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Review Article

Reviving the Pulp with PRP: A New Era in Endodontic Regeneration

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Abstract

Regenerative endodontics represents a rapidly advancing interdisciplinary domain that integrates stem cell biology, tissue engineering and dental science to restore the structure and functionality of compromised oral tissues through biological mechanisms. Among the various biomaterials explored, platelet-rich plasma (PRP) has emerged as a promising autologous product derived from the plasma fraction of the patient's own blood, characterised by a platelet concentration significantly higher than that found in whole blood. PRP serves as a concentrated reservoir of bioactive molecules, including essential growth factors and cytokines stored within platelet αgranules, which play an important role in modulating cellular proliferation, differentiation and tissue repair.

The therapeutic rationale for employing PRP lies in its capacity to function as a biological scaffold and delivery system for these regenerative mediators, thereby enhancing the healing and regeneration of diverse tissues. Owing to a deepened understanding of growth factor signalling pathways and cellular communication, PRP has been increasingly utilised across multiple medical and dental applications, including regeneration of bone, cartilage, tendon, hepatic tissue and dental pulp.

This review aims to explain the biological principles, preparation protocols and clinically applied PRP within the scope of regenerative dentistry. It further discusses the existing challenges, methodological inconsistencies, and emerging perspectives that shape the ongoing evolution of PRP-based regenerative strategies in oral and maxillofacial tissue engineering.

Keywords: Cytokines, Growth factors, Platelet-rich plasma, Regenerative dentistry, Tissue engineering.

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1. Introduction

1.1. Regenerative endodontics and the role of platelet-rich plasma

Regenerative endodontics represents a paradigm shift in contemporary dental practice, moving beyond traditional methods that merely eliminate infection and fill the root canal system. Rooted in the fundamental principles of tissue engineering, this biologically driven approach seeks to restore the vitality of the pulp–dentin complex, thereby enabling continued root development, strengthening of dentinal walls, and preservation of the tooth's innate defence mechanisms.[1] Unlike conventional endodontic therapies, regenerative procedures aim to recreate a functional pulp-like tissue within the canal space, restoring physiological function rather than replacing it with inert materials.

Central to regenerative endodontic therapy is the concept of the regenerative triad, which consists of stem cells, bioactive signalling molecules, and scaffolds. These three components act synergistically to initiate and sustain tissue regeneration. Stem cells provide the cellular foundation required for differentiation and tissue formation; signalling molecules regulate cellular behaviour and intercellular communication; and scaffolds offer a three-dimensional framework that supports cell attachment, migration, and organization.[2] Among these components, the scaffold plays a particularly critical role, as it not only provides structural support but also regulates the delivery and retention of biologically active mediators at the site of regeneration.[2,3]

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Scaffolds used in regenerative endodontics are designed to stabilize the regenerative environment within the root canal system. They facilitate the spatial and temporal release of growth factors, support platelet concentrates, and promote cellular activities such as adhesion, proliferation, and differentiation. In this context, platelet-rich plasma (PRP) has emerged as a biologically active autologous scaffold with significant regenerative potential.[3]

1.2. Platelet-rich plasma: Biological basis and evolution

Platelet-rich plasma is a first-generation platelet concentrate that was introduced into dental and medical practice in the late 1990s. It is derived from autologous whole blood through centrifugation, which separates plasma components and concentrates platelets above baseline physiological levels.[3] PRP is characterized by its high concentration of platelets suspended within a small volume of plasma, making it a potent source of biologically active molecules essential for tissue healing and regeneration.[4]

Platelets, once considered solely for their role in haemostasis, are now recognized as key regulators of wound healing. They function as reservoirs of more than 300 bioactive substances stored within α-granules and dense granules. Upon activation—either mechanically or chemically—these granules release a complex array of growth factors, cytokines, and enzymes that initiate and regulate a cascade of cellular and molecular events critical to tissue repair.[5] Because PRP is derived from the patient's own blood, it is inherently biocompatible and eliminates the risk of immunological rejection or disease transmission. These characteristics, combined with its relatively low cost and ease of preparation, have contributed to its widespread adoption in regenerative medicine and dentistry.

