



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Platelet-Rich Plasma for Burn Wound Healing in Preclinical Models: A Systematic Review of Efficacy and Biomolecular Mechanisms

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ARTICLE INFO

Keywords:

Burn wound
EGF
Fibroblast
Platelet-rich plasma
Preclinical models

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All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/bsm.v9i10.1398>

ABSTRACT

Background: Burn injuries represent a major global health issue, with complex pathophysiology that often leads to significant morbidity. Platelet-rich plasma (PRP) has been identified as a potential therapeutic agent due to its high concentration of growth factors that promote tissue renewal. This review synthesizes preclinical evidence on the efficacy of PRP for burn wounds. **Methods:** This systematic review followed PRISMA guidelines, searching PubMed, Scopus, and ScienceDirect for animal studies on PRP for burn wounds. The primary outcomes were wound healing, fibroblast scores, and VEGF/EGF levels. The SYRCLE tool was used for risk of bias assessment. **Results:** Eleven studies involving 526 animals were included. The risk of bias across studies was generally high or unclear, primarily due to poor reporting of randomization and blinding. Macroscopically, PRP was reported to accelerate wound closure in partial-thickness burns within 4-7 days and in full-thickness burns from day 8 onward. On a biomolecular level, PRP was associated with increased fibroblast scores and elevated tissue concentrations of VEGF and EGF from the first day post-treatment ($P < 0.05$ in multiple studies). **Conclusion:** While the included studies suggest PRP may enhance healing, definitive conclusions are precluded by the high risk of bias and methodological heterogeneity across the preclinical evidence base.

1. Introduction

Burn injuries, resulting from thermal, electrical, or chemical insults, constitute a severe form of trauma and a significant global public health challenge. The World Health Organization estimates that burns are responsible for approximately 180,000 deaths annually, with a disproportionate impact on low- and middle-income countries.¹ Beyond acute mortality, these injuries inflict profound long-term morbidity, including debilitating scar contractures, chronic pain,

and severe psychological trauma that fundamentally diminishes a patient's quality of life.²

The pathophysiology of a severe burn is a dynamic and evolving process. The initial thermal assault creates a central zone of coagulation, characterized by irreversible protein denaturation and cell death.³ Critically, this is surrounded by a zone of stasis, an area of compromised perfusion where tissue is initially viable but exquisitely vulnerable to progressive ischemia and subsequent necrosis. This zone is the

primary therapeutic target in acute burn care. The release of potent inflammatory mediators from injured cells initiates a robust inflammatory cascade, further impairing microvascular circulation and exacerbating tissue hypoxia.⁴ This complex interplay of ischemia, inflammation, and oxidative stress underscores the profound difficulty in managing these injuries effectively.

The standard of care for deep burns involves surgical excision of necrotic tissue followed by autologous skin grafting.⁵ Although life-saving, this approach is constrained by the availability of healthy donor skin, and the harvesting procedure creates a new, painful wound, increasing the patient's risk of infection and overall metabolic stress. Alternative modalities, such as allografts and xenografts, offer temporary wound coverage but are universally limited by immune rejection. Modern bioengineered skin substitutes represent a significant advance but are often associated with prohibitive costs and fail to fully recapitulate the complex architecture and function of native skin.⁶ Consequently, a critical, unmet clinical need persists for accessible and effective therapies that can accelerate healing and improve the quality of regenerated tissue.

