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PLATELET-RICH PLASMA AND PLATELET FIBRIN: STANDARDIZED PREPARATION PROTOCOLS, MECHANISMS OF ACTIVATION, STORAGE STABILITY, AND REGULATORY FRAMEWORKS

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ABSTRACT

Objective. To summarize current methods for obtaining platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), their biological properties, activation protocols, and regulatory aspects of clinical application.

Methods. A comprehensive analysis of recent literature on the preparation, standardization, and clinical use of platelet-derived biomaterials was performed. Special attention was given to two-step centrifugation protocols for producing pure platelet-rich plasma (P-PRP), low-speed centrifugation techniques for injectable PRF (i-PRF), and methods for constructing fibrin-based matrices (P-PRF).

Results. Platelet-derived biomaterials represent a concentrated source of growth factors (PDGF, TGF-β, VEGF, IGF-1, EGF, FGF, HGF) that promote tissue regeneration, angiogenesis, and immunomodulatory effects. The efficacy of PRP/PRF depends on donor hematological parameters, centrifugation settings, activation strategies, and delivery methods. This review outlines optimal platelet concentration ranges, discusses the rationale for anticoagulant selection, and describes quality control methods as well as classification systems (PAW, DEPA, MARSPILL). Regulatory aspects of PRP application in Ukraine are also highlighted, including cases in which GMP certification is mandatory.

Conclusion. PRP and PRF occupy a prominent position in regenerative medicine; however, the lack of standardized protocols and unified guidelines hampers the comparability of clinical outcomes. Future development in this field requires methodological harmonization, large-scale clinical studies, and the implementation of GMP standards in commercial production.

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Keywords: platelet-rich plasma, platelet fibrin, P-PRP, PRF, regenerative medicine, growth factors, GMP.

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ЗБАГАЧЕНА ТРОМБОЦИТАМИ ПЛАЗМА ТА ТРОМБОЦИТАРНИЙ ФІБРИН: ГАРМОНІЗОВАНІ МЕТОДИ ПРИГОТУВАННЯ, ДИНАМІКА АКТИВАЦІЇ, СТАБІЛЬНІСТЬ ПРИ ЗБЕРІГАННІ ТА МІЖНАРОДНІ РЕГУЛЯТОРНІ ПЕРСПЕКТИВИ

Мета. Узагальнити сучасні методи отримання збагаченої тромбоцитами плазми (PRP) та тромбоцитарного фібрину (PRF), їхні біологічні властивості, протоколи активації та регуляторні аспекти використання у клінічній практиці.

Методи. Проведено аналіз літератури останніх років, присвяченої підготовці, стандартизації та клінічному застосуванню тромбоцитарних біоматеріалів. Розглянуто протоколи двоетапного центрифугування для отримання «чистої» збагаченої тромбоцитами плазми (P-PRP), методи низькошвидкісної сепарації для формування ін'єкційної PRF (i-PRF), а також технології виготовлення фібринових матриць P-PRF.

Результати. Тромбоцитарні біоматеріали є концентрованим джерелом факторів росту (PDGF, TGF-β, VEGF, IGF-1, EGF, FGF, HGF), які стимулюють регенерацію тканин, ангіогенез та проявляють імуномодулювальні властивості. Ефективність PRP/PRF залежить від гематологічних характеристик донора, параметрів центрифугування, способу активації та методики введення. В огляді наведено оптимальні діапазони концентрації тромбоцитів, розглянуто доцільність використання антикоагулянтів, описано підходи до контролю якості та сучасні класифікаційні системи (PAW, DEPA, MARSPILL). Окрему увагу приділено нормативно-правовим умовам застосування PRP в Україні, включно з випадками, коли виробництво має відповідати вимогам GMP.

Висновок. PRP та PRF є перспективними біоматеріалами у регенеративній медицині, проте відсутність уніфікованих протоколів і стандартів обмежує можливість порівняння клінічних результатів. Подальший розвиток напряму передбачає гармонізацію методик, проведення масштабних клінічних досліджень та впровадження GMP-стандартів при комерційному виробництві.

