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REVIEW ARTICLE

Clinical effectiveness of albumin-enriched platelet-rich fibrin (Alb-PRF) in periodontal and peri-implant regenerative surgery: a systematic review

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Abstract

Alb-PRF is a heat-induced autologous fibrin biomaterial generated by combining thermally denatured serum albumin with liquid platelet-rich fibrin. Although its clinical use in periodontal and peri-implant procedures has increased, the available evidence remains limited and methodologically heterogeneous. This systematic review aimed to synthesize the biological rationale, clinical effectiveness, and methodological quality of Alb-PRF in periodontal and peri-implant applications. A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and the Cochrane Library from January 2013 to December 2025 in accordance with PRISMA 2020 guidelines. Grey literature sources, including Google Scholar and OpenGrey, were also screened. Randomized and controlled clinical trials as well as relevant in vivo animal studies evaluating Alb-PRF were included. Study selection and data extraction were independently performed by two reviewers using Rayyan, and methodological quality was assessed using the RoB-2, Newcastle–Ottawa Scale, or SYRCLE tools. Due to substantial heterogeneity in study design, clinical indications, and outcome measures, a narrative synthesis was performed. Seven studies were included (six clinical and one animal study), comprising 156 human participants and 24 animal samples, with follow-up periods ranging from 7 days to 6 months. Alb-PRF showed consistent benefits in early soft-tissue healing and postoperative comfort. However, evidence supporting its role in hard-tissue regeneration remains limited and inconclusive. Based on current evidence, Alb-PRF should be biologically interpreted as a soft-tissue phenotype-modulating adjunct that stabilizes the early healing microenvironment rather than as a primary hard-tissue regenerative material. Its clinical utility appears to be indication-specific and mainly related to early soft-tissue outcomes. Well-designed, standardized randomized controlled trials with longer follow-up periods are required to clarify its therapeutic role. *PROSPERO registration number:* CRD420251237466 (registered on 21 November 2025, version 1.0)

Plain language summary

This systematic review found that albumin-enriched platelet-rich fibrin (Alb-PRF) improves early soft-tissue healing and postoperative comfort in periodontal procedures, although its long-term regenerative potential remains uncertain.

Keywords Albumin-enriched platelet-rich fibrin · Platelet concentrates · Periodontal regeneration · Peri-implant therapy · Soft-tissue healing

Introduction

The success of periodontal regeneration depends not only on effective mechanical debridement and defect morphology but also on the biocompatibility of the applied biomaterial and its influence on the surrounding immunological microenvironment. Among currently available biological agents, platelet-derived concentrates—particularly platelet-rich fibrin (PRF)—have emerged as some of the most promising

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biomaterials in regenerative dentistry[1]. PRF is an autologous, anticoagulant-free fibrin–leukocyte–platelet matrix obtained from whole blood. Through the sustained release of growth factors such as transforming growth factor-β1 (TGF-β1), platelet-derived growth factor-AB (PDGF-AB), and vascular endothelial growth factor (VEGF), as well as various cytokines, PRF supports wound healing, angiogenesis, and tissue regeneration[2]. Clinically, PRF has been used in a wide range of periodontal and oral surgical procedures and has been associated with favorable healing outcomes in both soft and hard tissues[3–17].

Low-speed or liquid modifications of conventional PRF protocols, such as advanced PRF (A-PRF), have been developed to prolong growth-factor release, further emphasizing the need for standardized preparation parameters to minimize clinical heterogeneity[18]. Since the biological activity of classical PRF matrices typically lasts only a few days, the development of next-generation fibrin variants with enhanced biochemical stability and extended bioactivity has become essential. In this context, Alb-PRF represents a heat-induced, biologically stabilized fibrin–albumin composite generated through controlled thermal processing of the plasma fraction to partially denature serum albumin, followed by recombination with liquid PRF. This thermal modification promotes fibrin cross-linking, resulting in a mechanically more stable matrix with slower degradation kinetics and a more gradual release of growth factors over approximately 10–14 days compared with conventional PRF [19, 20]. The material is produced by combining heat-treated platelet-poor plasma with liquid PRF, forming a stable fibrin–albumin network with increased resistance to degradation [21, 22].

The biological uniqueness of Alb-PRF arises not only from its fibrin–platelet growth factor profile but also from the immunomodulatory contributions of serum albumin, which may influence the local microenvironment to promote tissue repair. Experimental data indicate that albumin-based biomaterials may attenuate oxidative stress and promote macrophage polarization toward the M2 phenotype, thereby contributing to inflammation resolution; however, in vivo evidence directly supporting such immunomodulatory effects for Alb-PRF remains scarce and unvalidated [23]. Histologically, the denser and more homogeneous fibrin–albumin matrix has been reported to provide a stable scaffold for cell migration, supporting angiogenesis and fibroblast activity during the early healing phase [19].

Current clinical evidence is limited by short follow-up durations (<6 months), small sample sizes, and methodological shortcomings, all of which restrict the reliability of conclusions regarding Alb-PRF's clinical performance. Considerable variability in centrifugation parameters, heating times, and serum-to-PRF ratios substantially hampers comparability and generalizability across existing studies [21]. Moreover, most published data originate from single-center pilot investigations, and high-quality randomized trials are still lacking [24]. Nevertheless, in vivo observations regarding the prolonged biological stability and barrier-like characteristics of Alb-PRF suggest its potential utility as a biologically derived barrier membrane for soft-tissue engineering applications [25].

The available clinical literature exhibits substantial methodological heterogeneity, which limits the ability to draw definitive conclusions regarding the regenerative efficacy of Alb-PRF. Previous reviews have primarily focused on the biological formation mechanisms and growth factor release dynamics of the material, without systematically synthesizing clinical outcomes within periodontal and peri-implant regenerative contexts. Therefore, this systematic review aims to comprehensively evaluate the biological basis, clinical effectiveness, and methodological rigor of Alb-PRF across periodontal and peri-implant applications. Additionally, this work seeks not only to summarize the current level of evidence but also to provide clinicians with evidence-based guidance regarding indication selection, protocol standardization, and expected biological outcomes.

Conceptual framework: Alb-PRF as a soft-tissue phenotype–modulating biomaterial

Conventional platelet-derived concentrates have traditionally been interpreted as passive growth-factor reservoirs; however, emerging evidence suggests that Alb-PRF may function beyond this classical paradigm by actively modulating the early wound-healing phenotype rather than merely accelerating tissue closure or directly inducing hard-tissue regeneration[19, 21].

The thermally stabilized fibrin–albumin matrix of Alb-PRF provides a prolonged, low-intensity release of growth factors within a mechanically persistent scaffold. This unique combination appears to bias the healing microenvironment toward rapid epithelial maturation, controlled inflammatory resolution, and short-term soft-tissue volume preservation.

