Review Article

Use of Platelet-rich Plasma, Platelet-rich Fibrin and Their Combinations in Veterinary Orthopaedics: A Comprehensive Review

Nura Abubakar, Abubakar Sadiq Yakubu, Ekaete Ime Oviawe

Department of Surgery and Radiology, Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto, Nigeria

Abstract

Orthopaedic disorders are a major cause of lameness, pain and productivity loss in animals, presenting significant clinical and economic challenges. Advances in regenerative medicine have highlighted platelet-derived biomaterials**,** particularly platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), as promising autologous therapies for musculoskeletal healing. PRP, a first-generation concentrate, delivers a rapid release of growth factors such as platelet-derived growth factor, transforming growth factor-beta and vascular endothelial growth factor, promoting early angiogenesis and inflammation modulation. PRF, a second-generation biomaterial, provides a fibrin scaffold that supports sustained growth factor release, cellular proliferation and tissue remodelling. Both individually enhance bone regeneration, tendon and ligament repair and osteoarthritis management in various species. Their combination (PRP–PRF) shows synergistic effects, pairing PRP's immediate biochemical stimulation with PRF's structural support, improving bone density, collagen organisation and mechanical strength. Clinical application, however, is limited by variability in preparation protocols, platelet concentration and species-specific responses. Standardisation, objective outcome measures and multicentre trials are needed to establish the reproducible guidelines. Future strategies include integrating PRP and PRF with biomaterials, stem cells and controlled release systems to enhance bioactivity and optimise regeneration in complex orthopaedic defects. Collectively, PRP and PRF are safe, cost-effective and biologically potent adjuncts that can improve tissue regeneration and reduce recovery time in veterinary practice.

Keywords: Platelet-rich fibrin, platelet-rich plasma, regenerative medicine, tissue healing, veterinary orthopaedics

Introduction

Orthopaedic disorders remain a major cause of lameness, pain and reduced performance in animals, significantly impacting welfare, productivity and economic value. The conditions such as bone fractures, tendon and ligament injuries and degenerative joint diseases are common in both companion and production animals, and they often pose therapeutic challenges due to the limited regenerative potential of musculoskeletal tissues.(1) Traditional treatment modalities including surgical fixation, bone grafting and pharmacological interventions are effective to varying degrees but may not fully restore the structural and functional integrity of damaged tissues. (2) In recent years, regenerative medicine has emerged as a promising field in veterinary orthopaedics, aiming to enhance the body's innate healing capacity through the use of biologics and bioactive materials.(2)

Access this article online

Quick Response Code:

Website: https://journals.lww.com/ajvs

DOI: 10.4103/AJVS.AJVS_31_25

Amongst the various biological therapies, platelet concentrates such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) have gained considerable attention. These autologous preparations, derived from the animal's own blood, are rich in growth factors, cytokines and other signalling molecules that play vital roles in inflammation modulation, angiogenesis and tissue regeneration.(2,3) PRP represents a first-generation platelet concentrate, consisting primarily of plasma with a high platelet count and a fibrin network that releases bioactive factors upon activation.(2) PRF, on the

Address for correspondence: Dr. Nura Abubakar, Department of Surgery and Radiology, Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto, Nigeria.
E-mail: abubakar.nura@udusok.edu.ng

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How to cite this article: Abubakar N, Yakubu AS, Oviawe EI. Use of platelet-rich plasma, platelet-rich fibrin and their combinations in veterinary orthopaedics: A comprehensive review. Al-Anbar J Vet Sci 2026;19:7-16.

Received: 21-11-2025, **Revised:** 14-12-2025,
Accepted: 25-12-2025, **Published:** 31-07-2026

other hand, is a second-generation biomaterial that forms a three-dimensional fibrin scaffold capable of providing a more sustained release of growth factors, as well as serving as a natural matrix for cell migration and proliferation.(3,4)

The application of PRP and PRF in orthopaedics stems from their biocompatibility, ease of preparation, cost-effectiveness and autologous origin, which minimise the risk of immunogenicity and disease transmission.(2) These biomaterials have been applied in the management of diverse orthopaedic conditions in animals, including bone defects, osteoarthritis (OA), tendon and ligament injuries and wound healing, with encouraging outcomes reported across various species such as dogs, horses and cats (1, 4, and 6). Furthermore, the combination of PRP and PRF has recently been explored to harness the advantages of both liquid and solid platelet matrices, potentially yielding synergistic effects on bone and soft-tissue healing.(5)

Despite the growing body of the literature, there remains considerable variability in preparation protocols, dosage and clinical results among studies, making it difficult to establish the standardised guidelines for veterinary use.(6) Moreover, most current knowledge is extrapolated from human orthopaedic research, underscoring the need for species-specific investigations that address the unique biological responses of animals.(1,2)

This review aims to provide a comprehensive evaluation of the current evidence on the use of PRP, PRF and their combinations in veterinary orthopaedics. It discusses their biological principles, preparation techniques and clinical applications in different animal models, highlighting both the therapeutic potential and existing limitations. In addition, emerging trends, challenges in standardisation and future directions for research and clinical translation are explored to guide the evidence-based use of these regenerative therapies in veterinary practice.