Ключові слова: збагачена тромбоцитами плазма, тромбоцитарний фібрин, P-PRP, PRF, регенеративна медицина, фактори росту, GMP.

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ABBREVIATIONS

PDBMs (Platelet-Derived Biomaterials)
PRP (Platelet-Rich Plasma)
P-PRP (Pure Platelet-Rich Plasma)
L-PRP (Leukocyte-Platelet-Rich Plasma)
PRF (Platelet-Rich Fibrin)

P-PRF (Pure Platelet-Rich Fibrin)
L-PRF (Leukocyte-Platelet-Rich Fibrin)
i-PRF (Injectable Platelet-Rich Fibrin)
hPL (Human Platelet Lysate)
PRGF (Plasma Rich in Growth Factors)
PPP (Platelet-Poor Plasma)
GMP (Good Manufacturing Practice)
ATMP (Advanced Therapy Medicinal Products)
PAW (Platelets, Activation, White cells)
DEPA (Dose, Efficiency, Purity, Activation)
MARSPILL (Method, Activation, Red blood cells, Spin, Platelet concentration, Image guidance, Leukocytes, Light activation)
RCF (Relative Centrifugal Force)
RPM (Revolutions Per Minute)
ELISA (Enzyme-Linked Immunosorbent Assay)
MSC (Mesenchymal Stem Cells)

INTRODUCTION

Platelet-derived biomaterials (PDBMs) represent an innovative group of autologous or allogeneic preparations based on concentrated blood platelets, designed to stimulate tissue regeneration. Their application relies on the ability of platelets to release a broad spectrum of growth factors and bioactive molecules, including PDGF, TGF-β, VEGF, IGF-1, EGF, FGF, and HGF, which are involved in wound healing, angiogenesis, inflammation reduction, and tissue remodeling.

One of the pioneers in the development of autologous platelet-derived preparations is Dr. Eduardo Anitua, a Spanish dentist, researcher, and founder of the BTI Biotechnology Institute (Spain). Between 1999 and 2001, he proposed the concept of Plasma Rich in Growth Factors (PRGF), a biological preparation derived from “pure” PRP (P-PRP) that excludes leukocytes and provides a standardized platelet concentration. PRGF became the first PRP system adapted to clinical standards, featuring controlled preparation protocols, closed sterile systems, and reproducible characteristics. This method was widely introduced in dentistry, orthopedics, ophthalmology, and aesthetic medicine, and served as a reference framework for the evaluation and comparison of other PRP systems [1–3].

Following the pioneering publications of Eduardo Anitua, who introduced the concept of standardized P-PRP preparation, the field of platelet-derived biomaterials developed rapidly. Numerous researchers contributed to refining fractionation methods, classification systems, PRP activation strategies, and clinical applications. Modern classification frameworks were established, including the PAW system (Platelets, Activation, White cells) and the DEPA model (Dose, Efficiency, Purity, Activation), both emphasizing control of leukocyte and platelet content [4]. Considerable variability in practical application methods has been highlighted, underscoring the need for standardization [5]. More recently, research has focused on elucidating mechanisms of action as the basis for international recommendations [6].

Currently, various PDBM forms are in clinical use, classified by leukocyte content, activation method, and physical properties. The most common are: P-PRP (pure platelet-rich plasma), L-PRP (leukocyte- and platelet-rich plasma), P-PRF and L-PRF (platelet fibrin in gel or membrane form), as well as i-PRF (injectable PRF). In addition, growing interest has been observed in human platelet lysate (hPL), obtained from donor platelets, and engineered composites combining PDBMs with hydrogels, collagen, or bioceramic matrices to enhance delivery and efficacy [7–11].