1.3. Biological mechanisms and growth factor profile of PRP

Following activation, PRP releases a diverse spectrum of growth factors and bioactive mediators that function as signalling molecules within the regenerative microenvironment. These mediators play a crucial role in modulating cell–cell communication and interactions between cells and the extracellular matrix (ECM), thereby optimizing conditions for tissue regeneration.[5]

Key growth factors released from PRP include vascular endothelial growth factor (VEGF), which stimulates angiogenesis and enhances blood supply to regenerating tissues; platelet-derived growth factor (PDGF), which promotes cell proliferation and chemotaxis; and transforming growth factor-beta (TGF-β), which regulates cell differentiation and matrix synthesis. Additional growth factors such as fibroblast growth factor (FGF), epidermal growth factor (EGF), hepatocyte growth factor (HGF), and insulin-like growth factors 1 and 2 (IGF-1 and IGF-2) further contribute to tissue remodelling, collagen production, and cellular maturation.[6]

In addition to growth factors, PRP contains matrix metalloproteinases (notably MMP-2 and MMP-9) and inflammatory mediators such as interleukin-8 (IL-8). These molecules play important roles in extracellular matrix remodelling, regulation of inflammation, and recruitment of progenitor cells.[6] Collectively, these bioactive components orchestrate key regenerative processes, including angiogenesis, osteogenesis, dentin genesis, and modulation of inflammatory responses.

1.4. Clinical applications of PRP beyond dentistry

Due to its regenerative properties, PRP has been widely applied across multiple medical and dental disciplines. Its clinical use spans bone remodelling, wound healing, neural regeneration, dermatological rejuvenation, hair restoration, sports medicine, and the management of chronic ulcers.[7] In these applications, PRP has demonstrated the ability to accelerate healing, enhance tissue quality, and improve clinical outcomes.[7]

In dentistry, PRP has gained increasing attention for its potential to enhance tissue regeneration and healing following surgical and nonsurgical procedures. Recent research has focused on understanding its biological mechanisms, optimizing preparation protocols, and evaluating its clinical effectiveness in various dental applications, particularly within the field of regenerative endodontics.[8]

1.5. Classification systems for platelet concentrates

To address variability in PRP formulations and improve consistency in reporting, several classification systems have been proposed. These frameworks aim to standardize terminology and facilitate meaningful comparison of clinical and experimental outcomes. One of the most widely accepted classification systems was proposed by Dohen Ehrenfest and colleagues, who categorized platelet concentrates into four principal groups based on leukocyte content and fibrin architecture.[8]

The first category, Pure Platelet-Rich Plasma (P-PRP), consists of a plasma fraction with a high platelet concentration and minimal leukocyte content. This formulation is associated with reduced inflammatory response and is often preferred in applications where excessive inflammation is undesirable. The second category, Leukocyte- and Platelet-Rich Plasma (L-PRP), contains a significant number of leukocytes along with platelets, which may enhance antimicrobial activity and immune modulation but can also increase inflammatory reactions.[9]

The third group, Pure Platelet-Rich Fibrin (P-PRF), is characterized by a dense fibrin-based scaffold with high platelet concentration and low leukocyte levels. The fourth category, Leukocyte- and Platelet-Rich Fibrin (L-PRF), comprises a robust fibrin matrix containing both platelets and leukocytes, providing sustained release of growth factors

over time. These classifications highlight the importance of understanding PRP composition when selecting an appropriate formulation for specific clinical indications.[9]

1.6. Preparation techniques and influencing factors

The biological efficacy of PRP is highly dependent on the method of preparation. Although numerous protocols have been proposed, there remains significant variability in centrifugation parameters, blood volume processed, anticoagulants used, and platelet activation methods. This lack of standardization contributes to inconsistent clinical outcomes and challenges in interpreting research findings.[10]

PRP can be prepared using either a single-spin or double-spin centrifugation technique. The single-spin method, such as the plasma-rich growth factor (PRGF) technique which produces a leukocyte-poor PRP with moderate platelet concentration.[10] While simpler and faster, this method may yield lower platelet enrichment compared to double-spin protocols.