From a biological perspective, Alb-PRF should be conceptualized as an immuno-biologically active soft-tissue phenotype–modulating biomaterial rather than a direct osteogenic or attachment-inducing regenerative agent. In this model, Alb-PRF does not aim to maximize hard-tissue formation but instead stabilizes the early wound microenvironment, thereby reducing tissue collapse, edema, and postoperative morbidity.

This conceptual shift is critical for accurately interpreting current clinical outcomes and for defining realistic, indication-specific expectations regarding Alb-PRF application in periodontal and peri-implant therapy.

This systematic review was structured according to the PICO framework, as follows:

- **Population (P):** Patients presenting with periodontal or peri-implant tissue defects and corresponding in vivo animal models simulating these conditions.
- **Intervention (I):** Application of Alb-PRF.
- **Comparison (C):** Conventional PRF variants (leukocyte- and platelet-rich fibrin (L-PRF), A-PRF, i-PRF, H-PRF) or standard surgical treatment alone.
- **Outcomes (O):** Clinical outcomes (clinical attachment level (CAL), probing pocket depth (PPD), gingival thickness (GTH), keratinized tissue width (KTW), papilla volume), biological parameters (growth factor levels, inflammatory cytokine profile), and radiographic indicators (bone height, volumetric changes).

Research question:

"Does the application of Alb-PRF enhance clinical, biological, and histological healing outcomes in periodontal and peri-implant regenerative procedures compared with conventional PRF variants or control interventions?"

Material and methods

Study design

This systematic review was conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [26] and prospectively registered in the PROSPERO database (CRD420251237466; version 1.0, registered on 21 November 2025).

The primary aim of this review was to evaluate the clinical and biological effects of Alb-PRF in periodontal and peri-implant regeneration. The following research questions were addressed:

1. Does Alb-PRF application improve clinical healing outcomes compared with conventional PRF variants or control treatments?
2. To what extent are the biological and immunological mechanisms underlying Alb-PRF supported by current evidence?
3. Is the methodological quality of existing studies sufficient to ensure clinical validity and reliability?

Search strategy and information sources

The following electronic databases were systematically searched for eligible studies published between January 1, 2013, and December 1, 2025. The year 2013 was selected as the starting point because studies specifically addressing albumin-stabilized platelet-rich fibrin formulations and related heat-modified platelet concentrate protocols began to emerge only after the broader development of second-generation platelet concentrates. Earlier literature did not provide directly relevant evidence on Alb-PRF as a distinct biomaterial.

- PubMed/MEDLINE
- Scopus
- Web of Science Core Collection
- Cochrane Library

In addition, grey literature sources (Google Scholar, OpenGrey) and the reference lists of relevant journals were manually screened. The search strategy was constructed using combinations of the following keywords: "albumin platelet-rich fibrin," "albumin-stabilized PRF," "Alb-PRF," "periodontal regeneration," "peri-implantitis," and "socket healing," employing Boolean operators (AND, OR) to enhance retrieval sensitivity [27].

An example of a PubMed/MEDLINE search query was as follows:

("albumin"[MeSH Terms] OR albumin*[tiab]) AND ("platelet-rich fibrin"[tiab] OR PRF[tiab]) AND (periodont*[tiab] OR "peri-implant"[tiab] OR socket[tiab] OR regeneration[tiab])

Filters applied: human or animal studies; English language; publication date range 2013/01/01–2025/12/01. Equivalent search structures were adapted for Scopus, Web of Science, and Cochrane Library. The first 200 results from Google Scholar and corresponding records from OpenGrey were screened. All searches were documented, and duplicate records were removed by DOI and title matching using EndNote and Rayyan software.

Eligibility criteria

Inclusion criteria:

- Clinical or in vivo animal studies involving Alb-PRF, defined as a heat-stabilized fibrin matrix formed by mixing the albumin gel—derived from PPP heated at 75 °C for 10 minutes—with freshly prepared liquid PRF.
- Interventions aimed at periodontal or peri-implant regeneration, such as intrabony defect treatment, soft-tissue thickening, socket preservation, or peri-implantitis management.

- Comparison groups including conventional PRF variants (L-PRF, A-PRF, i-PRF, horizontal-PRF (H-PRF)) or standard surgical therapy alone.
- Reporting of at least one clinical, radiographic, histological, or biological outcome.
- Studies published in English with full-text availability.

Exclusion criteria:

- In vitro cell culture studies, case reports, literature reviews, or uncontrolled case series.

  In vitro cell culture studies were excluded because the primary purpose of this systematic review was to synthesize clinically and translationally relevant evidence regarding the use of Alb-PRF in periodontal and peri-implant regenerative procedures. Although cell culture studies may provide mechanistic support, they do not directly reflect clinical performance, tissue-level healing outcomes, or in vivo regenerative behavior, and were therefore not included in the formal evidence synthesis.
- Experimental models lacking in vivo or clinical data related to periodontal or peri-implant regeneration.
- Studies with inadequate methodology or insufficient statistical reporting.
- Investigations employing non–Alb-PRF variants (e.g., A-PRF, Titanium-PRF (T-PRF)) or formulations lacking albumin.
- Duplicate or overlapping datasets; in such cases, only the most comprehensive or recent publication was included.

Study selection

Titles and abstracts were independently screened by two reviewers (H.A. Biçakçioğlu and G. Çolak) using Rayyan QCRI (Qatar Computing Research Institute). Full texts of all potentially eligible studies were then assessed independently by the same two reviewers. Before formal screening, the eligibility criteria were pilot-tested on a subset of records to calibrate the reviewers and ensure consistency in study selection. Because this review involved bibliographic screening rather than repeated clinical measurements, intra-examiner and inter-examiner reliability tests in the conventional measurement sense were not directly applicable; instead, reviewer consistency was ensured through independent duplicate screening, calibration, and consensus-based resolution of discrepancies.

In total, 955 records were screened at the title–abstract level. Of these, 25 full-text articles were assessed for eligibility, and 7 studies met the inclusion criteria. The remaining 18 articles were excluded because they did not involve Alb-PRF intervention, lacked a control group, or were limited to in vitro experiments (see Supplementary Table S3). The study selection process is summarized in the PRISMA 2020 flow diagram (Fig. 1).

Data extraction

A standardized data collection form was used to record, for each included study, the study design, sample size, application protocol (method of Alb-PRF preparation, content of the control group, and treatment region), follow-up duration, clinical and biological outcome measures, analytical methods, and main findings. Data extraction was performed independently by two reviewers (H.A. Biçakçioğlu and G. Çolak), and any discrepancies were resolved through discussion and consensus. No attempts were made to contact study authors for additional information or clarification. All data were obtained exclusively from information provided in the published articles. Extracted data were summarized in structured tables to allow systematic comparison and, where appropriate, narrative (qualitative) synthesis.

Risk of bias assessment

- Randomized controlled trials were evaluated using the Cochrane Risk of Bias 2 (RoB-2) tool [28],
- Cohort studies were assessed using the Newcastle–Ottawa Scale (NOS) [29],
- Animal experiments were evaluated using the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) Risk of Bias tool [30].