Clinical effectiveness of PDBMs is being investigated across multiple disciplines, including orthopedics, dentistry, dermatology [12], neurology, ophthalmology, gynecology, and wound surgery. Promising applications include treatment of osteoarthritis, intra-articular injections, healing of bone and soft tissues, intradiscal injections for intervertebral disc degeneration, and therapy of chronic wounds and trophic ulcers [13–15].

The main advantages of PDBMs are their autologous nature, low risk of complications, biocompatibility, and high concentration of growth factors. At the same time, clinical efficacy is determined by preparation standards, activation protocols, dosage, and injection site. Ongoing randomized clinical trials aim to validate long-term effects and establish evidence-based protocols. A key publication by Chahla et al. (2017) provided a systematic review of PRP standards in orthopedic clinical literature, emphasizing the need for unified preparation and reporting protocols. The authors proposed standardized descriptions of PRP composition (platelet and leukocyte counts, activators, volume, storage time), classification systems (e.g., PAW, DEPA, MARSPILL), and detailed preparation methods in publications. This work remains a critical reference for PRP standardization, stressing that without biochemical characterization, the efficacy of PRP cannot be reliably evaluated, even within a single disease context [16].

Despite the growing popularity of PRP, the lack of a unified preparation approach, particularly regarding leukocyte content, volume of active fraction, and activation strategy, significantly complicates comparison of clinical outcomes. Substantial variability across protocols – even when using the same centrifugation technology – affects the final biological activity and clinical efficacy of the preparation. Therefore, there is a pressing need for a clearly defined,

clinically reproducible protocol for obtaining "pure" PRP (P-PRP), which minimizes inflammatory response, standardizes platelet concentration, and complies with regulatory requirements for medical applications [17, 18].

The aim of this review is to summarize current preparation methods of PRP and PRF, as well as their advantages and limitations in clinical practice.

Preparation of Pure PRP (P-PRP) by a Two-Step Centrifugation Method

The most reliable and reproducible method for obtaining pure platelet-rich plasma (P-PRP) is based on a two-step centrifugation procedure. In this approach, platelet-rich plasma collected after the first spin is transferred into a separate sterile tube and subsequently concentrated during the second centrifugation step. The typical outcome is a platelet concentration approximately 3–5 times above baseline, while leukocyte content is minimized if proper collection techniques are applied after the initial spin [19].

It should be noted that the characteristics of the resulting P-PRP largely depend on the properties of the initial venous blood sample. Even under identical centrifugation parameters, tube type, and volume, the quality and concentration of the preparation may vary depending on the patient's individual hematological profile [20].

Key factors influencing the efficacy of P-PRP

- Hematocrit level: A high hematocrit reduces the relative plasma volume, and the buffy coat may shift upwards.
- Baseline platelet count: In patients with thrombocytopenia, platelet concentration in PRP will remain low even after two-step concentration.
- Blood viscosity: May influence cell separation efficiency during centrifugation.
- Physiological state of the patient: Hydration status and medication use (e.g., anticoagulants) affect blood composition.
- Time between collection and processing: Delays may result in premature platelet activation before centrifugation.

Therefore, it is advisable to assess hematological parameters before each procedure – at least platelet count and hematocrit – and to consider them when interpreting PRP concentration and expected therapeutic efficacy.

Therapeutic platelet concentration in P-PRP

One of the critical determinants of P-PRP efficacy is platelet concentration. Numerous studies have demonstrated that therapeutic benefit requires P-PRP to contain at least 2 – 3 times the baseline platelet count. This level ensures an adequate supply of α-granules carrying growth factors (TGF-β, PDGF, IGF-1, FGF, CTGF, EGF, HGF) necessary for tissue regeneration. The generally accepted therapeutic threshold is $\geq 1{,}000 \times 10^9$ platelets / L, corresponding to 2 – 5 times baseline values. Optimal ranges, depending on the clinical indication, are considered to be $1{,}000 – 1{,}500 \times 10^9$ / L. Conversely, excessive concentrations (> 5 × baseline) have been associated in some models with suppressed cell proliferation or increased release of pro-inflammatory cytokines. Controlled rather than maximal enrichment is therefore recommended [21–24].

