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IMMUNOMODULATION GUIDED BY PLATELET CONCENTRATES: REGENERATIVE APPLICATIONS IN DENTISTRY

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Abstract: Autologous platelet concentrates (APCs) have been extensively investigated in dentistry for their potential to modulate inflammation, accelerate healing, and promote tissue regeneration. The objectives of this study were to critically review the main clinical applications of these biomaterials, identifying interventions with proven benefits and those whose performance proved limited or ineffective. This is a narrative literature review, in which randomized clinical trials and case reports published between 2015 and 2025 were analyzed in the PubMed and Google Scholar databases, involving PRP, PRF, and their variations, applied alone or in combination with biomaterials in periodontal surgery, implant dentistry, bone reconstruction, and bone sequelae management. Systematic and narrative reviews, dissertations, theses, and book chapters were excluded, as well as articles without clear and objective methodology, duplicates between databases, and those that did not match the guiding question of the study. It was evident that PRF, especially in association with bone grafts, performs better in infraosseous periodontal defects, alveolar preservation, and implant procedures because it provides a biostimulating matrix and tissue stability. On the other hand, injectable modalities, such as i-PRP and i-PRF, show inconsistent results or no effect. Emerging applications, such as or Alb-PRF and combinations with membranes, show promising potential, although not yet consolidated by robust clinical studies. In general, APCs demonstrate more consistent efficacy as adjuvants in soft and hard tissue regenerative therapies.

Keywords: Autologous platelet concentrates. PRP. PRF. Periodontal regeneration. Bone regeneration. Implant dentistry

INTRODUCTION

Bone regeneration requires spatio-temporal regulation of the inflammatory phases, culminating in resolution and the creation of an environment conducive to the formation of tissue functionally similar to native tissue (NEWMAN et al., 2021). Osteoprogenitor and immune cells, a structuring blood clot, pro-osteogenic and pro-angiogenic signaling molecules, adequate vascular supply, and mechanical stability are indispensable for bone maturation (DONOS et al., 2023). However, extensive defects, aging, infection, and metabolic diseases can compromise this process (LEE et al., 2019; NEWMAN et al., 2021).

In these clinical situations, the gold standard is the use of autogenous and allogeneic grafts, which, however, present risks such as infection and host rejection, as well as consequences such as increased morbidity at the donor site and challenges related to the limitation of available donor areas and the reduced regenerative capacity of the affected tissue (ZUMARÁN et al., 2018; LEE et al., 2019). In this context, therapeutic alternatives have been explored through tissue engineering, which seeks to design biomaterials capable of providing structural support favorable to osseointegration and modulating the complexities of the healing process, including immune response, osteogenesis, and inflammation (LEE et al., 2019), which is made possible by their ability to release biomolecules such as drugs, genes, cells, and growth factors (LEE et al., 2019; NEWMAN et al. 2021).

Among these strategies, platelet concentrates stand out as immunomodulatory materials that are easy to obtain and apply, derived from autologous blood after cen-

trifugation, which forms three layers: red blood cells, platelet-poor plasma, and the “buffy coat,” rich in platelets and leukocytes (DOHAN et al., 2006). Varying according to composition and preparation, they are classified as pure platelet-rich plasma (P-PRP), platelet-rich plasma and leukocytes (L-PRP), pure platelet-rich fibrin (P-PRF), and platelet-rich fibrin and leukocytes (L-PRF) (ZUMARÁN et al., 2018).

The first generation, Platelet-Rich Plasma (PRP), uses anticoagulants before centrifugation and the addition of bovine thrombin and calcium chloride for rapid polymerization, useful in hemostasis and reduction of hematomas (DOHAN et al., 2006). However, anticoagulants impair angiogenic and regenerative responses due to the early release of growth factors, reducing their integration into the fibrin matrix (DOHAN et al., 2006; IEVINA and DUBNIKA, 2024; MIRON et al., 2021).

