Bio Vet Innovator Magazine

Volume 2 (Issue 9) SEPTEMBER 2025

OPEN ACCESS WORLD RABIES DAY - 28th SEPTEMBER POPULAR ARTICLE

The Clinical Efficacy of Autologous Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF) in Wound Healing in Small Animals with Special Reference to Dogs

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DOI: https://doi.org/10.5281/zenodo.17328160

Received: September 29, 2025
Published: September 30, 2025

Abstract:

Autologous platelet concentrates — principally platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) — are increasingly used as adjunctive regenerative therapies in veterinary wound management. These haemo-components concentrate platelets and their growth factors (e.g., PDGF, TGF-β, VEGF, EGF), which modulate haemostasis, inflammation, angiogenesis, fibroplasia and re-epithelialization. This review synthesizes peer-reviewed experimental and clinical evidence on the clinical efficacy of autologous PRP and PRF for cutaneous wound healing in small animals, with emphasis on canine studies. Overall, experimental and clinical reports indicate that PRP/PRF accelerate granulation tissue formation, enhance angiogenesis and promote earlier re-epithelialization compared with standard care. However, heterogeneity of product preparation, small sample sizes, variable application protocols and inconsistent outcome metrics limit definitive conclusions and preclude universal clinical recommendations. Priority research needs include standardized production and reporting, randomized controlled trials in naturally occurring canine wounds, and head-to-head comparisons of PRP versus PRF formulations.

Keywords: platelet-rich plasma; platelet-rich fibrin; wound healing; dog; veterinary regenerative medicine.

Introduction:

Wound management in small animal practice remains a frequent and sometimes protracted clinical problem. Cutaneous defects in dogs arise from trauma, surgical dehiscence, tumor excision, burns and chronic ulcers (e.g., secondary to endocrinopathies). Second-intention healing may be lengthy, costly and predispose to infection and suboptimal cosmetic and functional outcomes. Platelet-based autologous products, chiefly platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), are attractive adjuncts because they: (a) are autologous (low immunogenicity), (b) concentrate platelet-derived growth factors and

cytokines implicated in tissue repair, and (c) can be prepared clinic-side with modest equipment. Use of these products has expanded rapidly in human medicine and, increasingly, in veterinary practice. This review examines the biological rationale, production variables, clinical application methods and the strength of the available experimental and clinical evidence for PRP and PRF in small animal (especially canine) cutaneous wound healing.

Biological Basis and Mechanism of Action:

- **Platelet cargo and immediate effects:** Activated platelets release a complex mixture of growth factors and cytokines (e.g., platelet-derived growth factor [PDGF], transforming growth factor-β [TGF-β], and vascular endothelial growth factor [VEGF], epidermal growth factor [EGF]) that regulate cell migration, angiogenesis, fibroblast proliferation and matrix deposition — processes central to wound repair. The initial fibrin clot also provides a provisional extracellular matrix supporting cell infiltration and neovascularization (Attili et al., 2021). PRF differs from PRP by virtue of its fibrin architecture (no anticoagulant used during collection) and slower, sustained release of growth factors due to the 3-D fibrin matrix and entrapped leukocytes (Caterino et al., 2022).
- **Cellular response relevant to skin repair:** In vitro and in vivo studies show PRP/PRF stimulate keratinocyte migration, fibroblast proliferation, endothelial cell tubulogenesis and increased collagen deposition — all necessary for timely granulation and re-epithelialization (Jee et al., 2016; Perego et al., 2020). PRF's fibrin scaffold additionally supports cell ingrowth and may prolong mediator availability at the wound bed compared with liquid PRP (Caterino et al., 2022; Soares et al., 2021).
- **PRP: types and preparation variables**: PRP is not a single standardized product. Methods vary (single-spin vs double-spin, commercial kits vs in-house protocols), producing leukocyte-rich PRP (L-PRP) or leukocyte-poor PRP (P-PRP) with different platelet enrichments and leukocyte content. Activation (calcium chloride, thrombin) can convert PRP to a gel for topical use. These differences directly affect growth factor concentrations, inflammatory cell content and clinical responses (Perego et al., 2020; Goodale et al., 2023).
- **PRF: variants and properties: P**RF is typically produced by immediate centrifugation of whole blood in tubes without anticoagulant; a fibrin clot forms that can be used as a membrane or plug (L-PRF, i-PRF, advanced PRF variants exist). PRF entraps platelets and leukocytes in a fibrin architecture that releases growth factors over days, potentially providing longer biologic activity than PRP (Caterino et al., 2022; Soares et al., 2021).