Platelet-derived Products: Biology and Mechanisms

Platelet composition and function

Platelets are small, anucleate cellular fragments derived from megakaryocytes and are rich reservoirs of bioactive molecules contained primarily in alpha granules, dense granules and the open canalicular systems.(7) Once activated, platelets degranulate to release growth factors, cytokines, chemokines and other signalling molecules into the peri-environment.(7,8) The growth factors commonly released include platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), VEGF, basic fibroblast growth factor (bFGF), insulin-like growth factor (IGF) and others.(1,7) These factors act in a paracrine or autocrine fashion to influence cell migration, proliferation, differentiation, extracellular matrix (ECM) synthesis and angiogenesis.(1,7)

In bone and soft-tissue repair, specific growth factors play critical roles: for example, TGF-β and bone morphogenetic protein (BMP) (members of the TGF super family) regulate osteogenesis and chondrogenesis; PDGF stimulates chemotaxis and mitogenesis of mesenchymal cells; VEGF promotes angiogenesis and enhances nutrient supply and IGF and bFGF support cell proliferation and matrix synthesis.(1,7) The relative concentrations and temporal release profile of these factors influence the regenerative cascade's success.

Mechanisms of action in bone and soft-tissue healing

When platelet concentrates such as PRP or PRF are applied to damaged tissues, several overlapping mechanisms contribute to healing. First, the initial inflammatory phase is modulated, as platelet-derived mediators can recruit leukocytes, monocytes/macrophages and progenitor cells to the injury site.(8) Second, the release of growth factors stimulates proliferation of local progenitor or stem cells, upregulating genes involved in matrix synthesis, differentiation and ECM remodelling.(7,8) Third, angiogenesis is promoted through VEGF and related factors, which is essential for bringing nutrients, oxygen and additional progenitor cells into the repair site.(7)

In osseous healing, platelet factor-mediated signals synergise with mechanical cues and endogenous bone healing pathways. For example, PDGF contributes to vascularisation and cell recruitment in early phases, while TGF-β and BMPs drive the differentiation of mesenchymal progenitors into osteoblasts.(7,9) VEGF is also implicated in coupling angiogenesis and osteogenesis, thus helping to support new bone formation.(7,9)

In soft tissues such as tendons, ligaments and cartilage, the matrix scaffold and growth factors help modulate catabolic and anabolic balance. They can suppress matrix metalloproteinase (MMP) activity, stimulate collagen synthesis and regulate cellular apoptosis or proliferation in chondrocytes and tenocytes.(1,7) Moreover, platelet concentrates may modulate inflammation, reducing excessive catabolic cytokine signalling.(8)

It is worthnoting that the kinetics of growth factor release differs between preparations. Some systems or activation strategies yield a rapid 'burst' release within hours, while scaffolded or fibrin-based systems allow sustained, controlled release over days to weeks.(4) This temporal aspect is critical: a too-rapid release may exhaust growth factor supply prematurely, while too slow a release may not sufficiently modulate early inflammation.(4) In addition, the cellular milieu (resident progenitors, vascular supply and inflammatory state) and mechanical environment (load and stability) critically influence the net effect of the platelet product.

The variability in biologic response is an important consideration. Differences in species, platelet baseline counts, donor physiological factors (age, sex and health status) and the precise composition of the platelet concentrate (leucocyte content and fibrin architecture) all modulate efficacy.(8,10) This underscores the necessity of standardisation and precise reporting in studies of platelet biologics.

Platelet-rich Plasma

Definition and classification

PRP is defined as an autologous blood derivative containing a platelet concentration above baseline levels, suspended in a small volume of plasma.(6,11) The product is prepared through centrifugation or filtration techniques designed to concentrate platelets and their associated growth factors.(11) PRP is broadly classified based on its leucocyte and fibrin content into pure PRP, leucocyte-rich PRP, pure PRF and leukocyte- and PRF (L-PRF).(12) This classification reflects differences in biological activity, viscosity and the release kinetics of growth factors, which subsequently influence their clinical applications and outcomes.(13)

Autologous PRP is the most common form used in veterinary medicine because it eliminates the risk of immune rejection and disease transmission.(8,11) However, studies have also explored the use of allogeneic or xenogeneic platelet preparations, particularly in large animals where the volume required for treatment exceeds safe autologous limits.(1)

Preparation techniques

PRP can be prepared from autologous whole blood using a standardised double-spin centrifugation technique. Five mL of blood is withdrawn from the animal using a sterile syringe and immediately transferred into sterile tubes containing citrate dextrose solution as an anticoagulant at a 9:1 blood-to-anticoagulant ratio**,** in accordance with established PRP preparation protocols to prevent premature platelet activation.(6,14)

The anticoagulated blood is first centrifuged at low speed (1200–1500 rpm for 10 min) to separate erythrocytes from plasma based on density differences.(6) Following centrifugation, the supernatant plasma layer, including the buffy coat rich in platelets and leucocytes, is carefully aspirated without disturbing the red blood cell layer and transferred into new sterile tubes.

