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Platelet-Rich Fibrin (PRF) and Its Advanced Formulations in Periodontal Plastic and Regenerative Surgery: A Clinical and Biological Review

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ABSTRACT

Periodontal regeneration aims to predictably restore the lost tooth-supporting apparatus, encompassing alveolar bone, root cementum, and functional periodontal ligament fibers. Over the past two decades, autologous platelet concentrates have undergone an extensive evolution from early anticoagulated platelet-rich plasma (PRP) to second-generation leukocyte- and platelet-rich fibrin (L-PRF), and more recently to third-generation advanced PRF (A-PRF) and injectable PRF (i-PRF). The fundamental biological advantage of PRF stems from its completely natural, anticoagulant-free preparation, resulting in a three-dimensional polymerized fibrin architecture that acts as a reservoir for the sustained release of essential autologous growth factors—including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-beta), and vascular endothelial growth factor (VEGF)—over a 10 to 14-day window. This review provides a focused synthesis of the biological rationale, cellular mechanisms, and modern clinical applications of PRF and its liquid formulations across periodontal plastic surgery, intrabony defect reconstruction, furcation management, socket preservation, and sinus floor augmentation. In addition, the synergy of combining liquid i-PRF with particulate bone grafts to create cohesive "sticky bone" is discussed alongside evidence-based outcomes from recent clinical trials. Overall, PRF serves as an accessible, cost-effective, and safe autologous biomaterial that significantly enhances soft-tissue healing and promotes periodontal and peri-implant tissue regeneration.

INTRODUCTION

The primary goal of periodontal therapy has transitioned from mere disease arrest to the predictable reconstitution of destroyed periodontal tissues. True periodontal regeneration requires the coordinated formation of new cementum with inserting Sharpey's fibers, a functionally oriented periodontal ligament (PDL), and supporting alveolar bone [1]. While guided tissue regeneration (GTR) using barrier membranes and bone replacement grafts has demonstrated clinical efficacy, conventional synthetic and xenogeneic biomaterials lack intrinsic bioactivity and osteoinductive signaling.

To overcome these biological limitations, autologous blood concentrates were developed to deliver concentrated physiological doses of growth factors directly into surgical sites. First-generation platelet-rich plasma (PRP), introduced in the late 1990s, required the addition of bovine thrombin and calcium chloride to trigger clotting. However, chemical additives often resulted in an unnatural, rapid burst release of growth factors within the first few hours, and risks of antibody cross-reactivity and coagulopathies hindered its widespread adoption [2].

In 2001, Choukroun and colleagues pioneered leukocyte- and platelet-rich fibrin (L-PRF), a second-generation concentrate produced by centrifuging whole blood without any anticoagulants or biochemical activators [3]. The absence of anticoagulants allows natural, slow physiological polymerization of fibrinogen into an elastic, robust three-dimensional fibrin meshwork. Over the past decade, further advancements based on the "low-speed centrifugation concept" (LSCC) have introduced advanced PRF (A-PRF) and injectable liquid PRF (i-PRF), vastly expanding their surgical versatility in periodontology and implant dentistry [4].

Biological Architecture and Growth Factor Dynamics

The biological superiority of PRF over earlier concentrates is dictated by its distinct fibrin matrix geometry and cellular composition:

1. Fibrin Architecture

Unlike the rigid, tetramolecular fibrin junctions formed during rapid artificial thrombin-induced clotting in PRP, natural clotting during PRF centrifugation produces flexible, equilateral trimolecular junctions. This creates a fine, elastic three-dimensional scaffold that is highly resistant to proteolytic breakdown, preserving structural integrity in periodontal pockets for up to two weeks [5].

2. Cellular Entrapment

The centrifugation protocol concentrates not only platelets but also leukocytes (neutrophils, monocytes, and lymphocytes) and circulating mesenchymal stem cells. Leukocytes play an indispensable role in local immune regulation, producing antimicrobial peptides, decontaminating the surgical site, and directing macrophage polarization toward a reparative M2 phenotype [6].