In 2001, Choukroun et al. developed Fibrin Rich Plasma (FRP) without the addition of anticoagulants, allowing natural platelet activation and gradual release of growth factors. As with the formation of a natural clot, circulating thrombin in the blood induces the transformation of fibrinogen into a firm fibrin mesh capable of retaining platelets and leukocytes (DOHAN et al., 2006; STRAUSS, STAHLI and GRUBER, 2018) and allowing the prolonged release of growth factors (MIRON et al., 2021), increasing the membrane’s potential to promote hemostasis and angiogenesis and, consequently, sustain the healing process (DOHAN et al., 2006; ZUMARÁN et al., 2018). The clot obtained is stable, resistant, and adhesive, allowing adaptation to different anatomical sites and applications in

oral and maxillofacial surgery (ZUMARÁN et al., 2018).

In implant dentistry, bone quantity and quality are essential for predictable osseointegration (SOHN et al., 2015; GUAN et al., 2023). Calcium phosphates are biocompatible and osteoconductive, but have low mechanical strength, while synthetic polymers, although more resistant, have poor cell adhesion and limited integration. The combination of these biomaterials with platelet concentrates, especially PRF, improves graft molding and stability, promoting bone repair (IEVINA and DUBNIKA, 2024).

Given the search for predictable and biocompatible regenerative therapies in implant dentistry and oromaxillofacial surgery, this literature review aims to bring together scientific advances on the immunomodulatory role of platelet concentrates and their applications in association with biomaterials. The objective is to analyze the performance of autologous concentrates, such as PRF, L-PRF, and PRP, and their interactions with inflammatory and regenerative processes, contributing to the improvement of therapies and consolidation of knowledge in the field.

METHODOLOGY

This is a literature review study with a qualitative and descriptive approach, which aimed to gather scientific advances on the clinical performance of platelet concentrates, whether or not associated with biomaterials, in regenerative therapies in dentistry.

In order to guide the research, the following guiding question was outlined: “What are the main applications that have

demonstrated real benefits and which therapies have proven ineffective or failed in clinical practice?”

As a search strategy, a search was conducted in the PubMed/MEDLINE (National Library of Medicine) and Google Scholar electronic databases between October and November 2025, identifying relevant studies from 2015 to 2025.

A combination of the following keywords was used: “autologous platelet concentrates,” “PRP,” “PRF,” “L-PRP,” “healing,” and “guided tissue regeneration,” combined using the Boolean operators “and” or “or.” Disagreements between authors were resolved after analysis of the abstracts and discussion.

Thus, the inclusion criteria comprised articles published between 2015 and 2025, available in Portuguese or English, that addressed or discussed the application of platelet concentrates in tissue regeneration and reconstruction protocols. Case reports and randomized clinical trials were included, provided they presented experimental or clinical data or scientific discussions related to the topic addressed. Studies outside the established period, those that did not present a relationship between platelet concentrates and tissue repair, as well as studies that fit the proposed theme but did not involve the oral cavity were excluded. Systematic reviews, narrative reviews, dissertations, theses, and book chapters were also disregarded, as were articles without clear and objective methodology, duplicates between databases, and those that did not match the guiding question of the study.

The selection of studies was initially based on reading the titles and abstracts in order to identify those that addressed the

theme. When the title and abstract met the inclusion criteria, the article was read in its entirety.

