in Regenerative Therapies

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Introduction

The Fundamental Purpose of Autologous Concentrated Blood Products Platelets play a crucial role in natural wound healing because they contain growth factors and cytokines that initiate tissue repair processes. Recently, techniques such as Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF), developed to concentrate these growth factors and apply them directly to the damaged area, have strengthened tissue regeneration and accelerated the healing process [1].

PRF, which is obtained entirely from the patient's own blood and is free of foreign substances, supports healing through a natural inflammatory process. When centrifuged in glass or glass-coated tubes, silica acts merely as a catalyst for platelet activation but may also cause minor side effects. The resulting fibrin is generally absorbed by human tissues within 7-11 days. While this duration is usually sufficient for soft tissue repair, its efficacy in hard tissue regeneration remains uncertain when used alone [2].

Blood is one of the most valuable autologous resources the body resorts to for both hard and soft tissue repair [3].

PRF offers a specific molecular structure that allows fibroblasts and endothelial cells to migrate. Research has demonstrated that PRF membranes accelerate vessel formation (angiogenesis) and facilitate the remodeling of fibrin; these properties make PRF an effective option in the treatment of various superficial skin and mucosal wounds. Beyond being a simple fibrin covering, PRF is a rich matrix equipped with the molecular and cellular components required for an ideal healing environment. This matrix is capable of retaining all beneficial components from the collected blood sample. Furthermore, because PRF can be obtained without adding any chemical substances or requiring extra processing, it is defined as a strictly "biological healing material." The polymerized fibrin network with a tetramolecular structure, containing platelets, leukocytes, cytokines, and possibly circulating stem cells, forms the basis of PRF. Although the slow release of cytokines trapped within the matrix enhances the cellular response, it is thought that the true source of PRF's superior healing potential is this unique fibrin network [4].

Classification of Autologous Concentrated Blood Products Platelet concentrates obtained from a person's own blood are grouped into four main categories based on their leukocyte and fibrin content [5]:

Pure Platelet-Rich Plasma (P-PRP)

Leukocyte and Platelet-Rich Plasma (L-PRP)

Pure Platelet-Rich Fibrin (P-PRF)

Leukocyte and Platelet-Rich Fibrin (L-PRF)

Platelet-Rich Plasma (PRP) To prevent platelets from activating early and releasing their granules, venous blood collected in tubes containing anticoagulants undergoes a centrifugation process. As a

result of this process, the blood separates into three distinct layers:

At the very bottom, red blood cells occupy approximately 55% of the total volume.

At the very top is plasma poor in platelets (PPP), which contains plasma molecules, primarily fibrinogen; this layer makes up approximately 40% of the volume.

Between these two layers lies a thin intermediate layer where platelets are concentrated, accounting for only 5% of the total volume; this is called "Platelet-Rich Plasma" (PRP) [6].

The potential benefits of PRP have been widely researched, particularly in the fields of orthopedics and sports medicine [6]. In Oral and Maxillofacial Surgery, PRP has been used to treat periodontal bone defects, facilitate sinus augmentation, enhance soft and hard tissue regeneration, and support healing following third molar extractions. Targeted effects include improving graft vascularization, accelerating soft tissue healing, promoting bone regeneration, and reducing postoperative morbidity [6].

Various disadvantages of PRP have also been defined. The preparation process is costly, requires technical precision, and is largely operator-dependent. Additionally, the use of bovine-derived thrombin during clotting may raise both legal and biological concerns [7].

Platelet-Rich Fibrin (PRF) The disadvantages associated with first-generation blood concentrates led to the creation of more advanced alternatives. For PRF preparation, a 9-10 mL blood sample is drawn without interfering with the body's natural coagulation pathway and placed in glass-coated, pure glass, plastic-coated, or titanium tubes [8]. These tubes are placed opposite each other in the centrifuge and spun at 400g force for 12 minutes; this corresponds roughly to 2700 RPM.

Acting quickly is crucial: after blood collection, it must be placed in the centrifuge immediately, preferably within 60 seconds, to prevent spontaneous clotting before the process. This usually requires loading the centrifuge with two tubes simultaneously or, if a single tube is used, balancing it with another tube containing an equal volume of glycerin or saline.

After centrifugation, three distinct layers emerge:

The bottom layer containing red blood cells,

The top layer containing Platelet-Poor Plasma (PPP), and

The middle layer containing the fibrin clot rich in leukocytes and platelets.