Thus, clinical or experimental preparation of P-PRP should always be accompanied by platelet concentration measurement to allow evaluation and comparison of efficacy.

Centrifuge requirements for P-PRP preparation

To ensure high-quality and reproducible P-PRP, centrifuges must provide precise and controlled separation conditions. Validation of the centrifuge is essential, including calculation of the relationship between RPM and RCF for the selected rotor according to the formula: $RCF = 1.118 \times 10^{-5} \times r \times (RPM)^2$, where *r* is the radius in cm.

Main requirements:

- Adjustable RCF (g-force) or RPM, with precise settings.
- Availability of either swing-out (horizontal) or fixed-angle rotors with specified radius.
- Compliance with sterility: use of closed disposable tubes with caps and aerosol containment.
- Operating range of 200–1200 g, with adjustment increments no greater than ± 50 g.
- Preferable: integrated timer, digital interface, and imbalance protection [25].

Commonly used anticoagulants for P-PRP

To prevent coagulation, anticoagulants are added to venous blood intended for P-PRP preparation. The choice of anticoagulant is critical for maintaining platelet integrity in a non-activated state without interfering with their physiological activation.

- ACD-A (Acid Citrate Dextrose – Formula A): Contains citric acid, sodium citrate, and glucose. Maintains platelet stability for up to 2 hours, has minimal effects on cellular function, and does not inhibit growth factor release.
- Sodium citrate (3.2–3.8 %): Prevents clotting by binding calcium ions. Widely used in hematology laboratories and compatible with P-PRP protocols.
- Heparin: Rarely used for P-PRP, as it may alter granule release and platelet activation; not recommended for standard P-PRP protocols.

- EDTA: Not recommended, as it induces morphological changes in platelets and reduces their functional activity.

For clinical preparation of biologically active PRP, ACD-A or sodium citrate are recommended, as they preserve platelet integrity without inhibiting physiological activation. In contrast, EDTA irreversibly chelates calcium, thereby impairing growth factor release and limiting its suitability for PRP preparation. When using vacuum collection tubes, it is essential to confirm that the anticoagulant volume matches the collected blood volume [26].

Step-by-Step Protocol for Obtaining P-PRP

Required equipment and materials:

- Laboratory centrifuge with adjustable g-force (200–1200 g).
- Sterile tubes without gel separator (e.g., 10 mL, sodium citrate or ACD-A).
- Pipettes or syringes with fine tips.
- Vertical tube racks.
- Sterile gloves, wipes, antiseptics.
- Markers for tube labeling.
- PRP activation reagents ($CaCl_2$, thrombin).

1. Venous blood collection Collect 10–20 mL of venous blood into a sterile tube. Anticoagulant: ACD-A or sodium citrate 3.2–3.8 % (ratio ~ 1:9). Mix gently by inverting the tube (5–8 times), without shaking.

2. First centrifugation ("soft spin") Purpose: to separate platelet-containing plasma from erythrocytes and leukocytes. Conditions: 200–300 g, 10–15 minutes. Result: formation of a platelet-rich plasma layer above the buffy coat (leukocytes).

The first centrifugation step (soft spin) is critical for efficient separation of blood cellular elements and for obtaining platelet-rich plasma without leukocyte or erythrocyte contamination (Table 1).

Table 1. Optimal parameters of the first centrifugation step (Soft Spin)

Parameter	Value
RCF	200–300 g
RPM (at r = 10 cm)	1000–1500 rpm
Duration	10–15 min
Temperature	Room (18–22 °C)
Rotor type	Swing-out or fixed-angle

A low centrifugal force sediments erythrocytes while leaving platelets in plasma, minimizing buffy coat contamination. Exceeding recommended force may result in platelet loss or leukocyte inclusion.

3. Plasma transfer Carefully transfer platelet-rich plasma into a new sterile tube without disturbing the buffy coat layer.