Practical Considerations For Clinicians:

Clinic-side production requires aseptic venipuncture, validated centrifugation settings, and

standardized documentation of starting blood volume, centrifuge g-force/time, and final product yield. For larger dogs, multiple blood tubes may be necessary to yield clinically useful PRP/PRF volumes. Safety is generally favorable because products are autologous, but contamination risk and inconsistent platelet enrichment are practical concerns (Perego et al., 2020; Iacopetti et al., 2020).

Clinical Protocol for PRP/PRF Preparation and Application in Dogs

Step 1. Patient Preparation

- Ensure stability and hydration, No NSAIDs or corticosteroids 7 days prior.
- Use aseptic technique during collection and application.

Step 2. Blood Collection (by Weight)

- **<10 kg:** PRP = 6–8 mL | PRF = 5–6 mL
- **10–25 kg:** PRP = 12–16 mL | PRF = 8–10 mL
- **>25 kg:** PRP = 18–24 mL | PRF = 10–12 mL

☞ Collect into: **PRP:** Sodium citrate tubes. **PRF:** Plain glass tubes (no anticoagulant).

Step 3. Centrifugation Protocols

PRP preparation (Double Spin)

1. **Soft spin:** 1,500 rpm (~200 g), 10 min. → Collect plasma + buffy coat.
2. **Hard spin:** 3,500 rpm (~800 g), 10 min. → Re-suspend platelet pellet in lower 1/3 plasma.
3. **Yield:** 2–4 mL PRP.

PRF preparation (Single Spin)

1. Spin immediately after collection → **Spin:** 3,000 rpm (~400 g), 10–12 min.
2. Harvest fibrin clot (middle layer) → Compress between sterile gauze → PRF membrane.
3. **Yield:** 1–3 clots per 10 mL blood.

Step 4. Application

PRP

- Inject intra-lesionally/peri-lesionally (0.1–0.3 mL/cm²) OR drip topically.
- Repeat every 7–10 days until epithelialization.

PRF

- Place PRF membrane/clot directly on wound.
- Cover with non-adherent dressing.
- Replace every 5–7 days until closure.

Step 5. Post-Application

- Use PRP/PRF within 30 min of preparation and Avoid heparinized tubes.
- Aim for PRP platelet concentration 2–5 times the baseline.
- Standard wound dressing and monitor contraction, granulation, epithelialization.

Figure: Steps depicting the preparation and application of PRP and PRF

Evidence From Experimental Studies In Dogs:

Controlled experimental work in canine and other mammalian models has repeatedly shown that platelet concentrates accelerate measurable wound healing endpoints (wound contraction, granulation, angiogenesis, collagen organization) compared with controls (Jee et al., 2016; Angelou et al., 2022). These data provide mechanistic and proof-of-concept support but are often conducted in healthy animals with standardized wounds that do not fully replicate the heterogeneity of clinical cases.

Evidence From Clinical Canine Reports And Case Series:

Clinical evidence in dogs comprises case reports, case series and a smaller number of controlled clinical studies:

1. **Intra-lesional PRP in experimental canine wounds:** Jee et al. (2016) performed intralesional PRP injections into full-thickness wounds in beagles and reported more granulation tissue, increased angiogenesis and faster epithelialization versus saline controls.
2. **Topical autologous PRP in naturally occurring wounds:** Iacopetti et al. (2020) reported on repeated topical application of autologous PRP in large subacute cutaneous wounds of dogs and observed accelerated contraction and re-epithelialization with no major complications.
3. **Canine PRF clinical uses:** Soares and colleagues described canine-origin PRF products and reported beneficial effects on granulation and epithelialization in feline and canine wounds in preliminary studies and a clinical case series (Soares et al., 2021; Soares et al., 2024).
4. **Production and characterization studies:** Multiple veterinary studies have focused on standardizing production (centrifugation parameters, membrane handling) and quantifying growth factor release from canine PRF/PRP (Caterino et al., 2022; Perego et al., 2020).