A second centrifugation is then performed at higher speed (3000–3500 rpm for 10 min) to concentrate platelets, resulting in the formation of a platelet pellet at the bottom of the tube.(14) The upper portion of platelet-poor plasma is discarded, leaving approximately 1 mL of plasma to resuspend the platelet pellet. Gentle mixing is performed to obtain a homogeneous PRP preparation.

In veterinary applications, centrifugation parameters are commonly adjusted to accommodate species-specific haematological characteristics. For instance, equine PRP protocols may require lower centrifugation speeds and longer centrifugation times compared with canine protocols due to differences in red blood cell size and haematocrit values.(14) Despite the availability of various commercial PRP preparation systems, there is currently no universally standardised protocol for PRP preparation in animals**,** which complicates direct comparison between studies and contributes to variability in reported biological outcomes.(8,11) The prepared PRP is typically used immediately after preparation without the addition of exogenous activators.

Biological properties and mechanisms

PRP contains a concentrated mix of growth factors and cytokines, including PDGF, vascular endothelial growth factor (VEGF), TGF-β, IGF-1, fibroblast growth factor (FFG) and epidermal growth factor., all of which play key roles in wound healing and bone regeneration.(7,11) Upon activation using calcium chloride, thrombin or mechanical stimuli, platelets release these bioactive molecules, initiating a cascade that promotes angiogenesis, stem cell recruitment, ECM formation and collagen synthesis.(7,8)

The regenerative effects of PRP are mediated through multiple mechanisms: (1) Enhancement of local cell proliferation and differentiation, (2) modulation of inflammation by balancing pro- and anti-inflammatory cytokines and (3) promotion of neovascularization, which supports nutrient and oxygen delivery to the injured site.(11,13) PRP's anti-inflammatory action is particularly relevant in chronic joint diseases, as it can suppress Interleukin-1 beta (IL-1β) and Tumour Necrosis Factor-alpha (TNF-α) expression, while enhancing IL-10 production.(15)

Applications in veterinary orthopaedics

Bone healing and fracture repair

PRP has been used to accelerate fracture repair and enhance graft incorporation in animals. Studies have shown improved bone mineral density, faster callus formation and increased biomechanical strength when PRP is used alone or combined with bone substitutes.(9,14) The growth factor release profile of PRP supports osteoblast proliferation and differentiation, which contributes to more rapid bone bridging.(9)

Tendon and ligament injuries

Tendinopathies are common in performance animals such as horses and dogs. PRP application has demonstrated improvements in tendon fibre alignment, vascularisation and tensile strength.(1,8) In equine superficial digital flexor tendon injuries, intralesional PRP injections have resulted in reduced re-injury rates and shorter recovery periods compared to conventional therapies.(1)

Joint disorders (e.g., osteoarthritis)

Intra-articular administration of PRP has gained popularity for managing OA in dogs and horses. It exerts chondroprotective effects by enhancing hyaluronic acid production, reducing oxidative stress and suppressing catabolic enzymes such as MMP-13.(7,5) Comparative studies have shown that PRP can be as effective as or better than corticosteroids or hyaluronic acid in improving joint function and pain scores.(15,16)

Spinal and cartilage regeneration

Experimental studies indicate that PRP can support intervertebral disc regeneration and cartilage matrix restoration through the activation of mesenchymal stem cells (MSCs) and upregulation of collagen type II and aggrecan synthesis.(13,16)

Limitations and variability

Despite promising outcomes, several challenges hinder PRP's consistent clinical success. These include variability in platelet concentration, activation method and delivery techniques, all of which influence therapeutic efficacy.(6,11) Differences amongst animal species in platelet count and growth factor release kinetics further complicate standardisation.(8) Moreover, the lack of large randomised controlled trials in veterinary patients limits the establishment of evidence-based protocols.(8,11)

Future work should focus on defining optimal PRP formulations, identifying biomarkers predictive of treatment response and integrating PRP with complementary biomaterials or cell-based therapies to enhance and prolong the regenerative outcomes.(8,11)

Platelet-rich Fibrin

Definition and evolution

PRF is a second-generation autologous platelet concentrate obtained from whole blood without anticoagulants, forming a three-dimensional fibrin matrix that entraps platelets, leucocytes and growth factors, enabling a sustained release of bioactive molecules at the application site.(3,12) Variants of PRF have been developed to modulate cellular content and release kinetics; notable examples include L-PRF, advanced PRF (A-PRF) and injectable PRF (i-PRF). Each differs in centrifugation parameters and clinical handling properties.(4,17)

Preparation protocols

PRF is typically prepared by collecting venous blood in plain tubes and centrifuging immediately. The absence of an anticoagulant allows clot formation during centrifugation, producing a fibrin clot that is then separated from red blood cells.(3,17) Specific protocols (Revolutions Per Minute/Relative Centrifugal Force and time) determine the final architecture and cell content.(18) For example, A-PRF uses lower centrifugation speeds and longer times to increase leukocyte and growth factor retention, whereas i-PRF is produced at low speed for a short duration to yield a flowable product suitable for injection.(4,18) Species-specific hematologic differences (platelet size and baseline counts) and tube type also influence PRF yield and must be considered when adapting protocols for veterinary patients.(3,18)