The double-spin technique, which is more commonly employed, involves two sequential centrifugation steps. During the first spin, whole blood is separated into three layers: an erythrocyte-rich layer at the bottom, a buffy coat containing leukocytes, and an upper plasma layer rich in platelets.[11] Depending on the desired leukocyte content, the plasma layer with or without a portion of the buffy coat is transferred for a second centrifugation. This second spin concentrates platelets into a pellet, which is subsequently resuspended in a defined volume of plasma.

Centrifugation parameters such as relative centrifugal force (RCF), spin duration, and rotational speed play a critical role in maintaining platelet integrity. Excessive centrifugal force can result in premature platelet activation or rupture, reducing growth factor availability.[12] Studies have demonstrated that optimizing centrifugation conditions can significantly enhance platelet yield and growth factor release. For instance, increasing centrifugation duration has been shown to improve platelet recovery, whereas excessively high forces may lead to platelet aggregation and diminished biological activity.[3]

1.7. Importance of standardization

Evidence consistently indicates that variations in PRP preparation protocols significantly influence platelet viability, growth factor kinetics, and therapeutic effectiveness. As a result, standardization of preparation methods remains a major challenge and a critical requirement for achieving reproducible clinical outcomes.[14] Establishing consensus guidelines for PRP preparation would not only improve comparability among studies but also enhance its reliability as a regenerative biomaterial in clinical practice.

1.8. Role of PRP in Regenerative endodontics

In regenerative endodontics, the primary objective is the biological restoration of the pulp–dentin complex following injury or necrosis. This includes regeneration of pulp tissue, continued root development, and restoration of normal pulpal vitality. After thorough canal disinfection, regeneration can be achieved through activation of resident dental stem cells, provided that an appropriate scaffold and a growth factor-rich microenvironment are present.[14]

Autologous PRP fulfils both of these requirements, functioning as a reservoir of growth factors while simultaneously serving as a three-dimensional scaffold. The release of growth factors and cytokines from activated platelets creates an environment conducive to neovascularization, tissue organization, and reparative dentin formation within the root canal space.

Recent studies have highlighted PRP as a valuable adjunct in regenerative endodontic procedures due to its ability to accelerate wound healing, promote angiogenesis, and support matrix remodelling. Clinically, PRP has been associated with improved postoperative healing, reduced intraoperative bleeding, and enhanced bone formation. Its autologous nature and relative ease of preparation further contribute to its cost-effectiveness and clinical appeal.[15]

1.9. Broader dental applications and future perspectives

Within dentistry, PRP has been successfully applied across multiple specialties. In regenerative endodontics, it has been utilized in procedures such as pulpotomy, apexification, and periapical surgery. In periodontology, PRP has been employed in the management of infrabony defects and periodontal plastic surgeries. In oral and maxillofacial surgery, its applications include extraction socket preservation, bone grafting, soft tissue reconstruction, and implant site development.[16]

Given its biological versatility and regenerative potential, PRP continues to be a promising biomaterial in modern dental practice. Ongoing research aimed at refining preparation protocols, elucidating molecular mechanisms, and establishing evidence-based clinical guidelines will further enhance its role in regenerative dental medicine. Ultimately, PRP offers a biologically driven, patient-centred, and cost-effective strategy for achieving predictable and long-lasting regenerative outcomes.[17]

2. Discussion

Platelet-rich plasma was first introduced into clinical practice by Whitman and colleagues in 1997, marking an important milestone in regenerative medicine.[17] Since its inception, PRP has been widely investigated for its ability to enhance tissue healing due to its high concentration of platelet-derived growth factors. These biological mediators play a central role in orchestrating cellular events involved in wound repair,

angiogenesis, and tissue remodelling. In dentistry and oral and maxillofacial surgery, PRP has been explored extensively as an adjunctive therapeutic modality to improve clinical outcomes following surgical interventions.[18]

