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Platelet Rich Fibrin :-A Literature Review

Dr. Anurag Hasti[1], Dr. Ayushi Mishra[2], Dr. Tanu Gupta[3], Dr. Rashi[4], Dr. Rajvi Tayal[5], Dr. Manisha Dayma[6]

[1]Professor, Department Of Prosthodontics, Sharda University
[2]Post Graduate, Department Prosthodontics, Sharda University
[3]Assistant Professor, Department Of Prosthodontics, Sharda University
[4]Assistant Professor, Department Of Prosthodontics, Sharda University
[5]Assistant Professor, Department Of Prosthodontics, Swami Vivekanand Subharti University
[6]Post Graduate, Department Prosthodontics, Sharda University

***CorrespondingAuthor:**
Dr. Ayushi Mishra
EmailID: mishra.ayushi.105@gmail.com

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ABSTRACT
Platelet-rich fibrin (PRF), a second-generation platelet concentrate, has emerged as an increasingly popular option in regenerative medicine. This biological material offers several advantages - it comes from the patient's own body, requires simple preparation steps, is cost-effective, and provides sustained release of growth factors over time, making it superior to conventional platelet concentrates. While researchers have developed various PRF preparation methods that yield different concentrations of growth factors and biomolecules essential for wound healing, there soft tissues. This article examines recent developments in understanding the physiological effects of PRF components and explores innovative approaches to its use. Additionally, it traces the development of platelet concentrates over time and examines the biological characteristics of different PRF preparation techniques.

Keywords: *platelet-rich fibrin, platelets, growth factors, wound healing, bone formation, bone graft, membrane*

1. INTRODUCTION

In the last few decades a variety of biomaterials have been introduced in dentistry that can fill in osseous defects and accelerate wound healing. Materials like hydroxyapatite, freeze dried bone graft, tricalcium phosphate, bioactive glass etc. have been widely used and tested for their contribution in healing and regeneration of soft and hard tissues. It was first described by Dr. Joseph Choukroun in France to promote wound healing in implants. Currently, the studies have been focussed on the use of an autogenous material called Platelet Rich Fibrin that provides an osteoconductive scaffold along with growth factors to stimulate patient's own cells towards a regenerative response.(1)

Platelet rich fibrin (PRF) is a fibrin matrix in which platelet cytokines, growth factors and cells are (1)trapped and may be released after a certain time and that can serve as a resorbable membrane. It can be obtained from blood with the help of a simple process. PRF is basically a concentrate of growth factors that promote wound healing and regeneration which is used in various disciplines of dentistry to repair various lesions and regenerate dental and oral tissues. Growth factors are mitogenic (proliferative), chemotactic (stimulate directed migration of cells) and angiogenic (stimulate new blood vessel formation). Therefore, they appear to be critical to the wound-healing process(2).

PRP & PRF and its subgroup

The classification of platelet-rich forms is presented as follows (3):

1. Platelet-rich plasma (PRP):

- Pure platelet-rich plasma (P-PRP)
- Leukocyte- and platelet-rich plasma (L-PRP)

2. PLATELET-RICH FIBRIN (PRF)

- Leukocyte Platelet-Rich Fibrin (L-PRF)
- Injectable Platelet-Rich Fibrin (I-PRF)
- Advanced Platelet-Rich Fibrin (A-PRF)
- Advanced Platelet-Rich Fibrin Plus (A-PRF +)

Methods Of Preparation Of PRF

The initial protocol for PRF production, introduced by Choukroun et al. in 2001, requires 10 mL of blood sample to be collected without anticoagulant in glass-coated plastic tubes, which is immediately subject to centrifugation at 2,700 rpm (around 400 g) for 12 min. The obtained PRF is usually termed as Choukroun's PRF or leukocyte and PRF (L-PRF). However, in the last few years, the PRF protocol underwent several modifications. These protocols led to the formation of various products with different biology and potential uses.