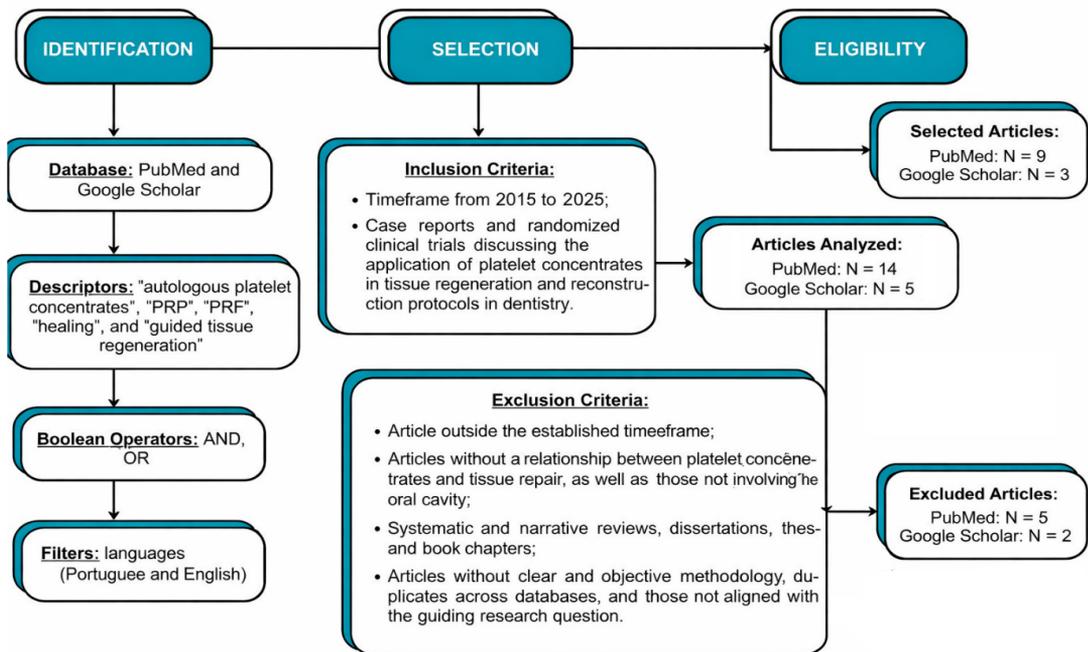
The search process is shown in the flowchart below, which also presents the inclusion and exclusion criteria.

DISCUSSION

The growing search for biomaterials that increase clinical predictability, reduce surgical morbidity, and remain affordable has driven interest in autologous platelet concentrates (APCs). In this context, it is essential to understand in which applications these biomaterials offer consistent benefits and where their performance remains limited, critically analyzing the available evidence on their different modalities.

APCs, especially PRF and PRP, have been investigated as adjuvants in bone graft integration (GUAN et al., 2023 and SOHN et al., 2015), although the results remain heterogeneous. While Cieplik et al. (2017) observed no benefits from the combination of PRP + calcium beta-triphosphate (-TCP) in intraosseous periodontal defects, Theodosaki et al. (2022) identified a synergistic effect between PRF and particulate grafts, with improved healing speed and radiographic filling. This variability suggests that performance depends on the CPA modality, the associated biomaterial, and the clinical context, such as baseline periodontal condition, defect extent, gingival biotype, and bone quality.

In the orthodontic context, injectable PRP (i-PRP) used alone has also not been shown to be effective in preventing bone resorption or periodontal defects during rapid maxillary expansion (ALOMARI and SUL-



Source: Authorial, 2026

RESULTS

N	Authors (Year)	Main Findings
1	CIEPLIK, et al (2017)	This is a prospective, randomized, controlled clinical study with a split-mouth design that evaluated, after 13 years of follow-up, the clinical results of guided bone regeneration procedures performed with β -tricalcium phosphate (β -TCP) biomaterial, with or without Platelet-Rich Plasma (PRP). The study included 25 patients with two deep intraosseous periodontal defects, interproximal and located in contralateral regions of the arch, presenting a minimum probing depth of 6 mm and radiographic evidence of minimum angular bone loss of 4 mm. At the test site, PRP was applied with β -TCP previously soaked in PRP, while at the contralateral control site, the graft was soaked only in autologous blood and no platelet concentrate was added; both were covered with a bioabsorbable membrane. Segment losses allowed for the analysis of tooth survival in 22 patients, demonstrating functionality rates of 81.8% at the test sites and 86.4% at the control sites. In the split-mouth analysis, conducted with 15 patients, it was observed that periodontal clinical parameters, including clinical attachment loss, improved in the first year, followed by a slight regression after 13 years. There were no statistically significant differences between the groups in terms of long-term healing.