Platelet-rich plasma (PRP) has emerged as a promising autologous biotherapy. PRP is a concentrate of platelets derived from the patient's own blood, containing a supraphysiological concentration of growth factors and cytokines stored within platelet alpha-granules.⁷ Upon activation at the wound site, these platelets release a cocktail of bioactive molecules that orchestrate the healing cascade, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF- β), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF).⁸ These factors collectively promote cell proliferation, migration, and differentiation, while the resulting fibrin matrix provides a provisional scaffold for tissue regeneration. Already utilized in diverse medical fields, PRP's autologous nature minimizes risks of immunogenicity and disease transmission, and its reported bactericidal properties are an added

benefit for infection-prone burn wounds.⁹

Despite a strong therapeutic rationale, the preclinical evidence for PRP in burn care is scattered across numerous studies with disparate methodologies. This makes it difficult for researchers to draw firm conclusions.¹⁰ This review aims to systematically synthesize the available evidence from animal studies on the efficacy of PRP for treating burn wounds. To our knowledge, this is the first systematic review to specifically synthesize evidence by simultaneously analyzing the macroscopic, microscopic, and molecular dimensions of PRP-mediated repair. The specific objectives are to evaluate the effect of PRP on macroscopic wound closure, microscopic fibroblast proliferation, and the local concentration of key signaling molecules like VEGF and EGF. This multi-faceted approach is critical because it connects the observable outcome (wound closure) to the underlying cellular process (fibroplasia) and the molecular drivers (angiogenesis and re-epithelialization signals), providing a more holistic understanding of PRP's potential mechanism of action. By consolidating these findings, this review seeks to clarify the preclinical efficacy of PRP and provide a robust evidence base to guide future research.

2. Methods

This systematic review was conducted and reported in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Studies were selected based on a predefined set of eligibility criteria, structured around the population, intervention, comparison, and outcome (PICO) framework: Population (P): In vivo preclinical animal models (rodents) with an experimentally induced burn wound; Intervention (I): Application of any formulation of platelet-rich plasma (PRP) or platelet-rich fibrin (PRF) to the burn wound; Comparison (C): A concurrent control group receiving either a placebo, standard dressing, or no treatment; Outcomes (O): Studies had to report at least one of the following: wound healing

rate, histological assessment of fibroblast proliferation, or quantitative measurement of VEGF or EGF.

Exclusion criteria included studies lacking a full-text version, articles not written in English, reviews, human clinical studies, and studies without a comparative control group. A comprehensive literature search was conducted across three major electronic databases: PubMed, Scopus, and ScienceDirect. The search strategy combined keywords and subject headings related to PRP, burn wounds, and animal models. For full reproducibility, the exact search strings used for each database are provided in a supplementary appendix. The search string for PubMed was: (((("platelet-rich plasma"[MeSH Terms]) OR "platelet-rich plasma"[Title/Abstract] OR "PRP"[Title/Abstract] OR "platelet-rich fibrin"[MeSH Terms])) AND (("burns"[MeSH Terms]) OR "burn"[Title/Abstract]) AND (("animals"[MeSH Terms:noexp]) OR "animal"[Title/Abstract] OR "rodent"[Title/Abstract])).

Two reviewers independently screened all identified records, first by title and abstract and then by full-text assessment, to determine final eligibility. Any disagreements were resolved by consensus or consultation with a third reviewer. A standardized form was used to extract data from each included article. Extracted variables included study identifiers, animal and burn model specifics, detailed intervention and control protocols, and all relevant outcome data. Where data were missing, an attempt was made to contact the original authors. The methodological quality of each study was independently assessed by two reviewers using the SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) Risk of Bias tool, which is specifically designed for animal intervention studies. This tool evaluates 10 domains related to selection, performance, detection, attrition, reporting, and other sources of bias.

A quantitative meta-analysis was considered but ultimately deemed inappropriate due to substantial

clinical, methodological, and statistical heterogeneity across the included studies. A narrative synthesis of the evidence was therefore performed. The decision to forego meta-analysis was based on several key sources of heterogeneity. The studies employed different animal models (Wistar rats, Sprague-Dawley rats, mice, and diabetic rats). Furthermore, the methods for inducing burns varied significantly, as did the resulting burn depths (partial-thickness vs. full-thickness). This clinical diversity means that the biological responses and healing potentials were likely different from the outset. There was no standardization in the PRP interventions. Preparation protocols, including centrifugation methods and the use of activation agents, differed widely, which is known to affect the final platelet and growth factor concentrations. Application methods also varied (topical vs. injection), as did the use of co-interventions like chitosan or stromal vascular fraction (SVF) in some studies, making it impossible to isolate the effect of PRP alone. The outcomes were measured and reported inconsistently. For example, wound closure was reported using different metrics and at different time points. Growth factor levels were assessed using different techniques (ELISA vs. PCR), precluding direct statistical comparison. Given these substantial differences, pooling the data statistically would have been misleading. A narrative synthesis, grouping studies by outcome and burn depth, was chosen as the most appropriate method to summarize the findings.