The methodological quality and overall certainty of evidence for each study were summarized in Supplementary Files X and Y (GRADE Summary of Findings tables), while item-level RoB assessments were presented in Supplementary Appendix S2 (Tables S2a–S2c).

Data synthesis

Due to the substantial methodological and clinical heterogeneity observed among the included studies—particularly regarding study design, population characteristics, Alb-PRF preparation protocols, outcome measures, and follow-up duration—a quantitative meta-analysis was not performed. The findings were analyzed using a narrative synthesis approach.

A meta-analysis was initially planned if three or more homogeneous randomized controlled trials reported comparable outcomes. In such cases, statistical heterogeneity would have been evaluated using Cochran's Q and I^2 tests, and when appropriate, the DerSimonian–Laird random-effects model would have been applied. For continuous variables, the mean difference (MD) or standardized mean difference (SMD) was to be calculated, while for dichotomous variables, the risk

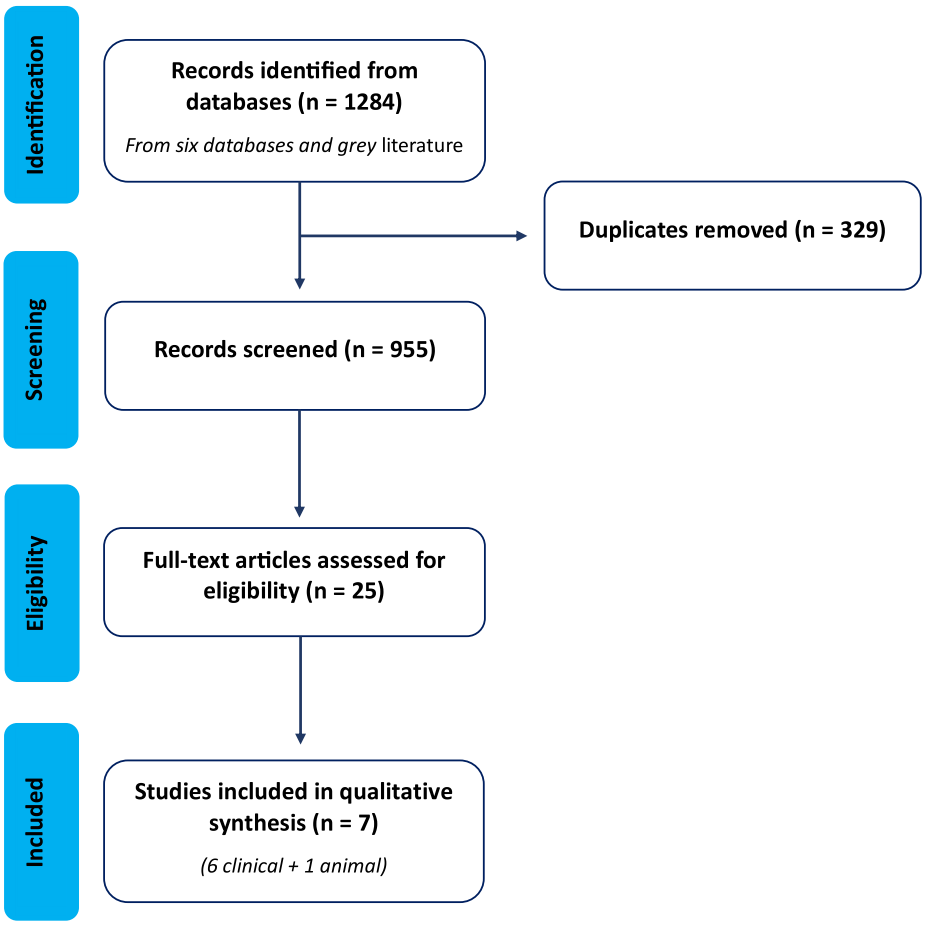

Fig. 1 PRISMA 2020 flow diagram illustrating study identification from six electronic databases and grey literature sources (records identified = 1284; duplicates removed = 329; screened = 955; full-text = 25; included = 7 [6 clinical + 1 animal])

Source	Total Records (n)	Dublicates (n)	Unique (n)
PubMed	6	2	3
Scopus	6	3	3
Web of Science	114	19	95
Cochrane Library	19	4	15
Google Scholar	139	29	110
CrossRef	≈1000	272	728
Total	1.284	329	955

ratio (RR) with 95% confidence intervals would have been used. Publication bias and small-sample effects were to be assessed by funnel plot inspection and the Egger test. Sensitivity (leave-one-out) and subgroup analyses (defect type, follow-up duration, Alb-PRF preparation protocol) were also planned. Because the included studies differed substantially in design, intervention protocols, comparators, and reported outcomes, the conditions required for a valid quantitative synthesis were not met. Therefore, the findings were synthesized narratively. The certainty of evidence for each clinical outcome was evaluated according to the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach, and the results were summarized in the Summary of Findings table (Supplementary File Y) [27, 31, 32].

Results

General findings

A total of seven studies (six clinical and one in vivo animal investigation) evaluating the effects of Alb-PRF on periodontal and peri-implant tissues were included in this systematic review (Table 1). Some of the studies focused on in vivo animal models, whereas others investigated early healing and soft-tissue changes in clinical settings. The clinical trials collectively included 156 participants, with follow-up periods ranging from 7 days to 6 months.

The number of clinical studies remains limited; only one randomized controlled trial specifically addressed the esthetic periodontal region, assessing Alb-PRF injection in interdental papilla reconstruction. Although an increase in papillary volume was reported, Alb-PRF did not demonstrate significant superiority over conventional PRF in terms of CAL, PPD, or periodontal stability [33]. In another randomized controlled trial conducted in intrabony defects, the adjunctive use of Alb-PRF with open-flap surgery showed a modest but consistent short-term (1-month) improvement

Table 1 Main characteristics and key findings of the included clinical and in vivo studies evaluating the effects of albumin-enriched platelet-rich fibrin (Alb-PRF) on periodontal and peri-implant tissues