2	MORAES et al. (2024)	<p>This randomized, controlled, prospective, triple-blind clinical trial, with a split-mouth design, aimed to evaluate the effects of the application of Platelet-Rich Fibrin and Leukocytes (L-PRF) in lower third molar extraction surgeries, investigating possible benefits in soft tissue and periodontal healing, postoperative pain control, and the quality and quantity of alveolar bone formed. Bilateral mandibular third molar extractions with similar clinical characteristics in terms of position, degree of impaction, and root formation pattern were performed in 28 patients with no signs of periodontal inflammation or other associated pathology. L-PRF significantly reduced postoperative pain at seven days ($p=0.019$), according to the visual analog scale (VAS). In cases where L-PRF was applied to the tooth socket after extraction, 96.4% had grade 5 healing rates after one month — the maximum level of repair, characterized by complete closure of the socket and absence of inflammation — compared to 67.9% in the control group, with a statistical power of 81.29%, confirming the reliability of the results. At three months, the sites treated with L-PRF showed less probing depth on the distal face of the adjacent second molar and better alveolar ridge stability, while the control group showed a more pronounced volumetric reduction. These results suggest the clinical superiority of L-PRF in alveolar preservation and acceleration of soft tissue repair, which may represent a relevant advantage in third molar surgeries with higher morbidity and in sites planned for rehabilitation with implants.</p>
3	ALOMARI and SULTAN (2019)	<p>This is a randomized, controlled clinical trial with a split-mouth design, whose objective was to evaluate the effects of injectable Platelet-Rich Plasma (PRP) on alveolar bone resorption in patients undergoing rapid maxillary expansion (RME). This procedure is associated with lateral flexion of the alveolar ridge and vestibularization of the anchor teeth through the intermittent application of high forces, causing damage to the periodontium. The sample consisted of 18 patients, aged 12 to 16 years, with transverse deficiency of the maxilla and with the first fully erupted molars and premolars, in which a Hyrax-type palatal expander was cemented. In the test group, PRP was injected along the roots of these teeth, and both groups were evaluated by cone beam computed tomography (CBCT) before expansion (T0) and after 3 months of retention (T1) to analyze the thickness of the buccal bone plate, alveolar bone crest level, and occurrence of dehiscence and fenestration. The results showed a reduction in the thickness of the buccal plate in the anchor teeth in both groups, with no statistically significant difference, as well as a loss of alveolar crest height due to ERM, more evident in the buccal root of the first premolars ($p > 0.05$). In addition, an increase in the occurrence of dehiscences at T1 was observed in both groups, being more pronounced in the intervention group (13.2%) compared to the control group (9.7%), while fenestrations also increased, except in the premolar region, where there was a slight reduction. Thus, it was concluded that injectable PRP was not able to prevent alveolar bone resorption or periodontal defects induced by ERM, indicating an absence of measurable clinical benefits in the context studied.</p>