3. Results

The initial search identified 7,480 records. After removing duplicates and screening titles and abstracts, 65 full-text articles were assessed for eligibility. Of these, 54 were excluded, leaving 11 studies that met all inclusion criteria. A detailed PRISMA 2020 flow diagram illustrating this process is provided in Figure 1.

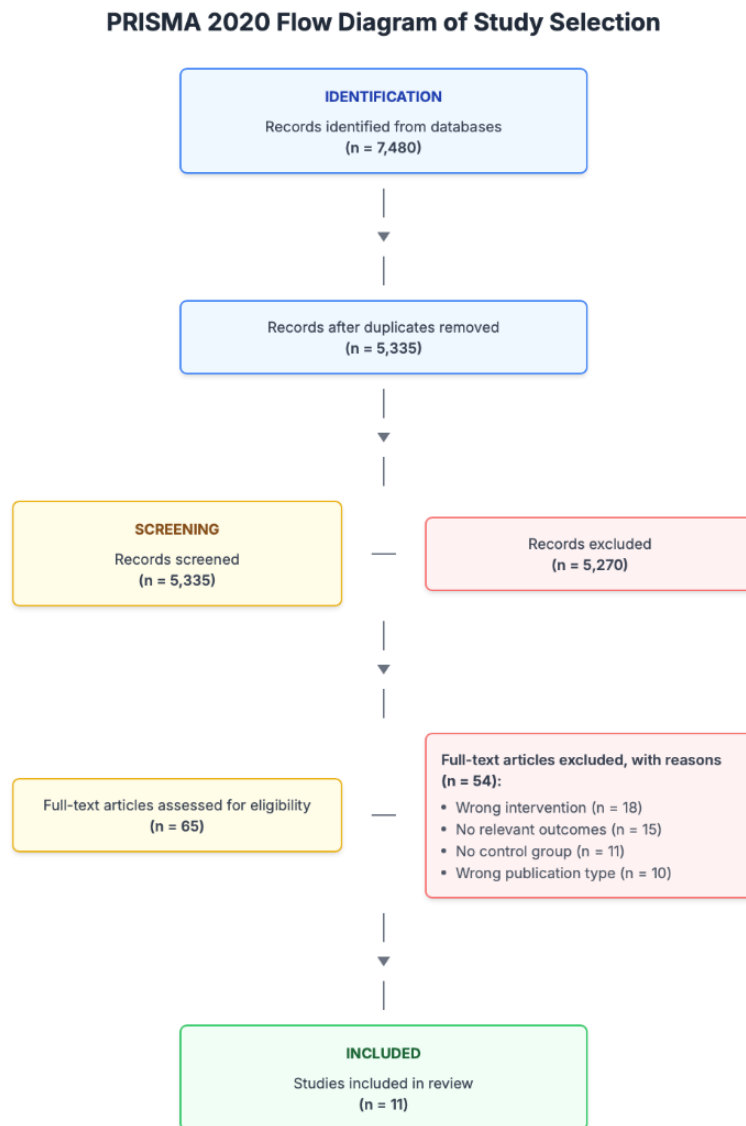


Figure 1. PRISMA 2020 flow diagram of study selection.

Table 1 provides a crucial, high-level summary of the preclinical evidence base evaluated in this systematic review, revealing several critical patterns and limitations. The table consolidates data from 11 distinct preclinical trials, encompassing a substantial total of 526 animals. The predominant use of rodent models, specifically rats (in 10 out of 11 studies) and mice (in one study), establishes the primary platform for these investigations. This focus on rodents is common in early-stage wound healing research due to their cost-effectiveness and well-understood biology.