Across clinical reports, PRP/PRF were generally associated with improved early granulation, increased angiogenesis, reduced time to re-epithelialization and acceptable safety profiles (Iacopetti et al., 2020; Jee et al., 2016; Soares et al., 2024). However, most clinical reports are small, nonrandomized and often lack blinded outcome assessment.

Antimicrobial And Immune-Modulatory Properties:

In vitro and some in vivo data indicate platelet concentrates may exert bacteriostatic/bactericidal effects or modulate local inflammation (Attili et al., 2021). While promising, these findings require careful translation to clinical practice because results depend on activation status, leukocyte content and bacterial species.

Outcome Measures Reported And Safety:

- **Common endpoints:** Studies report endpoints such as percent wound area reduction, time to complete epithelialization, histologic indices (collagen maturity, neovascular density), pain/comfort scores, infection rates and need for secondary interventions. Lack of standardization across studies impedes pooled quantitative synthesis.
- **Safety and adverse events:** Autologous PRP/PRF exhibit favorable safety in reported veterinary studies; no consistent major adverse immune reactions have been documented. Transient local inflammation is occasionally observed, particularly with leukocyte-rich formulations (Iacopetti et al., 2020; Soares et al., 2024). Strict asepsis during collection and application is essential.

Current Evidence Based Practical Clinical Recommendations:

1. **Indications:** PRP/PRF are reasonable adjuncts for subacute or chronic cutaneous wounds, second-intention healing where granulation is delayed, and selected non-healing ulcers after standard debridement and infection control. They are not a substitute for definitive surgical reconstruction

when indicated. (Iacopetti et al., 2020; Jee et al., 2016)

2. **Product selection:** Choose PRF for a structural membrane/scaffold and sustained release of growth factors (e.g., poorly vascularized chronic wounds). Use PRP when injectable application or gel formation is desired. Consider leukocyte content: leukocyte-rich products may have antimicrobial benefits but might increase local inflammation.
3. **Protocol tips:** Document starter blood volume, centrifugation g-force and time, product volume and platelet counts (if available). Typical clinical schedules reported include initial application and repeat treatments at 7–14 day intervals until satisfactory progress is observed.
4. **Adjunctive care:** PRP/PRF should be deployed alongside proper wound bed preparation (debridement, control of infection, maintenance of a moist wound environment) and management of systemic comorbidities impairing healing.
5. **Documentation:** Use standardized digital planimetry (photography with scale) and predefined timepoints for objective wound area measurements to support outcome assessment and contribute to the evidence base.

Key Limitations:

Heterogeneity of products and protocols: Variation in centrifugation, activation and leukocyte content leads to inconsistent biologic products and outcomes (Perego et al., 2020; Caterino et al., 2022).

1. **Small, nonrandomized clinical studies:** Many canine studies are case series with limited sample sizes and potential biases (Iacopetti et al., 2020; Soares et al., 2024).
2. **Outcome heterogeneity and lack of standardized reporting:** Diverse endpoints and measurement techniques limit cross-study comparisons and meta-analysis.

Research Priorities:

a) Randomized controlled clinical trials comparing PRP, PRF and standard care in naturally occurring canine wounds with predefined, clinically relevant endpoints.

b) Standardization of PRP/PRF production parameters and minimum reporting requirements (blood volume/kg, spin settings, platelet enrichment, leukocyte profile).

c) Head-to-head comparative studies of PRP vs PRF and leukocyte-rich vs leukocyte-poor formulations.

d) Special population studies (e.g., diabetic dogs, endocrinopathies) to define safety and efficacy across comorbid states.

e) Economic analyses to assess cost-benefit in routine clinical practice.

Conclusion:

Autologous PRP and PRF are promising adjuncts for cutaneous wound healing in small animals, particularly dogs. Experimental and clinical studies demonstrate consistent biologic plausibility and

frequently report accelerated granulation and epithelialization with favorable safety. Nonetheless, heterogeneity in product manufacture, limited randomized data and variable outcome measures restrict definitive clinical guidance. Clinicians using PRP/PRF should do so as adjuncts to established wound care, document outcomes rigorously and, where possible, contribute cases to standardized clinical trials or registries. Standardization of production and reporting, together with well-designed randomized trials, are essential to define the precise role of PRP and PRF in canine wound management.

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