Structural and biological characteristics

The fibrin matrix of PRF acts as a natural scaffold that supports cell migration and provides mechanical stability, while entrapped platelets and leukocytes release growth factors such as PDGF, TGF-β, and VEGF over an extended period compared with typical PRP preparations.(4,19) This sustained release profile reported to persist for days to weeks depending on preparation and species is thought to better match the temporal demands of tissue repair, promoting angiogenesis, matrix deposition, and modulation of inflammation.(4,20) Proteomic studies of animal-derived PRF confirm a complex mixture of proteins involved in matrix remodelling, cell proliferation and immune regulation, supporting its multifunctional role in regeneration.(3,20)

Applications in veterinary orthopaedics

PRF has been applied across a range of veterinary musculoskeletal problems. In wound and soft-tissue management, canine and feline clinical reports demonstrate accelerated epithelialisation and improved collagen organisation following topical PRF application.(21,22) For bone and periodontal defects, PRF membranes or composites have been used as graft adjuncts to enhance bone fill and graft incorporation in preclinical and clinical cases.(9,23) i-PRF is emerging as a minimally invasive option for intralesional treatment of tendon, ligament and early osteoarthritic lesions in animals, with preliminary studies showing improved histological organization and functional outcomes compared to controls.(8,24) However, most studies remain small or experimental and species-specific randomised trials are limited.

Combination use and composite strategies

PRF is frequently combined with other biomaterials (autografts, allografts, bone substitutes and polymers) to produce composite scaffolds that leverage PRF's biologic signalling and the mechanical properties of synthetic or natural carriers. Recent reviews and experimental reports highlight improved cell infiltration, neovascularisation and bone formation when PRF is used with calcium phosphates, titanium scaffolds or polymeric matrices in animal models.(5,23)These combination strategies are attractive in veterinary orthopaedics where larger defects or load-bearing reconstructions require additional structural support alongside biologic enhancement.(5)

Limitations, safety and standardisation needs

Despite broad interest, PRF faces several limitations: heterogeneous preparation methods across studies, variable reporting of centrifugation parameters and product characterisation and limited high-quality clinical trials in animals.(17,18) Autologous PRF is generally safe, but where autologous sourcing is impractical (e.g., in small or critically ill patients), recent studies suggest screened allogeneic PRF may be a viable alternative with low immunogenicity, although this requires careful donor screening and further validation.(25) Finally, to reliably translate PRF into veterinary practice, standardised production protocols, clear product characterisation (platelet/leucocyte counts and growth factor release profiles) and rigorous outcome studies are urgently needed.(3,18)

Combined Use of Platelet-rich Plasma and Platelet-rich Fibrin in Orthopaedics

Rationale for combination

The combined use of PRP and PRF is an emerging strategy designed to synergise the distinct biological and mechanical advantages of each product. PRP offers a rapid release of PDGFs that stimulate early cellular recruitment and angiogenesis, whereas PRF provides a fibrin-based scaffold

capable of sustained growth factor release and mechanical support at the defect site.(8,19) The integration of both materials is hypothesised to yield a dual-phase healing effect, an immediate biochemical boost from PRP followed by prolonged trophic support from PRF.(4,19)

This concept mirrors tissue-engineering principles that emphasise the temporal coordination of growth factor availability and structural stability during repair. Several authors have proposed that combining liquid PRP with solid or i-PRF allows for better retention of bioactive molecules and improved handling characteristics, particularly for irregular bone or cartilage defects.(5,17)

In vitro and *in vivo* evidence

In vitro studies using animal-derived MSCs have demonstrated enhanced proliferation, osteogenic differentiation and collagen synthesis when cultured with combined PRP–PRF preparations compared to either material alone.(5,13) The fibrin mesh in PRF provides an ideal substrate for cellular adhesion, while soluble factors in PRP potentiate cellular metabolic activity and gene expression related to osteogenesis and angiogenesis.(4,21)

In vivo experiments further support this synergy. For instance, in rabbit critical-size bone defects, PRP + PRF composites resulted in significantly higher bone volume fraction and vascular density than single-material controls.(5) Similar outcomes have been reported in canine and equine defect models, where combined applications accelerated mineralisation and enhanced histologic bone maturity.(8,21) The combined matrix also shows promise in enhancing cartilage repair, where sustained delivery of growth factors promotes chondrocyte proliferation and ECM deposition.(16,19)

Applications in veterinary orthopaedics

Critical-size bone defects

Large bone defects remain challenging to treat due to poor vascularisation and limited osteogenic potential. The PRP–PRF composite has been applied as biologically active filler in conjunction with bone substitutes, significantly improving defect bridging and callus organization in animal models.(5,9) In animal trials, PRP–PRF combinations have been shown to support faster mineralisation and more uniform bone regeneration than single materials.(5,9)