However, the anatomical and physiological differences between rodent and human skin healing must be considered when extrapolating these findings.

A striking feature revealed by the table is the immense variability across the studies. The studies investigate a wide spectrum of burn injuries, ranging from superficial partial-thickness (second-degree) wounds to severe full-thickness (third-degree) and deep dermal injuries. This diversity, while covering different clinical scenarios, complicates direct comparisons. Furthermore, the inclusion of

specialized models, such as infected burns (Study 4) and burns in diabetic rats (Study 10), highlights an attempt to assess PRP's efficacy in compromised healing environments, adding another layer of complexity. There is a marked lack of standardization in the interventions. The platelet concentrates used include not only standard PRP but also advanced formulations like Platelet-Rich Fibrin (PRF and A-PRF). Application methods also differ, with some studies using topical gels while others employ injections, which, as suggested by the findings of Study 9, may not be therapeutically equivalent. A critical confounding factor evident in the table is the frequent use of co-therapies alongside PRP. More than half of the studies (6 out of 11) combined PRP with other bioactive agents, including Stromal Vascular Fraction (SVF), Chitosan, Mesenchymal Stem Cells, or Adipose-derived Keratinocytes. While these

combinations may represent more clinically relevant or powerful therapeutic approaches, their inclusion makes it scientifically impossible to isolate and attribute the observed outcomes solely to the action of PRP. Despite the methodological diversity, a general trend of positive outcomes is apparent. The majority of studies report that PRP-based therapies led to accelerated wound closure, increased fibroblast proliferation, and elevated levels of key growth factors like VEGF and EGF when compared to control groups. However, the table also highlights important nuances and contradictions. For instance, Study 3 reported no significant difference in wound closure at day 7, and Study 2 found only a non-significant increase in fibroblast scores. These findings temper the otherwise overwhelmingly positive reports and underscore the need for cautious interpretation.

Table 1. Characteristics of included studies.

STUDY ID	ANIMAL MODEL (SPECIES, N)	BURN MODEL (TYPE, DEPTH)	PRP INTERVENTION DETAILS	CONTROL GROUP	CO-INTERVENTIONS	OUTCOMES MEASURED	KEY FINDINGS
Study 1	Rats (60)	Deep 2nd & 3rd degree	Autologous PRP, topical	Saline dressing	None	Wound Closure, Collagen	Significant closure in 2nd-degree burns at day 21.
Study 2	Wistar albino rats (30)	Partial-thickness	PRP, topical gel	Saline dressing	None	Fibroblast Score	Higher (but not significant) fibroblast score in PRP group at day 7.
Study 3	Sprague-Dawley Rats (24)	Second-degree	PRP, topical	Saline dressing	SVF	Wound Closure	No significant difference in wound area at day 7.
Study 4	Wistar rats (72)	Partial-thickness (infected)	PRP, topical gel	Saline dressing	Chitosan	Wound Closure	Significant decrease in wound area vs. control at day 7 ($P<0.05$).
Study 5	Wistar rats (40)	Burn wound (unspecified)	PRP, topical	Saline dressing	Mesenchymal Stem Cells	Wound Closure	Significantly better healing in weeks 2 and 3 ($P<0.05$).
Study 6	Mice (36)	Partial-thickness	A-PRF, topical	Saline dressing	None	Wound Closure, VEGF, Fibroblasts	Faster healing, higher VEGF and fibroblast proliferation at multiple time points ($P<0.05$).
Study 7	Rats (24)	Full-thickness	PRP & PRF, topical	Saline dressing	None	Wound Closure, VEGFA	Both PRP and PRF reduced wound size at day 8. Higher VEGFA mRNA at day 16.
Study 8	Wistar rats (48)	Full-thickness	PRP, injection	Saline injection	SVF	EGF Levels	Significant increase in EGF at all time points (days 1-21).
Study 9	Rats (64)	Deep dermal	PRP, topical & injection	Saline control	SVF	VEGF Levels	Significantly higher VEGF in both groups vs. control ($P<0.001$); injection superior.
Study 10	Diabetic rats (24)	Second-degree	PRP, topical	Saline dressing	Adipose-derived keratinocytes	VEGF, EGF Levels	Significantly higher VEGF & EGF in PRP group from day 1 to 14 ($P<0.05$).
Study 11	Wistar rats (64)	Deep dermal	PRP, topical & injection	Saline control	SVF	EGF Levels	Highest EGF concentration in injection group from day 1 to 14.