Advanced Platelet-Rich Fibrin (A-PRF)

Research has shown that high centrifugal forces cause cells to accumulate at the tube's bottom during centrifugation. This led to the development of Advanced PRF (A-PRF), which uses lower centrifugation speeds to potentially preserve cells and enhance leukocyte concentration in the PRF matrix. A-PRF can be prepared using either 1,500 rpm (230 g) or 1,300 rpm (200 g) for 14 minutes in glass vacuum tubes.

Studies have demonstrated that A-PRF contains more viable cells than L-PRF, particularly showing increased concentrations of neutrophils, lymphocytes, and platelets. These immune cells play a crucial role in macrophage development and differentiation. In turn, macrophages support bone and soft tissue regeneration by releasing growth factors. Research has established that macrophages are essential for osteoblast differentiation, with bone formation being severely limited in their absence.

Regarding growth factor release, there are conflicting findings in the literature. Some studies report that A-PRF releases higher levels of growth factors (including TGF-β1, VEGF, PDGF, EGF, and IGF1) compared to L-PRF, while others suggest the opposite. Given these contradictory results and the limited available research, more studies are needed to fully understand the comparative advantages and limitations of A-PRF versus L-PRF

Advanced Platelet-Rich Fibrin Plus (A-PRF +)

The development of advanced rich plasma plus (A-PRF+) emerged as a refinement of the A-PRF protocol. Researchers discovered that by reducing both centrifugation speed to 1,300 rpm (200 g) and time to 8 minutes, they could minimize cell loss since centrifugal force directly impacts cell retention within the PRF matrix. This modified protocol, introduced by Fujioka-Kobayashi and colleagues, demonstrated remarkable improvements over its predecessors. When compared to A-PRF and L-PRF, A-PRF+ exhibited notably higher concentrations of key growth factors, including TGF-β1, VEGF, PDGF, EGF, and IGF1. The enhanced release of growth factors was likely attributed to the increased presence of leukocytes within the fibrin network, facilitated by the gentler centrifugation parameters. Studies showed that A-PRF+ outperformed L-PRF in promoting human gingival cell migration and proliferation. Additionally, when gingival fibroblasts were cultured with A-PRF+, they showed increased expression of collagen1 mRNA at both 3 and 7 days. Given collagen's essential role in wound healing and tissue remodelling, these findings suggest that PRF formulations using reduced centrifugation parameters offer significant regenerative potential.

Injectable Platelet-Rich Fibrin (I-PRF)

Injectable PRF (i-PRF) represents a significant advancement that addresses one of PRF's primary limitations compared to PRP - its gel-only form. While PRP's liquid state allows versatile applications across regenerative medicine, either independently or combined with biomaterials, i-PRF now offers similar flexibility. The i-PRF protocol involves centrifuging anticoagulant-free blood at 700 rpm (60 g) for 3 minutes in specialized plastic tubes. These tubes' hydrophobic surfaces minimize coagulation activation, enabling blood component separation that produces a yellow upper layer containing plasma, clotting factors, and platelets, which can be easily extracted for injection. Growth factor analysis reveals that i-PRF exhibits higher initial growth factor release, while traditional PRF demonstrates superior long-term release of PDGF-AA, PDGF-AB, EGF, and IGF-1 over a 10-day period. Additionally, i-PRF shows enhanced expression of TGF-β at 7 days, PDGF at 3 days, and collagen1 at both 3 and 7 days compared to PRP. Although these findings suggest PRF may have stronger biological effects than PRP, additional research is needed to confirm this hypothesis.