Author (Year)	Study design/ sample	Intervention (Alb-PRF application)	Comparator	Follow-up/outcomes	Main findings	Risk of bias
Javid et al. (2023) [39]	Split-mouth RCT, n=20	Alb-PRF applied to extraction socket after mandibular 3rd molar removal	L-PRF	7 days	↓ Pain & swelling (VAS, $p<0.05$); faster epithelial closure	Low
Vadiati Saberi et al. (2024)[33]	RCT, n=30	Interdental papilla reconstruction with Alb-PRF gel injection	Hyaluronic acid gel	3 months	↑ Papillary height; no significant CAL or PPD difference ($p>0.05$)	Low
Abdulhak et al. (2024)[22]	RCT, n=32	Gingival phenotype modification (Alb-PRF vs CTG)	CTG	3 & 6 months	↑ GTH at 3 mo ($p<0.05$); no diff. at 6 mo; KTW higher in CTG ($p<0.05$)	Moderate
Kumari et al. (2025)[34]	RCT, n=28	Intrabony defect treatment using Alb-PRF	L-PRF	1 month	↓ PPD and ↑ CAL gain; modest but consistent benefit	Some concerns
Barakat et al. (2025)[40]	Prospective, n=15	Two-stage sinus lifting with Alb-PRF	No control	6 months	≈ 5 mm vertical bone gain at 6 months; however, due to the non-comparative design and low methodological quality (NOS = 1/9), these findings should be interpreted with caution	High
Shokry et al. (2025) [42]	RCT, n=24	Cystic bone defect regeneration with Alb-PRF	Blood clot	6 months	No sig. bone volume gain; fewer complications; safe adjunct	Low
Lourenço et al. (2024)[38]	In vitro + animal	Alb-PRF membrane	Conventional PRF	14 days	↑ PDGF, VEGF, ALP, OPG/RANKL; enhanced osteogenesis	– (preclinical)

RCT randomized controlled trial; *PPD* probing pocket depth; *CAL* clinical attachment level; *GTH* gingival thickness; *KTW* keratinized tissue width; *PDGF* platelet-derived growth factor; *VEGF* vascular endothelial growth factor; *ALP* alkaline phosphatase; *OPG/RANKL* osteoprotegerin/receptor activator of nuclear factor-κB ligand ratio.

in PPD reduction and CAL gain compared with conventional PRF [34]. The methodological quality and risk-of-bias assessments of all included studies are summarized in Table 2. Overall, the certainty of evidence across clinical outcomes was rated as low to moderate, primarily due to small sample sizes, short follow-up durations, and heterogeneity among study designs (see Supplementary Files X and Y).

Biological and mechanistic evaluation

Partial thermal denaturation of serum albumin enhances protein–protein cross-linking, thereby strengthening the mechanical stability of the fibrin–albumin matrix. This modification slows material resorption and prolongs the release of bioactive molecules, including TGF-β1, PDGF, VEGF, insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), fibroblast growth factor-2 (FGF-2), and interleukin-10 (IL-10). Experimental studies reported that Alb-PRF was associated with enhanced cell migration, collagen synthesis, and prolonged release of bioactive molecules [23, 25, 35].

Furthermore, albumin-based hydrogels exhibit high biocompatibility, controlled degradation, and mechanical durability, providing a microenvironment conducive to balanced tissue repair through regulated growth-factor release and attenuation of inflammatory responses [36]. Fujioka-Kobayashi et al. [19] reported that Alb-PRF sustained a longer and more gradual release of TGF-β1 and PDGF-AA/AB compared with classical PRF, supporting the link between mechanical stability and biological efficacy. Similarly, an in vitro study by de Lima Barbosa et al. [37] demonstrated that Alb-PRF induced enhanced alkaline phosphatase (ALP) activity and an increased osteoprotegerin/receptor activator of nuclear factor-κB ligand (OPG/RANKL) ratio in osteoblast-like cells, indicating pronounced osteogenic potential. However, when combined with nanostructured carbonated hydroxyapatite microspheres, this activity significantly decreased, suggesting that interactions between Alb-PRF and graft matrices may modulate biological performance and should be considered in combined applications [37].

Recent in vitro studies have also shown that Alb-PRF membranes exhibit higher PDGF and VEGF release, along with significantly increased ALP activity and OPG/RANKL ratios in MG-63 osteoblast-like cells, emphasizing the regenerative potential of Alb-PRF at the cellular level [38]. The prolonged release pattern of growth factors provides a biological basis for regulating inflammation during the early healing phase, although direct in vivo or clinical confirmation of M2 macrophage polarization specific to Alb-PRF is still lacking.

The biological behavior of Alb-PRF is influenced by alterations in growth-factor activity resulting from heat treatment of plasma fractions. Notably, unheated platelet-poor plasma and buffy-coat lysate have been shown to induce expression of TGF-β target genes such as IL-11 and NADPH oxidase 4 (NOX4) in oral fibroblasts, whereas heat-treated plasma does not elicit this response. These findings indicate that growth-factor activity may differ between heated and non-heated plasma-derived fractions used in Alb-PRF preparation [21].

Alb-PRF represents a heat-stabilized form of PRF developed to overcome the short degradation period of conventional variants. In vivo data demonstrate that, unlike

Table 2 Risk-of-bias assessment of the included studies. The Cochrane RoB-2 tool was applied to randomized controlled trials, the Newcastle–Ottawa Scale (NOS) to non-randomized prospective studies, and the SYRCLE tool to animal experiments

Study (Year)	Study design	Assessment tool	Randomization	Allocation concealment	Blinding	Incomplete data	Reporting bias	Overall risk level
Javid et al. (2023)[39]	RCT	RoB-2	*Low*	**Unclear**	*Low*	*Low*	*Low*	*Low*
Vadiati Saberi et al. (2024) [33]	RCT	RoB-2	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*
Abdulhak et al. (2024)[22]	RCT	RoB-2	*Low*	**Unclear**	*Low*	*Low*	*Low*	**Moderate**
Kumari et al. (2025)[34]	RCT	RoB-2	*Low*	*Low*	*Low*	*Low*	*Low*	*Low*
Barakat et al. (2025)[40]	Prospective Clinical	NOS (1/9 stars)	N/A	N/A	N/A	Limited follow-up	N/A	**Moderate**
Shokry et al. (2025)[42]	RCT	RoB-2	*Low*	**Unclear**	*Low*	*Low*	*Low*	*Low*
Lourenço et al. (2024)[38]	Animal Experiment	SYRCLE	*Low*	*Low*	–	*Low*	*Low*	*Low*

Italic = Low risk; Bold = Some concerns/Moderate; Bolditalic = High risk.

traditional PRF matrices that typically degrade within 2–3 weeks, Alb-PRF remains stable for approximately 4–6 months, functioning as both a soft-tissue barrier and a biologically active filler [25]. At the clinical level, a split-mouth randomized controlled trial on mandibular third molar extractions reported that Alb-PRF application resulted in faster edema reduction and more favorable early healing outcomes compared with L-PRF at day 7, with distinct differences observed in the kinetics of soluble growth-factor release between the two biomaterials [39].

Heat-induced albumin gelation delays the degradation of the fibrin–albumin matrix compared with classical PRF, reinforcing the mechanical and biological rationale underlying Alb-PRF's clinical use [18]. Experimental studies have shown that while conventional L-PRF and H-PRF samples are completely resorbed within 21 days, Alb-PRF maintains volumetric stability, supporting the notion that heat-induced albumin cross-linking enhances the material's biological durability [25]. The current biomaterial literature acknowledges the advantages of albumin-based structures in terms of biocompatibility and matrix stabilization; however, these findings should not be directly generalized to Alb-PRF. Therefore, interpretations regarding the biomodulatory properties of Alb-PRF should remain cautious and confined to the available experimental evidence [23].