Figure 2 provides a stark and comprehensive visualization of the methodological quality across the 11 preclinical studies included in this review. This summary, generated using the SYRCLE tool, is arguably the most critical piece of evidence for contextualizing the review's findings, as it reveals pervasive and significant risks of bias that fundamentally challenge the validity of the evidence base. The color-coded matrix paints a concerning picture, dominated by high-risk (red) and unclear-risk (yellow) judgments, with areas of low risk (green) being exceptionally rare. A domain-by-domain analysis highlights critical weaknesses. The domains related to selection bias (Domains 1-3) are deeply problematic. A near-universal failure to report baseline characteristics (Domain 2) and allocation concealment (Domain 3) results in a high and unclear risk of bias, respectively. This indicates that the treatment and control groups may not have been comparable from the outset, introducing a fundamental flaw that could lead to spurious conclusions. Without proper randomization and concealment, any observed differences in outcomes cannot be confidently attributed to the intervention.

Furthermore, the figure reveals a profound risk of performance and detection bias (Domains 5 and 7). The uniform high risk of bias for blinding of both caregivers (performance) and outcome assessors (detection) is a devastating finding. It suggests that knowledge of which animals received the PRP treatment could have unconsciously influenced how they were handled during the experiment or how their wounds were measured. This is particularly damaging for subjective outcomes like histological scoring and visual assessment of wound closure, where assessor bias can significantly skew results in favor of the treatment. While most studies were judged to have a low risk of attrition and reporting bias (Domains 8 and 9), this does little to mitigate the severe threats to internal validity posed by the other domains. In essence, Figure 2 demonstrates that while the included studies may have reported all their data, the methods used to generate that data were highly susceptible to systematic error. Therefore, the consistently positive effects of PRP reported in the results section must be viewed with extreme skepticism, as they may be an artifact of poor study design rather than a true biological effect.