The regenerative potential of PRP arises primarily from its capacity to accelerate wound healing, improve osseointegration during implant placement, and assist in the reconstruction of osseous defects, including mandibular discontinuities.[19] Numerous clinical and experimental studies have demonstrated that the application of PRP to extraction sockets significantly enhances both soft tissue healing and hard tissue regeneration. This is achieved through improved neovascularization, increased collagen deposition, and early stabilization of the surgical wound. Enhanced angiogenesis ensures an adequate blood supply, which is essential for nutrient delivery, immune response, and recruitment of progenitor cells to the healing site.[19]

In oral and maxillofacial surgery, PRP has been shown to promote bone regeneration in various clinical scenarios. Of particular interest is its application following third molar extraction, where it has been reported to facilitate bone formation at the distal aspect of mandibular second molars. This effect is especially pronounced during the early stages of healing, typically between three and six weeks postoperatively. The early regenerative advantage provided by PRP is thought to be mediated by the rapid release of growth factors that stimulate osteoblastic activity and extracellular matrix synthesis.[20]

In vitro investigations further support these clinical observations. Studies evaluating the interaction between PRP and human mesenchymal stem cells (MSCs) have demonstrated that PRP induces dose-dependent chemotaxis and proliferation of these cells. Importantly, PRP does not adversely affect the osteogenic differentiation potential of MSCs, suggesting that it can enhance cell recruitment and expansion without compromising lineage-specific maturation. These findings underscore the biological compatibility of PRP with stem cell-based regenerative processes.[20] However, despite these promising outcomes, the literature also reports inconsistent and sometimes contradictory results. Variability in study design, PRP preparation protocols, platelet concentration, and outcome measures contribute to this lack of consensus. Consequently, while preliminary data suggest a beneficial role for PRP in oral and maxillofacial regeneration, there remains a critical need for well-designed, randomized, and controlled clinical trials to conclusively establish its efficacy.[20]

In recent years, PRP has gained considerable attention in regenerative dentistry, particularly in the domains of oral surgery and endodontics. Its potential to enhance healing and stimulate tissue regeneration has prompted investigators to explore its application as an alternative scaffold in regenerative endodontic therapy (RET). RET aims to biologically replace damaged or necrotic pulp tissue, thereby restoring vitality, sensory function, and continued root development.[21]

Evidence from preclinical animal models and limited clinical case reports suggests that PRP can induce the formation of vascularized connective tissue within disinfected root canal systems. The angiogenic growth factors present in PRP, particularly VEGF, are believed to facilitate neovascularization, which is a prerequisite for sustained tissue survival and regeneration. The presence of newly formed blood vessels enhances nutrient diffusion and supports the metabolic demands of regenerating tissues.[21]

Despite these advantages, PRP exhibits a limited capacity to induce true dentin genesis. While connective tissue formation and revascularization have been observed, the differentiation of odontoblast-like cells and the deposition of tubular dentin remain minimal. Consequently, currently available PRP formulations are insufficient to fully regenerate the complex architecture of the dentin–pulp complex. This limitation underscores the need for adjunctive strategies or combination therapies to achieve complete functional regeneration.

The primary goal of regenerative endodontics is the re-establishment of a functional pulp–dentin complex using advanced tissue engineering principles. This includes restoration of pulp vitality, sensory innervation, immune defence, and continued root maturation. Although PRP offers several biological advantages, regenerative endodontics remains an evolving field, and many aspects of PRP-based therapy require further investigation.

One of the major challenges lies in the lack of standardized protocols for PRP preparation and application. Variations in platelet concentration, choice of platelet activators, leukocyte content, and delivery methods can significantly influence biological outcomes. Furthermore, the optimal concentration of platelets required to achieve maximal regenerative effects remains uncertain. Excessively high platelet concentrations may paradoxically inhibit cell proliferation due to supraphysiological growth factor levels.[22]

To address these challenges, further translational research is essential. Well-designed experimental studies and clinical trials are needed to evaluate the long-term regenerative outcomes of PRP in endodontic therapy and to establish evidence-based guidelines for its clinical use.