Osteochondral and cartilage regeneration

Combined platelet matrices have been used intra-articularly to treat early osteoarthritic lesions and full-thickness cartilage defects. Studies demonstrate improved lameness scores, increased cartilage thickness and higher expression of cartilage-specific markers such as collagen type II and aggrecan following PRP–PRF therapy.(7,16) The fibrin matrix helps maintain chondrocyte phenotype and enhances nutrient retention within the joint microenvironment.(3)

Spinal fusion and fracture management

In spinal arthrodesis and long-bone fractures, PRP–PRF composites have been utilised to augment graft fixation and enhance osteointegration. Experimental data indicate improved bone–implant contact and higher mechanical strength at the fusion site.(7,9)

Limitations and Future Directions

Despite encouraging preclinical evidence, the clinical translation of PRP–PRF combinations in veterinary orthopaedics remains limited by methodological inconsistencies and a lack of standardized protocols.(8,18) Critical variables such as platelet concentration, PRP-to-PRF ratio and activation timing have not been universally optimised.(3,8) Moreover, species-specific responses suggest that dosing and kinetics may vary significantly between small and large animals.(1,8)

Future research should focus on comparative trials evaluating combined PRP–PRF formulations across species, as well as on controlled-release systems and bioengineered scaffolds designed to further modulate growth factor delivery.(5,26)Integration with stem cell therapy and 3D-printed biomaterials represents another promising frontier, aiming to replicate physiological healing dynamics more closely.(5,26)

Comparative Evaluation of Platelet-rich Plasma, Platelet-rich Fibrin and Their Combination in Veterinary Orthopaedics

Overview of Comparative Studies

Direct comparisons between PRP, PRF and their combination have provided valuable insights into their relative efficacy in musculoskeletal repair. While both PRP and PRF contain similar growth factors such as PDGF, TGF-β and VEGF, their release kinetics, fibrin architecture and biological interactions differ significantly.(4,8) Comparative studies in veterinary orthopaedics have demonstrated that PRF often exhibits superior tissue integration due to its three-dimensional fibrin network, which supports cellular migration and sustained factor delivery.(13) Conversely, PRP's high fluidity allows for easier injection and rapid early angiogenic signalling, but its growth factor release is short-lived.(5,8) The combination of PRP and PRF therefore seeks to exploit the early action of PRP and the prolonged effect of PRF, offering a balanced healing environment.(4)

Comparative efficacy in bone healing

Studies involving bone regeneration in animal models such as rabbits and dogs have shown that PRP–PRF composites can outperform either PRP or PRF alone in terms of radiographic bone density, callus maturity and biomechanical strength.(5,9) Histological evaluations in these studies often reveal greater osteoblastic activity and more organised collagen deposition in the combination group, suggesting synergistic osteoinductive and osteoconductive effects.(5) In canine long-bone fractures, PRF alone improved early stability and soft callus formation, whereas PRP accelerated initial inflammation and vascularisation. However, when combined, the materials produced significantly higher bone volume fraction and earlier cortical bridging, reflecting an optimal healing sequence.(8,9)

Comparative outcomes in cartilage and tendon repair

Cartilage repair remains a major challenge due to the tissue's avascular nature and limited intrinsic regenerative potential. Comparative trials in equine and canine OA models indicate that both PRP and PRF can reduce pain and improve joint function, but their effect profiles may differ.(1,16) When combined intraarticularly, a synergistic effect is often observed, with PRP rapidly modulating inflammation and supplying early growth factors, while PRF sustains a slow release of growth factors that supports chondrocyte differentiation and matrix synthesis.(3,7) In tendon healing studies, PRF has been shown to provide superior tensile strength at the repair site due to its fibrin density, whereas PRP primarily influences neovascularization and early fibroblast proliferation.(1,19)

Biomechanical and histological comparisons

Biomechanical assessments in various animal models indicate that PRP–PRF composites can produce greater ultimate load to failure and enhanced stiffness compared to individual applications.(5,9) Histologically, the combination exhibits better collagen alignment, reduced fibrous tissue deposition and higher osteoid formation.(9,13) Furthermore, scanning electron microscopy reveals that the PRF matrix serves as a microstructural scaffold that traps PRP-derived cytokines, resulting in a gradual release and spatially distributed healing stimulus.(3,5) These findings confirm that the integration of PRP and PRF modifies both the biochemical microenvironment and mechanical behaviour of healing tissues.

Cost, practicality and clinical translation

From a clinical standpoint, PRP preparation is generally faster and easier, but its storage stability is poor and requires strict anticoagulant handling.(10) PRF, on the other hand, is simpler to prepare (without anticoagulants) and potentially more cost-effective but may yield smaller volumes and less uniformity.(18) The combination of PRP and PRF offers a middle ground improved biological performance with acceptable clinical feasibility. In small animal practice, combined PRP–PRF treatments are gaining popularity for fracture repair, joint therapy and ligament reconstruction, while large animal studies are exploring standardised protocols for field application in horses and cattle.(1,8)

Mechanisms of Action and Growth Factor Dynamics in Platelet-rich Plasma and Platelet-rich Fibrin

