Chapter 2

Biomimetic Approach and the Role of Platelet Products in Wound Healing

Osman Bulut[1]

Ceyda Çakar[2]

Abstract

Biomimetic science seeks inspiration from the flawless and functional structures of nature to develop innovative materials and therapeutic strategies. Since the 1990s, this approach has gained importance in the fields of wound healing and tissue regeneration. Blood is considered the most essential autologous source in the repair of both soft and hard tissues.

The medical use of platelet derivatives has been explored for nearly four decades. Initially applied only as tissue adhesives, they are now widely recognized as regenerative tools. Platelets play a pivotal role in all stages of wound healing; hemostasis, inflammation, proliferation, and maturation by releasing growth factors such as PDGF, VEGF, EGF, and TGF-β from their granules. These bioactive molecules stimulate fibroblast proliferation, collagen synthesis, angiogenesis and epithelialization, thereby accelerating tissue repair.

Platelet concentrates are classified into several categories: pure PRP (P-PRP), leukocyte and platelet-rich plasma (L-PRP), pure PRF (P-PRF), leukocyte and platelet-rich fibrin (L-PRF), advanced PRF (A-PRF), injectable PRF (i-PRF) and titanium-prepared PRF (T-PRF). While PRP provides a rapid release of growth factors, PRF offers sustained release through its natural fibrin matrix, which also supports immune modulation and antimicrobial activity.

In conclusion, both PRP and PRF enhance wound healing by supporting fibroblast proliferation, collagen deposition, epithelial differentiation, and vascular growth. Their autologous, biocompatible, and cost-effective nature makes them safe and promising biomaterials for the treatment of acute and chronic wounds.

1 DVM.; Muğla Sıtkı Koçman University, Faculty of Milas Veterinary Medicine, Department of Surgery, obulut@mu.edu.tr ORCID No: 0000-0003-2773-8243

2 VM.; Aydın Adnan Menderes University, Faculty of Veterinary Medicine, Department of Surgery, ceydaacakarr@gmail.com ORCID No: 0000-0002-1057-1523

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1. INTRODUCTION

Biomimetic science is based on the premise that natural structures are flawless and functional, drawing inspiration from them to develop novel materials and therapeutic methods. Since the 1990s, this approach has gained momentum, particularly in the fields of wound healing and tissue regeneration. From a biomimetic perspective, when the repair mechanisms of the body are examined, blood emerges as the most fundamental element. Blood is regarded as the most important autologous source used by the body in the healing of both soft and hard tissues (Choi et al., 2015; Chantre et al., 2019; Joorabloo & Liu, 2023).

The concept of using blood-derived products in medicine has been explored for nearly 40 years. Initially, platelet-rich products were employed solely as tissue adhesives; however, they are now widely used as biological materials to accelerate wound healing and tissue regeneration. Among these, platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) are the most commonly preferred autologous biomaterials (Fernandez-Moure et al., 2017; Ding et al., 2024; Valenzuela-Mencia & Manzano-Moreno, 2025).

Platelet derivatives act as regenerative tools by releasing growth factors at levels above physiological concentrations, thereby stimulating wound healing (Miron et al., 2017). The alpha and delta granules of platelets contain polypeptides and small molecules that attract both factors and cells to the site of injury. Alpha granules contain von Willebrand factor, fibrinogen, platelet-derived growth factor (PDGF), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), transforming growth factor beta (TGF-β) and insulin-like growth factor (IGF), which activate stem cells, stimulate chemotaxis, mitogenesis and cellular differentiation (Melville et al., 2019). Concentrated platelets accelerate various phases of wound healing, including angiogenesis, cellular repair, proliferation and differentiation (Miron et al., 2017).

2. WOUND HEALING PROCESS

A wound is defined as the disruption of tissue integrity due to trauma and its repair is achieved through a complex series of cellular and biochemical events. Wound healing is classically divided into three main phases: hemostasis and inflammation, proliferation and maturation (remodeling) (Guo & DiPietro, 2010).

2.1. Hemostasis and Inflammation Phase

Immediately following injury, vasoconstriction initiates coagulation. Platelets encounter subendothelial collagen at ruptured vascular sites, triggering platelet aggregation and the coagulation cascade. Cytokines stored within platelets (serotonin, kallikrein, growth factors) are released, leading to neutrophil and phagocyte migration into the wound area via chemotaxis. Increased vascular permeability allows serum proteins to accumulate, while the complement system is activated (Broughton et al., 2006; Schreml et al., 2010; Almadani et al., 2021).