4	PARISE et al. (2022)	Case-control study. The objective of the study was to evaluate the use of L-PRF in the prevention and treatment of bone necrosis. Patients diagnosed with medication-related osteonecrosis of the jaw (MRONJ) undergoing cancer treatment with zoledronic acid were included and divided into groups. The control group underwent conventional treatment without the use of L-PRF, presenting more pain, inflammation, and bone re-exposure. The test group, on the other hand, used L-PRF in the treatment and had better healing, without postoperative pain and with complete tissue closure in a short time. It was concluded that the biomaterial used allows the release of growth factors, which results in better healing, low risk of contamination, and no postoperative pain, and may be an ally in the prevention and treatment of ONJ.
5	MILUTINOVIC et al. (2020)	Case-control study. The study aimed to investigate the effectiveness of PRF in the treatment of infraosseous defects in patients with chronic periodontitis, evaluating the clinical outcome through periodontal depth and clinical attachment level at the beginning of the study and 6 and 9 months after surgery. The group treated with PRF had positive effects on the mean reduction in probing depth (4.00 ± 1.07 mm) when compared to the control group (4.83 ± 0.99 mm). It was concluded that the use of PRF in the surgical treatment of infraosseous defects demonstrated better parameters than open flap debridement alone.
6	TANUJA et al. (2022)	Case-control study. The study aims to determine the effectiveness of bovine hydroxyapatite and collagen (G-Graft) mixed with platelet-rich fibrin (PRF) as a barrier in post-extraction alveoli, compared to isolated extraction sites. In the test group, after extraction, the alveoli were preserved using hydroxyapatite with collagen (G-Graft), PRF, and chorion membrane, which were used with the graft material. In the control group, no additional treatment was performed after extraction. It was concluded that the use of G-graft with PRF was highly effective in preserving the alveolar ridge after tooth extraction. This material offers better healing and high regenerative capacity, improving graft handling and the quality of bone neoformation. In addition, the chorion membrane has antibacterial properties and improves the gingival biotype.
7	BOORA et al. (2015)	The prospective randomized controlled clinical trial aims to investigate the feasibility of using platelet-rich fibrin (PRF) and its performance in peri-implant healing in single-stage implants. The study group, which used PRF, showed significant changes in bone level, but still statistically lower than the control group, which did not use PRF. After the established three-month period following surgery, less probing depth was observed in the study group and a statistically insignificant change in the control group. It can be concluded that PRF has positive effects with potential and stimulating synergistic for bone neoformation around the implants.
8	ZOHARY et al. (2025)	The randomized clinical trial aimed to compare the performance of platelet-rich fibrin (PRF) and growth factor (CGF) when placed in front of previously infected implants. It involved 210 patients, whose affected teeth and periapical lesions were extracted and removed, respectively. The PRF and CGF groups showed higher mean bleeding on probing and pain when compared to the control group, which did not undergo any interventions. However, overall, both groups showed a decreasing pattern of pain, an increasing pattern of bone level stimulation, and a decreasing pattern of periapical lesions. The study group obtained positive results in the osseointegration of implants in pre-infected areas, with emphasis on the performance of CGF

9	HARTLEV et al. (2021)	<p>Randomized controlled pilot clinical study. The study aimed to analyze the clinical performance of implants that were applied in sites that had recently received autogenous bone grafts, which were covered by a platelet-rich fibrin membrane, representing the study group (PRF) group, and a graft covered with deproteinized bovine bone mineral together with a resorbable collagen membrane, representing the control group. Twenty-seven partially edentulous patients participated, 14 in the control group and 13 in the PRF group. Both groups showed similar results in terms of implant survival rate, peri-implant parameters, and patient satisfaction. The PRF group showed a slightly greater increase in cortical bone. It was concluded that the use of the PRF membrane stimulates effective guided bone regeneration around the implants.</p>
10	SHOKRY, MELEK, and AHMED (2025)	<p>This study is a randomized controlled clinical trial that aimed to analyze the effect of using autologous albumin-derived PRF (Alb-PRF) on bone regeneration after maxillary cyst enucleation. A 3D volumetric analysis of the bone cavity and bone density of the newly formed bone was considered. The research defined as a null hypothesis that there would be no significant difference between the groups treated with Alb-PRF and group treated only with enucleation without any additive for regeneration. Initially, the minimum sample size was set at 9 participants per group, but this number was later increased to 10. One group was treated with enucleation and application of Alb-PRF, while the other, the control group, was treated with enucleation alone. During the follow-up phase, two cone beam computed tomography (CBCT) scans were performed, one in the immediate postoperative period (T1) and another six months after surgery (T2). To obtain the volume, segmentation techniques were used through 3D software, and to obtain the bone density measurement, a region of interest (ROI) tool was used in three different and standardized positions in T1 and T2.</p> <p>In this study, Alb-PRF and conventional blood clots showed no significant differences in reducing the volume of the residual bone cavity or in the density of the bone formed. According to the author, the result can be attributed to the small sample size and insufficient follow-up period.</p>
11	PHAM (2021).	<p>The study is a randomized controlled clinical trial that aimed to evaluate and compare different approaches used in the treatment of intraosseous periodontal defects. Among these approaches, the results of treatment with platelet-rich fibrin (PRF) associated with debridement and open flap surgery (OFS), guided tissue regeneration (GTR), or OFS alone were evaluated. This analysis was performed considering clinical, radiographic, and healing parameters over a 12-month follow-up period. The null hypothesis was that the combination of PRF + OFD (open flap debridement) could present results similar to those of guided tissue regeneration and that this would be superior to the use of OFD alone. Thirty patients with chronic periodontitis were used. The study guarantees that the use of PRF can replace GTR with a resorbable membrane because it has similar potential results in the treatment of intraosseous defects. According to the author, this would be interesting because PRF is a simple, easy, and low-cost biomaterial when compared to bone grafts.</p>