4. Second centrifugation ("hard spin") Purpose: to pellet platelets. Conditions: 900–1200 g, 10 minutes. Result: separation into an upper layer – PPP (platelet-poor plasma) and a lower layer – PRP (platelet concentrate).

The second centrifugation step (hard spin) is used to sediment platelets at the bottom of the tube, reducing leukocyte content while avoiding premature activation.

5. Pellet resuspension After removing PPP, leave ~ 0.5–1 mL of plasma above the pellet. Carefully resuspend the platelet pellet to obtain a homogeneous suspension (Table 2).

Table 2. Optimal parameters of the second centrifugation step (Hard Spin)

Parameter	Value
RCF	900–1200 g
RPM (at r = 10 cm)	3200–3700 rpm
Duration	10 min
Temperature	Room (no cooling)
Rotor type	Swing-out or fixed-angle

Excessive force (> 1300 g) may damage or activate platelets. After the second spin, PPP should be removed, leaving ~ 0.5–1 mL for pellet resuspension [19, 27].

Fraction distribution after hard spin (~ 900–1200 g, 10 min):

1. Platelet pellet – concentrated at the bottom.
2. Residual leukocytes (buffy coat) – above the platelet pellet or at the interface.
3. PPP – upper plasma layer without cells.

Unlike erythrocytes, leukocytes do not sediment with platelets due to lower density and higher hydrodynamic drag [28].

Recommendations for platelet collection after centrifugation

- After first centrifugation:
  - The buffy coat appears as a thin gray-white band above erythrocytes – avoid disturbing it.
  - Collect 2 / 3–3 / 4 of the upper plasma layer, which contains up to 95 % of platelets.
  - Avoid the last 0.5–1 mL above the buffy coat to minimize leukocyte contamination.
  - Use a sterile syringe or pipette with a fine tip.

- Keep the tube vertical during aspiration to reduce mixing of layers.
- For L-PRP, partial buffy coat aspiration is allowed; for pure P-PRP, collect only the upper plasma fraction without touching the buffy coat.

- After second centrifugation:
  - Do not shake the tube after centrifugation.
  - Remove the upper PPP layer, leaving ~ 0.5–1 mL of plasma above the pellet.
  - Avoid disturbing the platelet pellet.
  - Resuspend the pellet in the remaining plasma to obtain a homogeneous suspension.
  - If needed, adjust volume by adding back part of the removed PPP.
  - Maintain sterility at all steps.

Main methods of PRP activation

- Calcium chloride (10 % $CaCl_2$): classical method; induces clotting and fibrin gel formation. Used for infiltrations or PRP gel preparation.
- Autologous or recombinant thrombin: rapid activation with immediate growth factor release; suitable for surgical applications requiring rapid effect.
- Physiological activation (contact with collagen/tissue): in vivo activation without prior in vitro stimulation; used for soft tissue or tendon injections.
- Mechanical activation: agitation or passage through a fine needle; limited efficiency.
- Photon/laser activation: experimental approach; studies ongoing.

Activation method depends on clinical goals: physiological activation is preferred for controlled release in tissue injections; chemical or thrombin activation is used in surgery. Premature activation should be avoided before injection [29, 30].

Freeze–thaw activation of PRP

The freeze–thaw method induces platelet lysis and release of α-granule contents without chemical reagents.

Advantages:

- Simple, reagent-free method.
- Allows PRP storage at −80 ° C.
- Effective release of growth factors for in vitro assays (e.g., ELISA).

Limitations:

- Uncontrolled release kinetics.
- Potential protein degradation (e.g., PDGF decrease, TGF-β changes).
- Not recommended for clinical injection or surgical use.

This method is mainly applied in laboratory research for quantitative assays [31].