Discussion

Interpretation of findings in the clinical context

The findings of this systematic review indicate that Alb-PRF provides notable advantages during the early healing phase, particularly regarding soft-tissue volume maintenance, edema control, and postoperative comfort. Evidence from studies on mandibular third molar surgery and interdental papilla reconstruction consistently supports these short-term benefits [25, 33, 39].

These findings are further supported by clinical investigations. In a split-mouth randomized controlled trial performed during mandibular third molar extractions, Alb-PRF resulted in significantly greater reductions in postoperative pain, edema, and inflammatory biomarker levels compared with L-PRF [39]. Similarly, in interdental papilla reconstruction procedures, Alb-PRF gel injection increased papillary height, although no superiority was observed over conventional PRF in terms of CAL or PPD [33]. In gingival phenotype modification procedures, Alb-PRF application led to a significant increase in GTH at three months compared with connective tissue graft (CTG); however, this difference was not maintained at six months, and KTW remained more stable in the CTG group [22]. Collectively, these findings suggest that Alb-PRF may represent a biologically less invasive adjunct for procedures targeting early soft-tissue healing, although additional high-quality randomized controlled trials are needed to clarify its long-term regenerative potential.

In a prospective two-stage lateral sinus-lifting procedure using Alb-PRF alone, a mean vertical bone gain of 5.07 ± 1.78 mm and a bone density of approximately 323 HU (Hounsfield units) were achieved at 6 months. Although limited in scope, available prospective data suggest that Alb-PRF maintains volumetric stability at the graft site for up to 4–6 months, behaving as a biologically active filler material. However, this conclusion is based on a single uncontrolled study and requires further validation [40].

A recent case report combining Alb-PRF with an alloplastic bone graft for alveolar ridge preservation demonstrated substantial maintenance of bone volume both clinically and radiographically at 6 months, suggesting that Alb-PRF may function as a biological carrier that supports not only soft-tissue repair but also hard-tissue regeneration when used in appropriate combinations. These findings also imply that incorporating Alb-PRF into "sticky bone"–like composites may improve graft stability and reduce postoperative alveolar resorption [41]. In contrast, results in cystic bone cavities remain inconsistent. A three-dimensional volumetric analysis–based randomized controlled trial found no significant additional bone gain at 6 months compared with conventional clot application, though Alb-PRF was safely used without increasing complication rates [42]. Collectively, the evidence suggests that Alb-PRF's regenerative effect depends on the defect type and surgical indication, and no current data confirm its superiority over classical PRF regarding attachment gain, probing depth reduction, or hard-tissue regeneration [33]. Thus, Alb-PRF should presently be regarded as an adjunctive biological material primarily supporting early soft-tissue healing rather than a primary regenerative agent.

Relationship between biological advantages and clinical outcomes

The thermally stabilized fibrin–albumin matrix supports the prolonged and controlled release of growth factors such as TGF-β1 and PDGF-AA/AB [19–21]. In addition to soluble growth factors, emerging evidence suggests that platelet-derived biomaterials may exert part of their biological activity through extracellular vesicles acting as paracrine mediators of immunomodulation and tissue repair [43]. These biological characteristics align well with Alb-PRF's observed soft-tissue benefits during early healing. Nevertheless, no direct clinical or in vivo evidence currently confirms its immunomodulatory actions—particularly those involving M2 macrophage polarization [23]. The discrepancy between favorable experimental osteogenic signals and the limited clinical hard-tissue outcomes suggests a translational gap

between laboratory-based observations and real clinical regenerative performance.

Recent experimental studies suggest that platelet-derived biomaterials can modulate the immune microenvironment by promoting a shift in macrophage phenotype from proinflammatory M1 to regenerative, anti-inflammatory M2, thereby accelerating healing [44]. Narrative syntheses have further contextualized these findings, proposing that such immunomodulatory effects may underlie interindividual variability in clinical outcomes and support phenotype-oriented and personalized periodontal therapy. Therefore, any potential immunoregulatory effects of Alb-PRF should currently be considered biologically plausible but unproven, and confirmation requires further controlled studies. In vitro evidence demonstrates that PRF membranes downregulate IL-1β and IL-6 expression while upregulating M2-associated markers such as arginase-1 and chitinase-like protein-3 (Chi3l3/YM-1), promoting inflammation resolution and tissue repair [45].

Despite its prolonged growth-factor release and enhanced mechanical stability, Alb-PRF lacks key biological prerequisites—such as osteoconductive architecture, space-maintaining capacity, and load-bearing rigidity—required for predictable periodontal hard-tissue regeneration. Specifically, the material does not provide sufficient space-maintaining capacity, osteoconductive architecture, or mechanical rigidity to support sustained bone formation under functional loading. Moreover, the gradual release of growth factors from Alb-PRF appears preferentially optimized for soft-tissue maturation and inflammation resolution rather than for the sustained induction of osteoblast differentiation and mineralized matrix deposition under regenerative conditions. These mechanistic limitations may explain why clinical studies have failed to demonstrate consistent improvements in bone fill, clinical attachment gain, or probing depth reduction when Alb-PRF is used as a stand-alone regenerative material.

Impact of protocol heterogeneity on outcomes

The included studies revealed substantial variation in Alb-PRF heating duration, gel-to-PRF ratio, and centrifugation parameters (Table 3). This methodological heterogeneity reduces the comparability of clinical outcomes and limits the strength of conclusions regarding Alb-PRF's regenerative potential. According to the GRADE framework (see Supplementary Files X and Y), the overall certainty of evidence was rated as *low to moderate* due to small sample sizes and protocol heterogeneity.

Notably, evidence indicating that heat-treated platelet-poor plasma may limit growth-factor activity suggests that preparation parameters exert a direct influence on clinical performance [21]. Therefore, future research employing Alb-PRF should prioritize multicenter collaboration under harmonized, standardized preparation protocols to improve reproducibility and validity.

Comparison with other PRF variants

Because different PRF variants vary in fibrin architecture, cellular composition, and growth-factor release kinetics, comparative analyses are essential to accurately position Alb-PRF in clinical practice. A-PRF, Alb-PRF, and i-PRF are third-generation modifications of PRF that aim to enhance mechanical stability and extend growth-factor release through thermal and centrifugation adjustments [25].

As summarized in Table 4, Alb-PRF demonstrates a distinct, prolonged release profile and marked soft-tissue biomodulatory potential, primarily attributed to the albumin gel formed from heat-treated platelet-poor plasma [21, 46]. Nonetheless, current evidence does not support the use of Alb-PRF as a primary agent for hard-tissue regeneration; instead, it should be applied in combination with grafts or barrier membranes for optimal outcomes.