12	TADEPALLI, et al (2022)	This is a clinical study that aimed to analyze and compare the benefits of using L-PRF and A-PRF (advanced platelet-rich fibrin) in the treatment of gingival recession defects. Thirty individuals with isolated gingival recession were selected and treated with L-PRF or A-PRF, both combined with coronally advanced flap. The clinical parameters observed were: recession height (RH), width of the recession width (RW), probing depth (PPD), clinical attachment level (CAL), width of attached gingiva (WAG), keratinized tissue height (KTH), percentage of root coverage (RC%), gingival thickness (GTH), visual analog scale for esthetics (VAS-E), and esthetic recession score (RES). There was a similar improvement in the parameters using both interventions, which showed a similar effect, with no significant differences, although the literature shows that A-PRF has more growth factor content and more uniform cell distribution than L-PRF.
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TAN, 2024). Methodological limitations of the trial, such as variations in the leukocyte count of participants—which influences blood separation during centrifugation and alters the final platelet yield—differences in oral hygiene, and the absence of prolonged follow-up, make it difficult to draw definitive conclusions. In addition, Miron et al. (2017) point out that anticoagulants and bovine thrombin used in the preparation of PRP may compromise healing. Similar results were observed in the participants of the study by Zeitounlouian et al. (2021), in which i-PRF did not improve bone quality or prevent fenestrations, dehiscences, or root resorptions during canine retraction. The authors suggest that adjustments in the type of retraction and protocol, such as the method of application and centrifugation parameters, could modify the results, arguing that failures may be related to the distinct cellular profile generated by each protocol, as proposed by Miron et al. (2017).

PRF stands out for its dense and moldable structure that acts as a biological scaffold (CHOUKRON et al., 2006; MIRON et al., 2021), offering mechanical advantages over other biomaterials (IEVINA and DUBNIKA, 2024; ZOHARY et al., 2025).

Tanuja et al. (2022) showed that PRF associated with bovine hydroxyapatite grafting with collagen in alveoli favors post-extraction ridge remodeling, reinforcing its role as an adjunct in bone regeneration. However, when used alone, its impact on hard tissues is limited, being more significant in soft tissue healing (BOORA et al., 2015; MO-RAES et al., 2024), which does not consolidate it as a substitute for osteoconductive biomaterials.

In implant dentistry, Hartlev et al. (2021) reported that PRF membranes provided greater marginal bone preservation and consequently better implant survival rates compared to conventional treatment with xenogeneic grafts and collagen membranes. Zohary et al. (2025) identified additional benefits when combining PRF and CGF, including less pain, better inflammation control, and a lower incidence of periapical lesions in newly infected implants, indicating that combined protocols tend to outperform PRF alone.