3. Sustained Growth Factor Kinetics

PRF acts as a slow-release drug delivery system. Trapped platelets gradually degranulate their alpha-granules, releasing high concentrations of platelet-derived growth factor (PDGF-AB and PDGF-BB), transforming growth factor-beta 1 (TGF-beta1), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor-1 (IGF-1) over an extended period of 10 to 14 days [7]. This continuous, prolonged biological signaling contrasts sharply with the rapid 1-hour burst release observed in PRP, providing sustained mitogenic and chemotactic stimuli to migrating fibroblasts, endothelial cells, and osteoblasts during the critical early phases of periodontal wound healing.

Evolution of Formulations: L-PRF, A-PRF, and i-PRF

Modifications in centrifugal speed, force, and tube composition have yielded distinct PRF formulations tailored for specific clinical tasks:

- **Leukocyte- and Platelet-Rich Fibrin (L-PRF):** Prepared using standard centrifugation (typically ~2,700–3,000 rpm for 10–12 minutes; ~700 g). It yields a dense, tough fibrin clot that can be easily compressed into strong, pliable membranes using a dedicated PRF box. L-PRF membranes serve effectively as biological resorbable barriers and soft-tissue grafts [3].
- **Advanced PRF (A-PRF and A-PRF+):** Developed by

reducing centrifugation speed and force (~1,300–1,500 rpm for 8–14 minutes; ~200 g). Decreasing the centrifugal force prevents cells from being forced down into the red blood cell layer, resulting in a more porous fibrin network containing higher concentrations of trapped neutrophils, monocytes, and up to three times greater total growth factor release over 14 days compared to standard L-PRF [4].

- **Injectable PRF (i-PRF):** Produced by spinning non-anticoagulated blood in specific hydrophobic plastic tubes at very low speeds (~700 rpm for 3–4 minutes; ~60 g). Centrifugation is halted before fibrinogen polymerizes into a solid gel, producing a dynamic liquid concentrate rich in platelets, leukocytes, and thrombin. The liquid remains uncoagulated for approximately 15 to 20 minutes, allowing it to be injected directly into soft tissues or mixed with particulate bone substitutes [8].

Clinical Applications in Periodontics and Implantology

The versatility of PRF has led to successful documentation across multiple periodontal and peri-implant procedures:

1. Periodontal Intrabony Defects and Furcations

The combination of L-PRF or A-PRF clots with bone grafting materials (autogenous, allograft, or xenograft) consistently yields superior clinical outcomes compared to bone graft alone. Clinical trials demonstrate significant reductions in probing pocket depth, greater clinical attachment level (CAL) gains (averaging 0.8–1.2 mm additional gain), and increased radiographic defect fill [9].

2. Periodontal Plastic Surgery & Root Coverage

L-PRF membranes are widely utilized as an alternative to subepithelial connective tissue grafts (SCTG) in the treatment of Miller Class I and II (RT1) gingival recession defects. When combined with coronally advanced flaps (CAF) or tunneling techniques, PRF significantly increases gingival biotype thickness, promotes rapid revascularization, and eliminates donor-site morbidity associated with palatal harvesting [10].

3. "Sticky Bone" Preparation and Alveolar Ridge Preservation

By mixing particulate bone grafts with liquid i-PRF and allowing natural polymerization to take place over 5 to 10 minutes, a cohesive, moldable, and non-friable graft mass known as "sticky bone" is formed. Sticky bone prevents graft particle migration, accelerates capillary ingrowth, and dramatically simplifies graft placement in socket preservation, horizontal ridge augmentation, and maxillary sinus floor elevations [11].

4. Healing of Palatal Wounds and Extraction Sockets

Compressing PRF membranes over palatal donor sites or securing them within fresh extraction sockets accelerates re-epithelialization, protects exposed nerve fibers, and dramatically reduces postoperative patient discomfort and analgesic consumption [12].

CONCLUSION

Platelet-rich fibrin represents a significant milestone in regenerative periodontics. By combining a completely natural autologous preparation with sustained growth factor delivery and an elastic biological scaffold, PRF enhances angiogenesis, supports osteogenesis, and accelerates soft-tissue wound healing. From dense L-PRF barrier membranes to injectable i-PRF and cohesive "sticky bone" matrices, these formulations give clinicians an accessible, safe, and cost-effective biological strategy for optimizing outcomes in routine periodontal, regenerative, and implant surgical practice.

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