Table 3 Main methodological parameters reported for Alb-PRF preparation across the included studies

Protocol parameter	Reported application in Alb-PRF	Description
Heating phase (platelet-poor plasma)	75 °C for approximately 10 minutes	Used to induce partial denaturation of serum albumin and formation of the albumin gel structure [21]
Cooling phase	Slow cooling to 25–30 °C	Stabilization of the gel matrix and reduction of thermal precipitation risk [19]
Serum gel : liquid PRF ratio	Approximately 1 : 1 (volume/volume)	Reported ratio used to obtain a clinically manageable consistency while preserving the liquid PRF component [39]
Centrifugation protocol for liquid PRF	Approximately 700 g for 3 minutes (same as i-PRF protocol)	Lower g-force helps preserve the cellular fraction of liquid PRF [18]
Clinical application form	Injectable gel and membrane-like condensed structure	Reported in the literature as an injectable gel or membrane-like condensed form [33]

Table 4 Comparative structural and biological characteristics of major PRF variants, including Alb-PRF. Alb-PRF is characterized by a dense fibrin–albumin matrix and a prolonged release profile; however, evidence supporting its superiority over other PRF variants in hard-tissue regeneration remains limited [2, 18, 19, 39, 47]

Characteristic	L-PRF	A-PRF/i-PRF	Alb-PRF
Preparation protocol	Standard centrifugation speed and duration	Lower centrifugation speed and longer duration	Combination of heat-treated platelet-poor plasma and liquid PRF
Fibrin matrix structure	Denser and more stable	More porous fibrin network	Dense, albumin-reinforced stable network
Cellular content	Moderate leukocyte and platelet levels	Higher cellular content	Moderate to high cellular contribution (derived from liquid PRF)
Growth-factor release pattern	High initial release within the first 7 days	Prolonged release (7–14 days)	Gradual and extended release profile
Primary clinical advantage	Easy preparation and tissue stability	Enhanced cellular activity and biological responsiveness	Early healing and soft-tissue biomodulation
Limitation	Short duration of effect	Lower mechanical strength	Insufficient evidence for hard-tissue regeneration efficacy

Strengths of the available evidence

The available literature provides several notable strengths. First, the biological rationale of Alb-PRF is relatively well characterized, particularly regarding the formation of a heat-stabilized fibrin–albumin matrix and its potential for sustained growth-factor release [21]. Second, despite the limited number of studies, clinical investigations across different indications have consistently suggested favorable effects on early postoperative healing, pain, and edema control [21, 33, 39]. Third, the inclusion of both clinical and preclinical in vivo evidence contributes to a broader understanding of the biological behavior and translational relevance of Alb-PRF.

Limitations of the present systematic review

Several limitations of the present systematic review should be acknowledged. First, the number of available studies was limited, and most clinical investigations were characterized by small sample sizes, single-center designs, and relatively short follow-up periods, thereby restricting external validity and long-term interpretation. Second, substantial heterogeneity existed across the included studies with respect to surgical indication, study design, comparator groups, Alb-PRF preparation parameters, and reported outcome measures, which precluded quantitative synthesis. Third, some included studies presented methodological concerns, including limited reporting of allocation concealment, non-comparative designs, or potential performance and detection bias. Fourth, evidence regarding hard-tissue regeneration remains especially limited, making it difficult to draw robust conclusions on the regenerative predictability of Alb-PRF beyond early soft-tissue healing. These limitations underline the need for future well-designed, multicenter randomized controlled trials with standardized protocols and longer follow-up periods.

Recommendations for future research

1. **Conduct** multicenter randomized controlled trials with follow-up periods of ≥12 months to verify the long-term stability and clinical predictability of Alb-PRF outcomes.
2. **Standardize** Alb-PRF preparation parameters—particularly heating duration, albumin-to-serum ratio, and centrifugation settings—to minimize methodological heterogeneity and enhance reproducibility across studies.
3. **Evaluate** biological and immunological markers (e.g., TGF-β1, IL-10, VEGF, pSTAT3, IL-17) in parallel with clinical endpoints to clarify the underlying mechanisms of action.
4. **Compare** Alb-PRF with other platelet-derived biomaterials (L-PRF, i-PRF, and A-PRF) and its combinations with grafts, membranes, or soft-tissue substitutes to determine its relative regenerative potential in different clinical indications, such as peri-implant phenotype management, papilla stability, and soft-tissue volume preservation after extraction.

Clinical positioning of Alb-PRF based on biological function

Based on the synthesis of current clinical outcomes and biological rationale, Alb-PRF should not be interpreted as a universal regenerative material but rather as a context-dependent adjunct with indication-specific utility. The indication-specific clinical positioning of Alb-PRF is summarized in Table 5. Overall, the currently available evidence suggests that Alb-PRF provides its most consistent

Table 5 Evidence-based clinical positioning of Alb-PRF according to its biological function in periodontal and peri-implant therapy. This table summarizes indication-specific recommendations regarding the use of Alb-PRF as a stand-alone material or as an adjunctive biomaterial in periodontal and peri-implant therapies

Clinical indication	Alb-PRF alone	Alb-PRF as adjunct	Rationale
Interdental papilla reconstruction	Recommended	–	Primarily soft-tissue–driven indication; clinical evidence supports early volume stability and epithelial maturation without the need for hard-tissue regeneration
Soft-tissue phenotype modification (gingival thickness, peri-implant mucosa)	Recommended	–	Alb-PRF enhances early soft-tissue stability and reduces postoperative morbidity; long-term hard-tissue gain is not the primary objective
Socket preservation	Use with caution	Recommended	Alb-PRF alone may preserve soft-tissue contours but does not consistently ensure alveolar bone maintenance; combination with graft materials is biologically more predictable
Periodontal intrabony defects	Not recommended	Optional	True periodontal regeneration requires osteogenic and space-maintaining properties; Alb-PRF may serve only as a supportive biological modifier
Peri-implant bone loss/peri-implantitis defects	Not recommended	Optional	Insufficient clinical and biological evidence supports Alb-PRF as a stand-alone regenerative material; adjunctive use may improve early healing only

Alb-PRF albumin-enriched platelet-rich fibrin.

benefit during the early healing phase, particularly by supporting soft-tissue stability, epithelial maturation, and postoperative comfort. In contrast, evidence for periodontal and peri-implant hard-tissue regeneration remains limited, heterogeneous, and insufficient for definitive clinical recommendations. Accordingly, Alb-PRF should presently be interpreted primarily as an indication-specific adjunctive biomaterial rather than a stand-alone regenerative substitute.

Conclusion

Current evidence indicates that Alb-PRF primarily supports early soft-tissue healing, wound stability, and postoperative comfort rather than predictable hard-tissue regeneration. Although its biological rationale is promising, the available clinical evidence remains limited by small sample sizes, protocol heterogeneity, and short follow-up periods. Therefore, Alb-PRF should presently be regarded as an indication-specific adjunctive biomaterial, and further well-designed randomized controlled trials are required before stronger regenerative recommendations can be made.

Clinical recommendations

Alb-PRF may be indicated in procedures requiring soft-tissue biomodulation (evidence level: low; most data derived from small-scale randomized controlled or prospective studies with ≤3–6 months of follow-up). Short-term benefits have been reported for papilla reconstruction, peri-implant phenotype augmentation, and early socket healing.