In the treatment of infraosseous defects, PRF exhibits angiotropic, hemostatic, and osteoconductive properties relevant to periodontal regeneration. Milutinovic et al. (2020) reported significant reductions in

probing depth (PD) and progressive improvement in clinical attachment level (CAL). Pham (2021) and Elbehwash et al. (2021) observed that PRF associated with open flap debridement (OFD) outperformed both OFD alone and guided tissue regeneration (GTR) in clinical and radiographic parameters. Elbehwash et al., 2021 further suggest that combining PRF with regenerative biomolecules, such as ascorbic acid (AA), enhances these effects. Mubarak et al. (2023) demonstrated that the combination of L-PRF + collagen membrane favors bone filling and clinical indices, such as PS, NIC, and bacterial plaque index, attributing the effect mainly to the mechanical protection of fibrin by the membrane, which ensures a more stable environment for healing. However, multicenter and controlled studies are needed to consolidate the real magnitude of these benefits.

In the management of medication-related osteonecrosis of the jaw (MRONJ), L-PRF has been used to improve local angiogenesis and osteogenesis. Clinical studies such as those by Parise et al. (2022) and Bracher et al. (2021) reported significant improvement in epithelialization, reduced inflammation, and pain relief, with no adverse effects reported. However, persistent methodological limitations, such as small sample sizes and the absence of control groups, still prevent definitive conclusions about its clinical efficacy.

Seeking to overcome the rapid degradation of CAPs and achieve greater three-dimensional stability, albumin-enriched platelet-rich fibrin (Alb-PRF) was developed with a denser matrix, formed after protein denaturation and reorganization, which can prolong PRF resorption for 4 to 6 months (MIRON et al., 2023). Despite this, Shokry,

Melek, and Ahmed (2025) observed no significant differences in bone volume or density after cystic enucleations using Alb-PRF, indicating no measurable clinical benefit in these parameters. In contrast, Lourenço et al. (2024) demonstrated that Alb-PRF releases lower levels of inflammatory cytokines and higher concentrations of PDGF (platelet-derived growth factor), which favors osteoblast proliferation, suggesting promising biological potential, although dependent on validation by more robust studies.

Another relevant modification of conventional PRF is advanced platelet-rich fibrin (A-PRF), obtained by slower centrifugation, resulting in a more porous matrix with a higher concentration of leukocytes and growth factors. In the treatment of gingival recessions, Tapadelli et al. (2022) showed similar clinical impacts similar clinical impacts between L-PRF and A-PRF. The systematic review by Saleh, Abdelhaleem, and Elmeadawy (2024) reports that, although A-PRF can enhance results when associated with surgical techniques, traditional methods, such as connective tissue grafting with a coronally advanced flap, continue to demonstrate greater efficacy in these treatments.

In summary, CPAs are biologically compatible tools that offer benefits mainly as adjuvants, especially in soft tissue healing and inflammatory modulation. Their impact on bone regeneration remains variable and dependent on the preparation technique, the form of application, and the associated biomaterials. Innovations such as Alb-PRF and A-PRF increase the stability and regenerative potential of platelet matrices, but still lack solid clinical validation.

CONCLUSION

The literature shows that the performance of autologous concentrates varies according to their physical form, preparation, and association with biomaterials. The most consistent results occur with solid PRF, especially when combined with particulate grafts or membranes, promoting better bone filling, ridge stability, and healing in periodontal, alveolar preservation, and implant dentistry procedures. These findings reinforce its role as a supportive biomaterial with significant biostimulating potential in inflammatory and regenerative processes.

On the other hand, liquid forms such as i-PRF and i-PRP have limited efficacy, especially in orthodontic applications and in extensive defects when used alone, indicating lower regenerative capacity without structural support. New formulations, such as albumin-enriched PRF, PRF associated with ascorbic acid, and combinations with collagen, show promising results, although the lack of methodological standardization remains a challenge. Thus, there is still a need for more robust clinical studies to consolidate the role of autologous concentrates and improve their therapeutic applicability.

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