As macrophages and lymphocytes migrate into the wound, inflammation is gradually controlled. During epithelialization, epithelial cells migrate from wound edges to cover the defect in partial-thickness wounds, while full-thickness wounds require longer healing within the dermal tissue. The basal layer of the epidermis thickens through mitotic activity, while the release of IGF-1 and colony-stimulating factors (CSF) further contribute to the healing process (Guo & DiPietro, 2010; Sorg et al., 2017; Almadani et al., 2021).

2.2. Proliferation Phase

The proliferative phase begins around day four and typically continues until day 21. Endothelial cells and fibroblasts are the key players in this stage. Fibroblasts produce fibronectin, collagen, glycosaminoglycans, and elastin, while endothelial cells promote angiogenesis. Wound contraction begins around days 8–10, aiding closure, with fibroblast proliferation and angiogenesis supporting granulation tissue formation (Broughton et al., 2006; Guo & DiPietro, 2010).

2.3. Maturation Phase

The maturation phase is characterized by the balance between collagen synthesis and degradation. This stage determines scar formation and the mechanical strength of the tissue. Collagen production peaks between days 14 and 21, ensuring functional restoration of the wound (Sorg et al., 2017; Almadani et al., 2021).

3. THE ROLE of PLATELETS in WOUND HEALING

Platelets are small, anucleate blood cells derived from megakaryocytes in the bone marrow, with an average diameter of 2 μm. Their trilaminar membrane contains glycolipids, glycoproteins and cholesterol between phospholipid layers. The glycocalyx on the platelet membrane plays a critical role in adhesion and aggregation. Their cytoplasm includes mitochondria, alpha, beta and lambda granules, as well as microtubules. The open canalicular system facilitates the release of active molecules into the extracellular environment (Etulain, 2018; Locatelli et al., 2021).

Alpha granules store a wide variety of bioactive proteins such as PDGF, EGF, IGF, VEGF, PF-4, IL-1, PDEGF, and ECGF. Additional components, including von Willebrand factor (VWF), ADP, thrombospondin-1, osteocalcin and serotonin, contribute to adhesion, activation and fibroblast proliferation. Platelets are therefore the primary source of the complex of growth factors essential for initiating hemostasis and wound healing (Stenberg et al., 1998; Sclafani et al., 2005; Opneja et al., 2019).

4. PLATELET-DERIVED PRODUCTS and THEIR CLASSIFICATION

Dohan Ehrenfest et al. (2009) classified platelet concentrates into the following categories (Dohan Ehrenfest et al., 2009):

1. Pure platelet-rich plasma (P-PRP)
2. Leukocyte- and platelet-rich plasma (L-PRP)
3. Pure platelet-rich fibrin (P-PRF) and leukocyte-poor PRF (LP-PRF)
4. Leukocyte- and platelet-rich fibrin (L-PRF)

Later, Tunali et al. (2013) introduced titanium-prepared PRF (T-PRF), while Choukroun (2014) described advanced PRF (A-PRF) with higher monocyte content and injectable PRF (i-PRF) (Tunalı et al., 2013; Ghanaati et al., 2014; Miron et al., 2017;). These developments expanded the clinical applications of platelet derivatives and optimized wound healing outcomes.

4.1. Fibrin Sealants

Fibrin sealants typically contain fibrinogen/fibrin monomers, thrombin, factor XIII (in most cases) and calcium; some formulations also include aprotinin or other stabilizers. Upon application, thrombin converts fibrinogen into fibrin polymers, forming a local three-dimensional fibrin network (provisional matrix). This structure provides both hemostasis and a cellular scaffold (Albala, 2003; Spotnitz, 2010, 2014).

Fibrin sealants influence various stages of wound healing (Albala, 2003; Spotnitz, 2014):

Hemostasis: fibrin networks rapidly reduce bleeding post-surgery or trauma, impacting the inflammatory phase.

Cell guidance: fibrin matrices provide ligands for fibroblast, endothelial and keratinocyte adhesion and migration, thereby accelerating granulation tissue formation.

Growth factor delivery: fibrin networks retain and gradually release endogenous or exogenous growth factors, enabling use as a local drug or cell delivery system.

The resorption rate of fibrin matrices depends on formulation and concentration, typically occurring within days to weeks; sufficient for cell infiltration and new matrix synthesis. Thus, fibrin sealants act as temporary scaffolds, eventually replaced by collagen and extracellular matrix (Spotnitz, 2014b).