Overview of platelet biology and activation pathways

Both PRP and PRF act primarily through the release of bioactive molecules stored in platelet α-granules, dense granules and lysosomes.(7,8) Upon activation, platelets secrete a wide array of growth factors, cytokines and adhesion molecules that collectively modulate inflammation, angiogenesis and tissue regeneration.(7,13)

In PRP, platelets are activated chemically usually with calcium chloride or thrombin resulting in an immediate burst release of growth factors such as PDGF, TGF-β, VEGF and IGF.(7,8) PRF, however, is prepared without anticoagulants, allowing for natural coagulation and gradual fibrin polymerization, which traps platelets and leucocytes within a dense fibrin network. This leads to a sustained release of growth factors over 7–10 days, mimicking physiological wound healing kinetics.(4,19)

Growth factor profile and release kinetics

Platelet-derived growth factor

PDGF plays a crucial role in recruiting MSCs and promoting fibroblast proliferation and collagen synthesis.(8) PRP exhibits a rapid, high-concentration release of PDGF within hours of activation, whereas PRF maintains lower but sustained levels over several days.(4,19) The prolonged PDGF availability from PRF supports continuous cellular proliferation during bone remodelling and cartilage regeneration.(19)

Transforming growth factor-beta

TGF-β modulates chondrogenesis, osteoblastic differentiation and ECM formation.(7) Its slow release from PRF matrices favours long-term modulation of cell behaviour, while PRP provides a rapid boost in the early inflammatory phase.(1,4) Combined PRP–PRF systems ensure early and sustained TGF-β activity, resulting in better tissue maturation.(5)

Vascular endothelial growth factor

VEGF is essential for angiogenesis and nutrient delivery in healing tissue.(7) PRP induces an early angiogenic surge that enhances granulation tissue formation, whereas PRF sustains endothelial cell migration and neovascularisation.(13) The complementary release kinetics are particularly beneficial in critical-size bone defects and avascular cartilage zones.(5,9)

Bone morphogenetic proteins and insulin-like growth factor

Recent proteomic analyses have detected BMP-2, BMP-7 and IGF-1 in both PRP and PRF preparations, contributing to osteogenic and anabolic effects in bone and tendon tissues.(7,9) The presence of these factors underscores the regenerative potential of platelet concentrates as natural bioreactors capable of guiding stem cell differentiation.(7)

Cellular and molecular interactions

At the cellular level, platelet-derived factors influence a network of signalling pathways, including mitogen-activated protein kinase, Phosphoinositide 3-Kinase/Protein Kinase B and Smad cascades, which regulate gene expression associated with proliferation, angiogenesis and matrix deposition.(7) In particular, the Smad pathway is activated by PDGFs such as BMPs, which bind to cell surface receptors, phosphorylate receptor-regulated Smads (R-Smads) and form complexes with Smad4 that translocate to the nucleus to drive gene transcription for osteoblast differentiation and bone matrix production. PRP primarily initiates these pathways during the early inflammatory and proliferative phases, while PRF extends their activation during tissue remodelling.(4) Leukocytes present in PRF contribute antimicrobial peptides

and immune-modulatory cytokines such as IL-1β and IL-6, which balance inflammation and promote tissue regeneration.(4) Moreover, the dense fibrin structure of PRF serves as a temporary ECM, facilitating cell adhesion, migration and mechanical stability at the injury site.(4,19)

Temporal dynamics and synergy in combined use

The temporal release dynamics of growth factors is a major determinant of healing success. PRP acts within the first 24–48 h, stimulating haemostasis and initiating angiogenesis, whereas PRF continues to release bioactive molecules for up to 2 weeks.(4,8) This sequential delivery, when combined, mimics the natural progression of wound healing from inflammation to proliferation to remodelling.(4) In osteochondral and tendon repair models, the PRP–PRF combination enhances both early angiogenic signalling and long-term matrix maturation, leading to improved biomechanical properties and more organised tissue architecture.(5,7)

Summary of mechanistic insights

The regenerative capacity of PRP and PRF is mediated by their distinct yet complementary growth factor kinetics, fibrin architectures and cellular interactions. PRP provides a rapid, high-intensity biochemical response, while PRF ensures prolonged trophic and mechanical support. Their combined application produces sequential and synergistic activation of cellular and molecular pathways essential for musculoskeletal tissue regeneration in animals.(5,8)

Clinical Applications of Platelet-rich Plasma and Platelet-rich Fibrin in Veterinary Orthopaedics

Overview

In veterinary orthopaedics, PRP and PRF have transitioned from the experimental models to clinical use for managing fractures, joint disorders and tendon or ligament injuries.(8,18) Their appeal lies in their autologous origin, biocompatibility and growth factor-mediated healing, reducing reliance on synthetic implants or pharmacological interventions.(8,18) These materials are increasingly employed in small and large animal practices due to ease of preparation, safety and adaptability to field conditions.(1,18)

Fracture repair and bone regeneration

Platelet-rich plasma and platelet-rich fibrin as biological adjuncts

Fracture healing involves complex biological events hematoma formation, inflammation, callus development and remodelling that can be enhanced by PDGFs.(9) PRP accelerates the early inflammatory and angiogenic phases, whereas PRF supports osteoconduction and osteoinduction due to its fibrin scaffold and sustained release of TGF-β and PDGF.(3,4)