Storage and shelf life of P-PRP

- Immediate use: ideally within a few hours after preparation; delayed use increases risk of spontaneous activation and platelet dysfunction [5].
- Cold storage (≈ 4 ° C): slows platelet metabolism and reduces activation; useful for short-term holding, but factor stability varies (e.g., PDGF may decrease, TGF-β1 may increase). Suitable for research, not prolonged clinical use [32, 33].
- Cryopreservation (− 20… −80 ° C): preserves growth factors up to 6 months; useful for biobanking, but may alter activation profile. Requires validated freezing/thawing protocols [34].

Additional standards and compliance

This protocol aligns with key PAW (DeLong et al., 2012) and DEPA (Magalon et al., 2016) classification criteria, and may be adapted to GMP requirements when closed sterile systems are used.

Quality control of P-PRP

At key steps, platelet and leukocyte concentrations should be measured for reproducibility and classification (Table 3).

Table 3. Main control points for platelet and leukocyte concentration in P-PRP

Step	Parameters	Purpose
Before centrifugation	Platelets, Leukocytes	Baseline reference values.
After first centrifugation (optional)	Platelets in plasma	Evaluate retention before transfer.
After second centrifugation (before application)	Platelets, Leukocytes	Final QC; fold-enrichment, classification (PAW, DEPA).

Automated hematology analyzers capable of assessing platelets/leukocytes in citrated blood or plasma are recommended.

Legal and practical aspects of PRP use without GMP (Ukraine)

In Ukraine, autologous PRP may be prepared and used without GMP if performed in licensed medical facilities under aseptic conditions, with informed consent and proper documentation, and without commercialization (Table 4).

Table 4. Key Ukrainian regulatory documents on autologous biomaterials

Document	Key provisions
Law №2427-VIII (2018, rev. 2025)	Defines scope (transplantation, bioimplants, xenomaterials); MOH authority.
Order №1388 (06.08.2024)	Quality standards for anatomical materials; packaging/ preservation.
ST-N 42-4.0:2020 (GMP)	Manufacturing of sterile medicinal products; EU adaptation.
ST-N 42-4.9:2020 (GMP ATMP)	Advanced therapy medicinal products; aligned with EU ATMPs.

Conditions allowing non-GMP PRP use:

- Autologous origin (patient's own blood).
- Application within a licensed healthcare facility.
- Qualified staff under sterile conditions.
- Approved local SOPs and documentation.

Cases requiring GMP certification:

- Centralized or commercial PRP production.
- Allogeneic (donor-derived) PRP.
- Combination with drugs/biologics or modified formulations.
- International clinical trials or export.

Protocol for Obtaining Injectable PRF (I-PRF)

Injectable PRF (I-PRF) is produced using the principle of low-speed centrifugation without anticoagulants. This preserves a liquid phase rich in platelets, leukocytes, and fibrinogen for subsequent injectable use [35, 36] (Table 5).

Biological properties of I-PRF [5]

- High concentrations of platelets, fibrinogen, and leukocytes (especially monocytes).
- Sustained release of growth factors.
- Stimulation of angiogenesis, chemotaxis, and mesenchymal stem cell (MSC) migration.

Critical conditions:

- Absence of anticoagulant enables natural fibrin polymerization.
- Centrifugation must start immediately to preserve liquid phase.
- Low RCF (~60 g) prevents premature platelet activation.

Clotting time of I-PRF

I-PRF retains its liquid phase only for a limited time after centrifugation, as no anticoagulants are used. Fibrinogen is activated by thrombin naturally present in the sample, initiating fibrin polymerization. Therefore, I-PRF must be applied within the defined time window to prevent gel formation [35, 36] (Table 6).

Table 5. Step-by-step protocol for obtaining injectable PRF

Step	Details
1. Blood collection	Volume: 10–20 mL venous blood into a glass or polymer tube without anticoagulant. Centrifugation should begin within ≤1 min after collection.
2. Centrifugation	RCF: 60 g (~700–800 rpm at r = 10 cm). Duration: 3 min. Rotor: swing-out.
3. I-PRF collection	Aspirate the upper orange layer (1.0–1.5 mL) immediately after centrifugation, avoiding the pellet.
4. Application	Used for injections or mixing with biomaterials. Coagulates into fibrin gel within 15 min after collection.