Alb-PRF should not be used alone for hard-tissue regeneration; in cases involving intrabony defects or peri-implant bone loss, it should be combined with grafts and/or membranes.

Alb-PRF may improve postoperative comfort by reducing pain and edema during early healing, making it a useful adjunctive biological agent in minimally invasive surgeries.

A standardized preparation protocol should be followed to ensure reproducibility across centers, including consistency in albumin gel heating duration, serum-to-PRF ratio, and centrifugation parameters.

Clinical and radiographic follow-up of at least 6–12 months is recommended for patients treated with Alb-PRF.

Meta-analysis: Not performed due to methodological and clinical heterogeneity.

Clinical significance: Alb-PRF appears to stabilize the early wound microenvironment and soft-tissue phenotype rather than directly inducing periodontal regeneration; however, current evidence does not substantiate its role in hard-tissue regeneration, and its use as a primary graft substitute should be postponed until robust, high-quality data emerge.

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Data Availability All data generated or analyzed during this study are included in this published article.

Declarations

Conflict of interest The authors declare that there is no conflict of interest related to this systematic review.

Ethical approval This article is a literature-based systematic review and did not involve human or animal subjects; therefore, ethical approval was not required.

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References

1. Miron RJ, Choukroun J. Platelet rich fibrin in regenerative dentistry: biological background and clinical indications. Chichester: John Wiley & Sons; 2017.
2. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol. 2009;27(3):158–67. https://doi.org/10.1016/j.tibtech.2008.11.009.
3. Hajibagheri P, Basirat M, Tabari-Khomeiran Z, Asadi-Aria A. The efficacy of platelet-rich fibrin (PRF) in post-extraction hard and soft tissue healing and associated complications: a systematic review and meta-analysis of split-mouth randomized clinical trials. BMC Oral Health. 2025;25(1):869. https://doi.org/10.1186/s12903-025-06238-1.
4. Laforgia A, Inchingolo AD, Riccaldo L, Avantario P, Buongiorno S, Malcangi G, et al. The use of platelet-rich fibrin (PRF) in the management of dry socket: a systematic review. Int J Mol Sci. 2024. https://doi.org/10.3390/ijms251810069.
5. Saleh W, Abdelhaleem M, Elmeadawy S. Assessing the effectiveness of advanced platelet rich fibrin in treating gingival recession: a systematic review and meta-analysis. BMC Oral Health. 2024;24(1):1400. https://doi.org/10.1186/s12903-024-05115-7.
6. Moreno X, Neira P, Strauss FJ, Mery MI, Gruber R, Cavalla F. Effect of leukocyte- and platelet-rich fibrin on peri-implant mucosal thickness in edentulous patients treated with mandibular implant-retained overdentures: a randomized controlled trial. J Clin Med. 2025. https://doi.org/10.3390/jcm14196917.
7. Giammarinaro E, Baldini N, Covani U, Menini M, Pesce P, Marconcini S. Does platelet-rich fibrin enhance the outcomes of peri-implant soft tissues? A systematic review. BMC Oral Health. 2025;25(1):615. https://doi.org/10.1186/s12903-025-05922-6.
8. Silva F, Chauca-Bajaña L, Caponio VCA, Cueva KAS, Velasquez-Ron B, Padín-Iruegas ME, et al. Regeneration of periodontal intrabony defects using platelet-rich fibrin (PRF): a systematic review and network meta-analysis. Odontology. 2024;112(4):1047–68. https://doi.org/10.1007/s10266-024-00949-7.
9. Park W-J, Han S-H, Kim NJ, Park J-B. The efficacy of utilizing platelet-rich fibrin for managing periodontal intrabony defects in conjunction with graft material: a systematic review and meta-analysis. Appl Sci (Basel). 2024;14(8):3371.
10. Guan S, Xiao T, Bai J, Ning C, Zhang X, Yang L, et al. Clinical application of platelet-rich fibrin to enhance dental implant stability: a systematic review and meta-analysis. Heliyon. 2023;9(2):e13196. https://doi.org/10.1016/j.heliyon.2023.e13196.
11. Zhao Z, Li Y, Zhang F, Gao L, Lin H. The impact of platelet concentrates in maxillary sinus lifts: a systematic review and meta-analysis. J Craniomaxillofac Surg. 2025;53(7):960–9. https://doi.org/10.1016/j.jcms.2025.03.009.
12. Babich O, Lugassy E, Babich M, Abayov P, Haimov E, Juodzbalys G. The use of platelet-rich fibrin in sinus floor augmentation surgery: a systematic review. J Oral Maxillofac Res. 2024;15(2):e1. https://doi.org/10.5037/jomr.2024.15201.
13. Molina-Barahona M, Castillo J, Freire-Meza E, Vásquez-Palacios AC, Morales-Navarro D, Avecillas-Rodas R. Radiographic evaluation in alveolar preservation using platelet-rich fibrin: a randomized controlled trial. Dent J. 2025. https://doi.org/10.3390/dj13060231.
14. Siawasch SAM, Yu J, Castro AB, Dhondt R, Teughels W, Temmerman A, et al. Autologous platelet concentrates in alveolar ridge preservation: a systematic review with meta-analyses. Periodontol 2000. 2025;97(1):104–30. https://doi.org/10.1111/prd.12609.
15. Rebimbas Guerreiro S, Marto CM, Paula A, Pereira JRA, Carrilho E, Marques-Ferreira M, et al. Platelet-rich plasma and platelet-rich fibrin in endodontics: a scoping review. Int J Mol Sci. 2025. https://doi.org/10.3390/ijms26125479.
16. Goswami P, Chaudhary V, Arya A, Verma R, Vijayakumar G, Bhavani M. Platelet-rich fibrin (PRF) and its application in dentistry: a literature review. J Pharm Bioallied Sci. 2024;16(Suppl 1):S5-s7. https://doi.org/10.4103/jpbs.jpbs_435_23.
17. Khattri S, Kaushik M, Tomar N, Ahmed S, Rana N, Khan M, et al. Effect of platelet-rich fibrin coating on secondary stability of dental implants: a systematic review and meta-analysis. Cureus. 2024;16(12):e75166. https://doi.org/10.7759/cureus.75166.
18. Miron RJ, Pikos MA, Estrin NE, Kobayashi-Fujioka M, Espinoza AR, Basma H, et al. Extended platelet-rich fibrin. Periodontol 2000. 2024;94(1):114–30. https://doi.org/10.1111/prd.12537.
19. Fujioka-Kobayashi M, Schaller B, Mourão C, Zhang Y, Sculean A, Miron RJ. Biological characterization of an injectable platelet-rich fibrin mixture consisting of autologous albumin gel and liquid platelet-rich fibrin (Alb-PRF). Platelets. 2021;32(1):74–81. https://doi.org/10.1080/09537104.2020.1717455.
20. Ambujakshi Manjunatha V, Damera T, K A, Singh R, Popat T, Vala D. Novel albumin gel-platelet-rich fibrin mixture (Alb-PRF); where do we stand? Int J Clin Biochem Res. 2022;8:239–41. https://doi.org/10.18231/j.ijcbr.2021.051.
21. Kargarpour Z, Nasirzade J, Panahipour L, Miron RJ, Gruber R. Liquid platelet-rich fibrin and heat-coagulated albumin gel:

bioassays for TGF-β activity. Materials. 2020. https://doi.org/10.3390/ma13163466.
22. Abdulhak S, Kassem T, Alsayed Tolibah Y. Comparison between autologous albumin gel and liquid platelet-rich fibrin mixture versus connective tissue graft to modify the gingival phenotype: a randomized controlled trial. Cureus. 2024;16(6):e61958. https://doi.org/10.7759/cureus.61958.
23. Kuten Pella O, Hornyák I, Horváthy D, Fodor E, Nehrer S, Lacza Z. Albumin as a biomaterial and therapeutic agent in regenerative medicine. Int J Mol Sci. 2022. https://doi.org/10.3390/ijms231810557.
24. Gummaluru SS, Gurumoorthy K, Kancharla AK, Boyapati R. Evaluating the predictability and regenerative capacity of novel platelet concentrate (PC)-titanium platelet rich fibrin (T-PRF) in the field of dentistry. Cumhuriyet Dent J. 2023;26(3):332–9. https://doi.org/10.7126/cumudj.1252781.
25. Song P, He D, Ren S, Fan L, Sun J. Platelet-rich fibrin in dentistry. J Appl Biomater Funct Mater. 2024;22:22808000241299588. https://doi.org/10.1177/22808000241299588.
26. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71.
27. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane Handbook for Systematic Reviews of Interventions London, UK: Cochrane; 2024 [Version 6.5 (updated August 2024):[Available from: https://www.cochrane.org/handbook.
28. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898.
29. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Non-Randomized Studies in Meta-Analysis. 2000. Available from: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
30. Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol. 2014;14:43. https://doi.org/10.1186/1471-2288-14-43.
31. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88. https://doi.org/10.1016/0197-2456(86)90046-2.
32. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924–6. https://doi.org/10.1136/bmj.39489.470347.AD.
33. Vadiati Saberi B, Khalighi Sigaroudi A, Kamani M, Rafiei E. Comparison of the effect of albumin with platelet-rich fibrin (Alb-PRF) gel and hyaluronic acid gel injection on interdental papilla reconstruction: a randomized clinical trial. J Adv Periodontol Implant Dent. 2024;16(2):109–15. https://doi.org/10.34172/japid.2024.018.
34. Kumari S, Sharma AK, Sunil MKS, Koppula SK, Sharma S. A randomized controlled study comparing albumin-enriched platelet-rich fibrin and conventional platelet-rich fibrin for the treatment of intrabony defects. J Pharm Bioallied Sci. 2025;17(Suppl 2):S1619–21. https://doi.org/10.4103/jpbs.jpbs_190_25.
35. Katarivas Levy G, Ong J, Birch MA, Justin AW, Markaki AE. Albumin-enriched fibrin hydrogel embedded in active ferromagnetic networks improves osteoblast differentiation and vascular self-organisation. Polymers. 2019. https://doi.org/10.3390/polym11111743.
36. Meng R, Zhu H, Deng P, Li M, Ji Q, He H, et al. Research progress on albumin-based hydrogels: properties, preparation methods, types and its application for antitumor-drug delivery and tissue engineering. Front Bioeng Biotechnol. 2023;11:1137145. https://doi.org/10.3389/fbioe.2023.1137145.
37. de Lima Barbosa R, Rodrigues Santiago Rocha N, Stellet Lourenço E, de Souza Lima VH, Mavropoulos E, Mello-Machado RC, et al. The association of nanostructured carbonated hydroxyapatite with denatured albumin and platelet-rich fibrin: impacts on growth factors release and osteoblast behavior. J Funct Biomater. 2024. https://doi.org/10.3390/jfb15010018.
38. Lourenço ES, Rocha NRS, de Lima Barbosa R, Mello-Machado RC, de Souza Lima VH, Leite PEC, et al. Investigating the biological efficacy of albumin-enriched platelet-rich fibrin (Alb-PRF): a study on cytokine dynamics and osteoblast behavior. Int J Mol Sci. 2024. https://doi.org/10.3390/ijms252111531.
39. Javid K, Mourão CF, Mello-Machado RC, Sartoretto SC, Torres M, Stellet Lourenço E, et al. Clinical and biochemical evaluation of the use of Alb-PRF versus L-PRF in mandibular third molar extractions: a split-mouth randomized clinical trial. J Funct Biomater. 2023. https://doi.org/10.3390/jfb14100505.
40. Barakat M, Khalil A, Albash Z. Efficacy of platelet-rich albumin and fibrin gel in two-stage lateral sinus lift: a prospective study. Ann Med Surg (Lond). 2025;87(9):5409–16. https://doi.org/10.1097/ms9.0000000000003589.
41. Moualla Z, Qasem T, Alnada A. Alveolar ridge preservation using a mixture of Alb-PRF and alloplastic bone graft: a case report. Case Rep Dent. 2025;2025:3007346. https://doi.org/10.1155/crid/3007346.
42. Shokry M, Melek LNF, Amer TA. Three-dimensional volumetric analysis of bone regeneration following jaw cyst enucleation with and without an autologous albumin gel-platelet-rich fibrin mixture (Alb-PRF): a randomized controlled clinical trial. BMC Oral Health. 2025;25(1):693. https://doi.org/10.1186/s12903-025-06027-w.
43. Biçakçioğlu H, Çolak G. Platelet-rich fibrin-derived extracellular vesicles: emerging biological mediators in periodontal regeneration. Odontology. 2025. https://doi.org/10.1007/s10266-025-01275-2.
44. Anitua E, Troya M, Alkhraisat MH. Immunoregulatory role of platelet derivatives in the macrophage-mediated immune response. Front Immunol. 2024;15:1399130. https://doi.org/10.3389/fimmu.2024.1399130.
45. Nasirzade J, Kargarpour Z, Hasannia S, Strauss FJ, Gruber R. Platelet-rich fibrin elicits an anti-inflammatory response in macrophages in vitro. J Periodontol. 2020;91(2):244–52. https://doi.org/10.1002/jper.19-0216.
46. Zheng X, Yan X, Cheng K, Feng M, Wang Y, Xiao B. Exploration of proper heating protocol for injectable horizontal platelet-rich fibrin gel. Int J Implant Dent. 2022;8(1):36. https://doi.org/10.1186/s40729-022-00436-0.
47. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin Oral Investig. 2016;20(9):2353–60. https://doi.org/10.1007/s00784-016-1719-1.

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