Preclinical and clinical findings

In canine femoral and tibial fractures, PRF application has been shown to improve callus density, radiographic healing scores and mechanical strength compared with untreated controls.(9)PRP may demonstrate faster initial callus formation but can show weaker structural integrity at later stages due to its rapid degradation.(8) The combination of PRP and PRF has yielded superior outcomes, particularly in critical-size bone defects, where synergistic effects enhanced both early vascularisation and later mineralisation.(5)

In equine orthopaedics, PRP and PRF are frequently used alongside bone grafts or implants to improve bone–implant integration and reduce non-union rates.(1) Studies have reported improved bone volume when PRP–PRF composites were used to fill segmental defects.(5)

Joint therapy and osteoarthritis management

Mechanisms and rationale

OA in animals involves chronic inflammation, cartilage degradation and synovial fibrosis. PRP and PRF modulate the joint microenvironment by downregulating inflammatory mediators (e.g., IL-1β and TNF-α) and stimulating chondrocyte proliferation and ECM synthesis.(7,16) PRP's high concentration of growth factors promotes synovial regeneration and lubrication, while PRF serves as a sustained intra-articular reservoir that maintains trophic factor release over several days.(4,16)

Clinical outcomes

In canine and equine OA models, intra-articular PRP or PRF injections have significantly improved lameness scores, joint range of motion and cartilage thickness compared with controls.(1,8) A combination of PRP and PRF has been observed to provide longer-lasting pain relief and improved cartilage quality.(3)

Tendon and ligament regeneration

Platelet-rich plasma and platelet-rich fibrin effects on tendon healing

Tendon injuries in animals are notorious for their slow healing and high recurrence rates. PRP enhances tenocyte proliferation and collagen type I synthesis, while PRF provides a fibrin-rich matrix that maintains cellular alignment and mechanical integrity.(1,5)

Experimental and clinical evidence

In equine superficial digital flexor tendon injuries, PRP injections have shortened recovery time and improved ultrasound echogenicity of the repair site.(1) PRF application has resulted in stronger and more organized collagen fibres, reducing the risk of reinjury.(13) Combined PRP–PRF treatment produced favourable biomechanical outcomes, with increased tensile strength and reduced scar tissue formation.(5,8)

Spinal fusion and orthopaedic implant integration

Recent studies have explored PRP and PRF as biologic coatings or fillers in spinal fusion and orthopaedic implants. In animal models, PRP–PRF constructs have improved vertebral fusion rates and bone–implant contact.(5,9) The fibrinous nature of PRF enhances biomechanical anchorage and may reduce micro motion at implant interfaces, improving long-term fixation.(5)

Summary

Clinical and preclinical evidence confirms that PRP and PRF alone or in combination enhance bone, cartilage, tendon and ligament regeneration across multiple veterinary species. PRP accelerates early inflammation and angiogenesis, PRF ensures prolonged trophic support and their combination can yield superior structural and mechanical recovery.(3,5)

Limitations, Standardisation Challenges and Future Perspectives

Variability in platelet-rich plasma and platelet-rich fibrin preparation protocols

A major limitation in the clinical and experimental application of (PRP) and (PRF) lies in the lack of standardisation in preparation methods, centrifugation parameters and platelet or leukocyte concentrations.(4,8) Variations in spin speed, duration and tube type significantly alter the cellular and growth factor composition of the final product.(1,11) In veterinary practice, this variability is further compounded by species-specific differences in platelet size, count and plasma volume.(18,24) Consequently, the biological potency of PRP and PRF preparations can vary widely, leading to inconsistent clinical outcomes across studies.(1,11) Although standardized classification systems such as the DEPA model (dose, efficiency, purity and Activation) have been proposed, their adoption in animal research remains limited.(2)

Inconsistent study designs and outcome measures

Many studies assessing PRP and PRF in animal orthopaedics suffer from small sample sizes, lack of control groups and variable follow-up durations.(8,11) Furthermore, quantitative parameters such as platelet counts, fibrin density and growth factor release are often omitted, making cross-study comparisons difficult.(18) Outcome assessments also vary, with some relying on radiographic or histologic scoring, while others use mechanical testing or subjective lameness evaluations. The absence of uniform evaluation criteria limits meta-analyses and the synthesis of evidence-based conclusions.(1,8)

Storage, handling and regulatory concerns

PRP requires the use of anticoagulants during preparation, which can influence platelet activation kinetics and storage stability.(18) PRF, while free from anticoagulants, must be prepared and applied immediately to preserve cell viability and fibrin integrity.(4) These logistical factors hinder clinical application, especially in field settings or large animal surgeries where immediate centrifugation is impractical.(8,18) In addition, regulatory frameworks governing the use of biologic materials in veterinary medicine remain underdeveloped.(15)