Practical aspects

- Prepare I-PRF immediately before use.
- Complete injection or mixing with biomaterials within 10 min post-centrifugation.
- Do not use I-PRF after 15 min, as it converts into a fibrin gel.

Table 6. Clotting time of I-PRF depending on temperature and tissue contact

Condition	Time to clot formation
Room temperature (~20–22 °C)	~10–15 min
Body temperature (~37 °C)	5–10 min
In vivo tissue contact	4–6 min

Protocol for Obtaining Pure Platelet-Rich Fibrin (P-PRF)

Pure Platelet-Rich Fibrin (P-PRF) is a bioactive fibrin clot without leukocytes, derived from venous blood without anticoagulants [37]. The method relies on immediate centrifugation after blood draw. Its efficacy has been confirmed by recent studies in regenerative medicine [38].

Key features of the process:

- Single-step centrifugation without anticoagulants.
- Rapid coagulation and fibrin matrix formation.
- High bioactivity due to gradual release of growth factors (up to 14 days) (Table 7).

Precautions

- Only use tubes without anticoagulants (glass or silica-coated).
- Start centrifugation within 2 min after collection.
- PRF is not injectable; it is suitable only for topical or implantation use.
- Use clot within 60–90 min; later it loses flexibility and bioactivity.

Table 7. Step-by-step protocol for obtaining P-PRF

Step	Description
1. Blood collection	10–20 mL venous blood in glass or titanium tubes without anticoagulants. Begin centrifugation within ≤2 min after draw.
2. Centrifugation	~700 g (~2700 rpm), 8–12 min. Swing-out or fixed-angle rotor.
3. Fraction separation	Three layers: upper – PPP, middle – fibrin clot (P-PRF), lower – erythrocytes.
4. PRF retrieval	Carefully remove fibrin clot with sterile forceps. Can be used as a membrane (after liquid removal) or immediately for implantation.
5. Application	Used in dentistry, orthopedics, surgery as a bioactive regeneration matrix.

CONCLUSIONS AND PERSPECTIVES

Platelet-derived biomaterials (PRP, I-PRF, PRF) occupy a leading position in modern regenerative medicine due to their high concentrations of growth factors, biocompatibility, and relative safety. However, their clinical efficacy strongly depends on preparation protocols, standardization, activation methods, and application conditions.

The most promising directions remain intradiscal injection for intervertebral disc degeneration, osteoarthritis and joint disease therapy, bone and soft tissue healing, and treatment of chronic wounds.

Future development requires:

- Implementation of unified preparation and quality control protocols (PAW, DEPA, MARSPILL).
- Broad application of GMP standards in commercial production.
- Randomized clinical trials to evaluate long-term efficacy.
- Development of combined biomaterials with scaffolds or carriers for controlled growth factor release.

Thus, PRP and PRF are powerful regenerative tools, but their successful clinical integration is possible only under conditions of strict standardization, legal regulation, and evidence-based recommendations [39].

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The authors declare that they have no conflict of interest that could have influenced the outcomes of the study, the interpretation of data, or the preparation of the manuscript. No financial, academic, personal, or other relationships exist that could be perceived as potential conflicts of interest.

ARTIFICIAL INTELLIGENCE DISCLOSURE

We, the authors of this publication, confirm that generative artificial intelligence (AI) tools were used during the research process and/or the preparation of the manuscript.

The use of AI was limited to supportive tasks, including:

- generating text fragments in scientific style;
- language editing and translation;
- creating structured tables and templates;
- technical formatting of certain materials.

All key scientific conclusions, data interpretation, and final editing were carried out by the authors. The use of AI was conducted under human oversight, in compliance with principles of research integrity, ethical standards, and data security requirements.

We hereby disclose the use of generative AI and confirm that the authors take full responsibility for the content, accuracy, and interpretation of the data.

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