Advantages and Shortcomings of PRF(1)

Advantages of PRF	Shortcomings of PRF
It is an autologous product.	The speed of blood handling decides the success of PRF preparation.
Minimum blood manipulation without biochemical handling	Since the structural integrity of PRF modulates over time PRF membrane should be used immediately
Since polymerization occurs naturally, it requires no bovine thrombin	Due to potential bacterial contamination and dehydration storage of PRF membrane is not possible
It shows extended growth factor release compared to other platelet concentrates	Not possible to be used in general surgery since it is an autologous product and the quantity of PRF is low.
Involved in healing process as PRF fibrin matrix contains growth factors, leukocytes, and cytokines	
Membrane possesses high flexibility and elasticity	
It is inexpensive and involves simple procedure.	

3. BIOLOGICAL EFFECT

Platelets are the key cellular component driving PRF's biological activity. While these cells are well-known for their role in blood clotting, they also contain important protein molecules that orchestrate wound healing. These molecules are stored in three distinct types of granules within platelets: alpha, delta, and lambda. The alpha granules are particularly significant as they are both the most numerous and serve as the primary storage site for growth factors.

When platelets become activated, they release their granular contents through exocytosis. The growth factors released from PRF include several critical signalling molecules that promote both soft and hard tissue regeneration:

- Transforming growth factor β (TGF-β)
- Platelet-derived growth factor (PDGF)
- Insulin-like growth factor 1 (IGF1)
- Vascular endothelial growth factor (VEGF)
- Epidermal growth factor (EGF)

In addition to these growth factors, PRF also contains important immune signalling molecules (cytokines) such as interleukin-1β, interleukin-6, interleukin-4, and tumor necrosis factor-α. Together, these molecular components create a powerful regenerative environment that supports tissue healing.

Certain growth factors and cytokines present in PRF and their function

Transforming growth factor-β (TGF-β)	Provokes the formation of new blood vessels while supporting the formation of structural proteins (fibronectin and collagen). Prevent degradation of collagen, thus maintains collagen levels. Captivate fibroblasts and immune cells to specific areas. Lower bone loss by blocking the development of osteoclasts (cells that break down bone tissue).
Platelet-derived growth factor (PDGF)	Promotes migration and proliferation of mesenchymatous cell lineage; Allow angiogenesis, macrophages chemotaxis, and activation; induces TGF-β secretion from macrophages

Insulin growth factor-1 (IGF-1)	Induces chemotaxis and activation of osteoblasts and bone formation; stimulates differentiation and mitogenesis of mesenchymal cells
Vascular endothelial growth factor (VEGF)	Stimulates endothelial cell proliferation and migration, induces angiogenesis; enhances permeability of the vessels.
Epidermal growth factor (EGF)	Provoke angiogenesis; induces proliferation and differentiation of epithelial cells; enhances cytokine secretion in epithelial and mesenchymal cells
Interleukin-1β (IL-1β)	Promotes expression of adhesive molecules on endothelial cells; stimulates helper T cell, chemotaxis of lymphocytes; activates osteoblasts
Interleukin-6 (IL-6)	Induces B-cell differentiation and antibody secretion; promotes differentiation of naive T cells in cytotoxic T lymphocytes
Tumor necrosis factor-α (TNF-α)	Induces neutrophil cytotoxicity; accelerates cell survival and proliferation; enhances the remodelling capacities of fibroblasts
Interleukin-4 (IL-4)	Promotes B-cell differentiation into plasmocytes, B-cell class switching to IgE, differentiation of naive helper T cells in Th2 cells

4. CONCLUSION

Platelet-Rich Fibrin (PRF) represents an advancement in platelet concentrate technology, offering expanded potential for improved healing and recovery outcomes. The natural way PRF's fibrin network forms creates a biologically appropriate structure that enhances its therapeutic benefits. PRF has gained traction in regenerative medicine due to several advantages: it's simple to produce, cost-effective, and derived entirely from the patient's own blood. The availability of multiple preparation techniques yields different PRF variants, making this concentrate adaptable for various medical applications. Yet, more research is needed to fully understand the role and importance of its platelet-based and inflammatory properties, as well as to determine what additional advantages this second-generation platelet concentrate might offer over its predecessors.

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