Biological limitations and patient variability

The efficacy of PRP and PRF treatments is influenced by animal-specific physiological variables such as age, breed, metabolic status and concurrent diseases.(8,24) Older or systemically compromised animals may demonstrate lower platelet activity and diminished growth factor release, which can reduce therapeutic effectiveness.(24,26) Moreover, PRP formulations with high leucocyte content can provoke excessive inflammation and fibrosis, negatively impacting tissue remodelling.(7,24) The short half-life of several growth factors may also necessitate repeated administrations to sustain biological activity.(8)

Future perspectives and research directions

Towards standardised veterinary protocols

Future research should prioritise the development of species-specific protocols defining optimal centrifugation parameters, platelet concentration ranges and activation strategies.(18,24) Establishing consensus guidelines for PRP and PRF preparation and reporting will improve reproducibility and clinical translation.(11)

Integration with regenerative technologies

Combining PRP and PRF with stem cell therapies, bioceramic scaffolds and 3D bioprinting technologies presents promising opportunities for repairing complex orthopaedic defects.(5,26) Platelet-derived matrices have been shown to enhance stem cell survival and differentiation, promoting improved tissue regeneration.(5)

Controlled-release and next-generation biomaterials

Emerging studies aim to design controlled-release PRF gels or nanocomposite carriers that prolong growth factor availability beyond the natural platelet lifespan.(5,26) These innovations could transform PRF from a transient biological scaffold into a sustained bioactive platform for orthopaedic tissue regeneration.(5)

Clinical translation and large-scale trials

Large multicentre veterinary trials comparing PRP, PRF and combined approaches across different species are essential. Emphasis should be placed on objective imaging techniques (CT, MRI), mechanical testing and molecular biomarkers to validate treatment efficacy and define dose–response relationships.(8,24)

Summary

Despite substantial preclinical and clinical progress, the application of PRP and PRF in veterinary orthopaedics remains limited by methodological variability, regulatory uncertainty and incomplete mechanistic understanding.(8,11) Nonetheless, current evidence supports their biological safety, regenerative efficacy and potential for clinical translation. Future innovations that integrate platelet concentrates with bioengineered scaffolds, growth factor delivery systems and cell-based therapies are poised to redefine regenerative orthopaedics in animals.(5,26)

Conclusion and Recommendations

The use of PRP and PRF in veterinary orthopaedics represents a major advancement in regenerative medicine, offering a biologically safe and autologous source of growth factors that

stimulate tissue repair, angiogenesis and osteogenesis.(3,8) Both biomaterials have shown encouraging outcomes in the healing of fractures, tendon injuries and joint disorders in multiple animal species, including dogs, horses and cattle.(1,5)

However, despite their promise, clinical efficacy remains inconsistent due to a lack of standardisation in preparation, centrifugation parameters and application methods.(11,18) Species-specific haematological variations and uncontrolled platelet or leucocyte concentrations often result in heterogeneous outcomes.(10,18) Therefore, establishing uniform preparation and reporting standards is essential for improving reproducibility and clinical confidence.(11,12)

Furthermore, the short bioactivity window of growth factors released from PRP and PRF limits their long-term regenerative effects.(4,8) Future studies should explore controlled-release formulations, nanocomposite scaffolds and hybrid systems integrating PRF with bioactive ceramics, stem cells or 3D-printed matrices to extend therapeutic efficacy.(5,21)

Regulatory and logistical challenges also persist in veterinary settings, particularly for field applications and large animals where on-site centrifugation or immediate use is difficult.(15,18) Addressing these issues requires collaborative efforts between veterinarians, bioengineers and policymakers to establish the clear guidelines for biologic use in animals.(11)

In addition, large-scale, controlled clinical trials are urgently needed to define optimal doses, treatment intervals and outcome measures.(1,11) Future research should adopt quantitative imaging, biomechanical evaluation and molecular biomarkers to objectively assess tissue regeneration.(5,16)

Overall, while PRP and PRF are not universal solutions, they hold substantial potential as cost-effective, autologous and minimally invasive adjuncts to conventional orthopaedic therapies. By addressing current methodological and regulatory gaps, these platelet concentrates can play a transformative role in advancing evidence-based regenerative orthopaedics for both companion and production animals.(3,5)

Recommendations

To strengthen the scientific and clinical foundations of PRP and PRF applications in veterinary orthopaedics, several measures are recommended. Standardised, species-specific protocols for the preparation and classification of PRP and PRF should be developed to ensure reproducibility and consistency across laboratories and clinical environments.

In addition, continuing education and professional training programmes for veterinarians should be established to enhance the understanding of platelet concentrate preparation, handling and clinical application. This will promote responsible and effective use of these biological therapies.

It is also essential to develop the clear regulatory guidelines specific to veterinary biologics to ensure product safety, quality control and ethical compliance.

Collaborative research amongst veterinarians, bioengineers and materials scientists should be encouraged to advance hybrid systems that combine PRF with bioactive scaffolds and stem cell therapy, thereby improving regenerative outcomes.

Finally, multicentre clinical trials using standardised outcome measures, including imaging, histological and biomechanical assessments, are needed to provide robust, evidence-based validation of PRP and PRF efficacy in various animal species.

Acknowledgements

The authors acknowledge the support of the staff and students of the Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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