2.1. Preparation of PRP

PRP is prepared through centrifugation of autologous whole blood, a process designed to separate erythrocytes and concentrate platelets within the plasma fraction. The centrifugation protocol plays a pivotal role in determining platelet yield, growth factor release, and overall bioactivity of the final PRP product. Variations in centrifugation speed, duration, and relative centrifugal force (RCF) have been shown to significantly affect PRP quality. The double-spin

centrifugation technique is widely regarded as superior to single-spin methods in achieving higher platelet concentrations. A commonly employed protocol involves an initial low-speed centrifugation (approximately 160 g for 10 minutes) to separate plasma from red blood cells, followed by a second higher-speed centrifugation (approximately 250 g for 15 minutes) to pellet and concentrate platelets. This approach has been shown to enhance cytokine concentration and promote cellular migration and proliferation.[22]

Animal studies further demonstrate that higher centrifugal forces can substantially increase platelet concentration. Protocols involving centrifugation at 1000 g for 5 minutes followed by 1500 g for 15 minutes have resulted in platelet concentrations up to six times higher than baseline values. However, excessively high centrifugal forces may compromise platelet integrity and reduce growth factor bioavailability, highlighting the need for careful optimization of preparation parameters.

A wide range of commercial PRP preparation systems is currently available, many of which claim to produce standardized and reproducible platelet concentrations. Despite these claims, significant variability exists among commercial kits in terms of platelet yield, leukocyte content, and growth factor concentration.

A comprehensive evaluation of 33 commercially available PRP systems revealed that only 11 met the minimum platelet concentration threshold of 1×10^6 platelets/µL. Furthermore, only 10 systems achieved a platelet concentration that was at least five times higher than baseline physiological levels. This variability raises concerns regarding the reliability and reproducibility of PRP products generated using commercial devices.[22]

In addition to variability in quality, the cost of commercial PRP systems represents a significant limitation.[23] The price of individual kits ranges from approximately USD 175 to USD 1150, which may restrict accessibility, particularly in resource-limited settings. In contrast, manual laboratory-based preparation methods, when performed under controlled conditions, can yield PRP with comparable biological activity at a substantially lower cost.[24]

2.2. Clinical implications of PRP

The heterogeneity observed among PRP preparation methods, coupled with inconsistent clinical outcomes, underscores the necessity for standardization.[25] Establishing universally accepted protocols for PRP preparation, characterization, and application is essential for improving reproducibility and facilitating meaningful comparison across studies.

In the context of regenerative endodontics, PRP should be viewed as a promising but incomplete solution. While it offers substantial benefits in terms of angiogenesis, cell recruitment, and early tissue organization, it alone cannot achieve full regeneration of the dentin–pulp complex. Future strategies may involve combining PRP with stem cell therapy, biomimetic scaffolds, or bioactive molecules to enhance odontogenic differentiation and dentin formation.

In conclusion, PRP remains a biologically driven, autologous, and cost-effective regenerative biomaterial with wide-ranging applications in dentistry and medicine. Continued research aimed at refining preparation techniques, elucidating molecular mechanisms, and validating clinical outcomes will be crucial in defining its precise role within regenerative endodontics and broader dental practice.[25]

3. Conclusion

Thus, PRP has demonstrated considerable potential as an autologous biologic adjunct across multiple regenerative dental procedures. Despite its promising outcomes certain clinical indications and its overall effectiveness remain subjects of ongoing debate. To optimise its clinical utility, standardised guidelines regarding patient selection, preparation techniques and application protocols are required. Moreover, well-designed randomised controlled trials with long-term follow-up are essential to validate its therapeutic benefits and determine its predictability in regenerative outcomes. Nevertheless, current evidence indicates PRP as a valuable regenerative biomaterial with significant prospects for future application in clinical dentistry.

4. Source of Funding

None.

5. Conflict of Interest

None.

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