The Leukocyte and Platelet-Rich Fibrin (L-PRF) clot can be carefully removed with the help of forceps. The remaining red blood cell layer can be gently cleaned off using a spatula-like instrument. To create stronger membranes, the clot is gently compressed for approximately five minutes to drive out the exudate (fluid) rich in growth factors. This process is typically performed using a metal box with a weighted press plate (PRF Box), yielding L-PRF membranes approximately 1 mm thick. These membranes can remain intact for several hours at room temperature, and it has been shown that they can withstand approximately 400g of force thanks to their dense fibrin networks [8].

L-PRF serves as a fibrin-based scaffold that supports cell migration, one of the key mechanisms underlying tissue regeneration. Furthermore, L-PRF membranes continuously release significant concentrations of growth factors for 7-14 days, contributing to their regenerative efficacy [9].

Subsequently, Concentrated Growth Factors (CGF), Advanced Platelet-Rich Fibrin (A-PRF), and Injectable Platelet-Rich Fibrin (I-PRF) were introduced as improved forms of PRF, with claims of offering enhanced biological activity. By modifying the centrifugation protocol—specifically by adjusting speed and time—stronger autologous regenerative products can be obtained [10]. In a comparative analysis involving PRP, PRF, and A-PRF incubated for 15 to 60 minutes, Kobayashi et al. reported that A-PRF consistently provided the highest cumulative growth factor release, with high levels persisting for up to 10 days. Their results showed that A-PRF produced significantly higher total growth factor concentrations than traditional PRP or PRF over a 10-day observation period [11].

In the case of I-PRF, plastic tubes are used to ensure the product remains in liquid form and to prevent fibrin membrane formation. Unlike L-PRF, the primary purpose of I-PRF is to produce a highly bioactive liquid that can be easily incorporated into graft materials to enhance their regenerative capabilities [12].

While researchers attempted to address the shortcomings of PRP, alternative platelet-derived options were examined, and Choukroun et al. introduced PRF in 2001. Platelets are at the center of the wound healing process due to their alpha granules, which contain numerous growth-promoting molecules. These include Platelet-Derived Growth Factor (PDGF), which attracts and activates endothelial cells, fibroblasts, and macrophages; Insulin-Like Growth Factor-1 (IGF-1); Epidermal Growth Factor (EGF); Vascular Endothelial Growth Factor (VEGF); and Transforming Growth Factor-β (TGF-β). L-PRF membranes have been shown to secrete these mediators in significant amounts continuously for at least seven days. Although PRP gels also contain these factors, their chemically induced activation causes a rapid "burst" release within the first few hours, followed by almost complete degradation within three days [13].

This distinction stems primarily from differences in fibrin matrix architecture. PRF is formed through a natural polymerization process that traps growth factors within an intrinsic fibrin network, ensuring a slow, sustained release. In contrast, PRP gels rely on extrinsically triggered polymerization that creates a fibrin structure which releases growth factors rapidly; this leads to the immediate consumption or degradation of the factors [14].

PRF demonstrates enhanced biological performance when combined with autologous or non-autologous graft materials. According to Tunalı et al. [15], when PRF is applied with non-autologous grafts, its natural inflammatory properties change; this is because the body's reaction to foreign substances may interfere with normal wound healing and reduce the efficacy of PRF.

Further research by Tunalı et al. revealed that using titanium instead of silica for platelet activation produces a denser fibrin network. This structure, named Titanium-Prepared Platelet-Rich Fibrin (T-PRF), exhibited extended resorption times, allowing it to be used as a standalone autologous graft. Researchers found that T-PRF could remain in tissues for more than 30 days and secrete growth factors in a controlled manner. Its long-term stability and natural matrix structure also facilitated the activation of bone regeneration mechanisms [16].

Conclusion Platelet concentrates have been applied in a wide variety of clinical areas, including soft tissue healing, plastic periodontal procedures, gingival augmentation, management of Medication-Related Osteonecrosis of the Jaw (MRONJ), bone defect regeneration, ridge preservation, sinus lift procedures, immediate implant placement, and enhancement of implant osseointegration. Their simplicity of application and cost-effectiveness make them a preferred option in patient care.

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Conflicts of Interest

No conflicts of interest.

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