They are widely used in surgery for hemostasis, tissue adhesion, skin graft fixation, fistula closure and more recently as carriers for local agents or cells. However, clinical evidence for direct and independent effectiveness in chronic wounds (e.g., venous ulcers, diabetic foot ulcers) is limited, partly due to heterogeneous protocols and adjunctive use. Supportive data exist for burn wounds and graft applications, although techniques and protocols influence outcomes (Albala, 2003; Spotnitz, 2010).

Despite advantages such as biocompatibility, natural matrix properties and scaffold function, fibrin sealants also present drawbacks: high costs of commercial products, theoretical infection risk when derived from pooled human plasma, immune reactions to bovine thrombin in older formulations, and rare but serious thromboembolic complications from improper use (e.g., intravascular injection) (Radosevich et al., 1997; Spotnitz, 2014).

4.2. Platelet-Rich Plasma (PRP)

PRP is produced by centrifuging autologous blood to concentrate platelets. Protocols differ among laboratories and commercial kits, varying in speed, time and g-force, but the target platelet concentration is generally ~3–5 times baseline (~1,000,000/μL). Activation (e.g., calcium chloride, thrombin) triggers the release of alpha granule contents. Platelets in PRP secrete PDGF, TGF-β, VEGF, EGF, IGF and other cytokines, stimulating fibroblast proliferation and collagen synthesis (PDGF, TGF-β), supporting angiogenesis (VEGF) and accelerating epithelial cell proliferation and re-epithelialization (EGF). They also modulate cellular communication during early inflammation. Overall, PRP enhances the proliferative phase and accelerates granulation tissue formation. Release kinetics depend on preparation and activation protocols (Oneto & Etulain, 2021; Patel et al., 2023).

PRP is generally autologous, reducing risks of immune reactions and infections, though strict asepsis is required. Its main limitations include methodological variability (preparation, activation, application), cost and inconsistent clinical evidence across wound types (Dohan Ehrenfest et al., 2009; Martinez-Zapata et al., 2016; Oneto & Etulain, 2021).

4.3. Platelet-Rich Fibrin (PRF)

PRF is a second-generation platelet concentrate obtained through single-step centrifugation without anticoagulants. Slow polymerization forms a natural fibrin network that entraps platelets, leukocytes and growth factors. This three-dimensional fibrin scaffold serves as a reservoir for the sustained release of growth factors (L. Alio et al., 2012; Mishra, 2021; Yang et al., 2025).

PRF provides prolonged release of platelet-derived growth factors, which is particularly important for maintaining the proliferative phase. Its leukocyte content contributes to immune modulation and antimicrobial activity, while the fibrin scaffold facilitates cell migration (fibroblasts, endothelial cells). PRF thus supports both soft tissue epithelialization and bone regeneration (Jayadev et al., 2013; Miron et al., 2017; Yang et al., 2025).

Numerous clinical studies, especially in dental, periodontal and alveolar surgery, report that PRF enhances soft tissue healing and in some cases, bone regeneration more effectively than PRP. More recent studies in diabetic and chronic wounds also show promising outcomes, suggesting that PRF accelerates wound closure (Dohan et al., 2006; Miron et al., 2017; Silveira et al., 2022; Yang et al., 2025).

Variants such as L-PRF, A-PRF, and i-PRF differ in cellular content and fibrin structure depending on centrifugation parameters and tube type, which influence biological behavior (e.g., leukocyte content, release kinetics). Therefore, reporting the exact PRF protocol is critical for comparative studies (Jayadev et al., 2013; Silveira et al., 2022).

PRF offers several advantages: it requires no anticoagulants, has a simple preparation process, ensures sustained growth factor release, is cost-effective, and is autologous. However, variations in protocols (centrifuge type, rpm, tube material) and heterogeneity in clinical studies remain limitations (Dohan et al., 2006; Yang et al., 2025).

5. CONCLUSION

PRP and PRF applications support epithelial differentiation, dermal matrix organization and vascular growth during wound healing. By enhancing fibroblast proliferation and collagen synthesis, they accelerate epithelialization. PRF, being derived from the patient's own blood, is safe and natural, with minimal scarring, no risk of malignant transformation, and low cost. Recent studies demonstrate that PRP and PRF can be safely and effectively applied in the treatment of wounds.

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