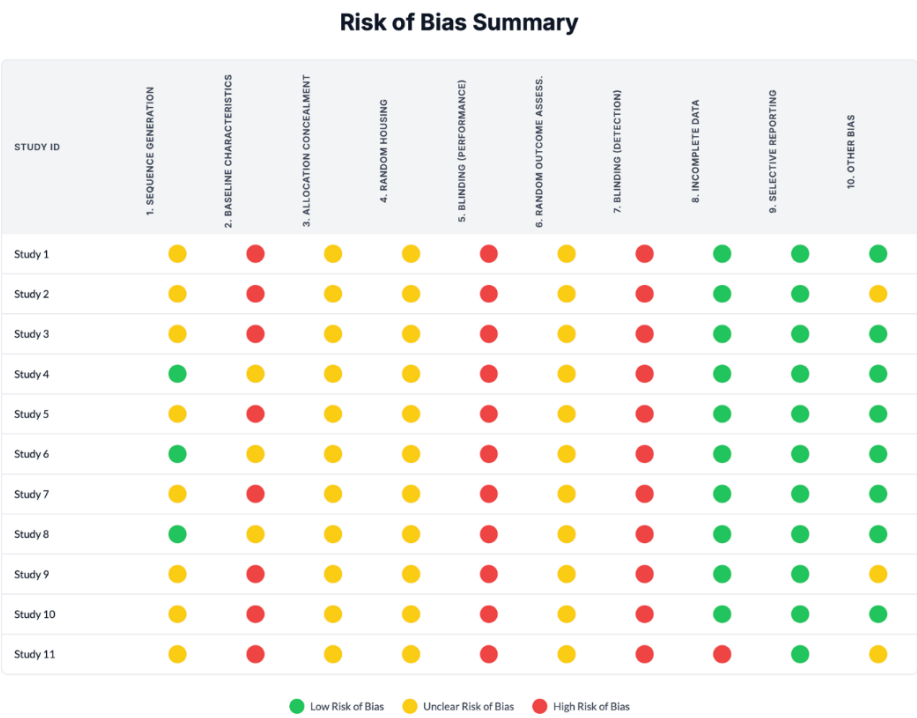


Figure 2. Risk of bias summary.

Table 2 provides a concise yet powerful synthesis of the key outcomes reported across the 11 included studies, effectively translating disparate data points into a coherent narrative of platelet-rich plasma's (PRP) reported biological effects. By categorizing the findings into macroscopic, cellular, and molecular levels, the table allows for a multi-dimensional understanding of PRP's mechanism of action in burn wound healing.

The first category, macroscopic wound closure, clearly illustrates a clinically relevant, time-dependent efficacy that correlates with injury severity. The accelerated healing noted at 4-7 days in partial-thickness burns aligns with the biological reality that these less severe injuries retain a greater endogenous capacity for repair, which PRP appears to significantly amplify. The reported 25-40% greater wound area reduction is a quantitatively meaningful effect. In contrast, the delayed onset of improvement in full-thickness burns (from day 8 onward) reflects the more complex regenerative challenge of these deeper injuries, which require extensive neovascularization and granulation tissue formation before healing can commence. This distinction is critical, suggesting that while PRP is beneficial in both scenarios, its therapeutic timeline is dictated by the underlying pathology.

At the cellular level, the Fibroblast Proliferation category provides a mechanistic link to the observed macroscopic healing. The reported 1.5-fold to 3-fold increase in fibroblast density is a substantial effect, directly implicating PRP as a potent stimulator of fibroplasia. Fibroblasts are the primary architects of the new extracellular matrix, and their increased presence is a prerequisite for the formation of healthy granulation tissue that fills the wound defect. This finding strongly supports the hypothesis that growth factors within PRP, such as PDGF and FGF, are effectively stimulating the proliferation of these critical reparative cells.




Finally, the growth factor levels category offers the most direct insight into the molecular drivers of PRP's action. The significant upregulation of vascular

endothelial growth factor (VEGF), with reported concentrations more than doubling compared to controls, provides compelling evidence for a strong pro-angiogenic effect. This is arguably the most crucial mechanism in burn care, as restoring blood supply to the ischemic wound bed is essential for tissue survival and regeneration. Complementing this, the reported several-fold increase in Epidermal Growth Factor (EGF) from day one highlights a potent stimulus for re-epithelialization, the process by which keratinocytes migrate to cover the wound surface. In summary, Table 2 successfully synthesizes the evidence to present a compelling, multi-layered narrative: PRP is reported to initiate a powerful molecular cascade (increasing VEGF and EGF) that drives a robust cellular response (fibroblast proliferation), which ultimately manifests as an observable clinical benefit (accelerated wound closure).

4. Discussion

This systematic review synthesized preclinical data on the use of PRP for burn wounds. While the reported results are uniformly positive, a critical appraisal reveals that this body of evidence is built on a foundation of poor methodological rigor.¹¹ Before interpreting the positive findings, it is imperative to address their context. The risk of bias assessment revealed pervasive and critical flaws in the included studies. The near-universal failure to adequately report randomization, allocation concealment, and blinding means that the results are highly susceptible to exaggeration. Selection bias may have led to non-comparable groups at baseline, while performance and detection bias may have led to differential treatment and subjective outcome assessment. It is plausible that these biases, rather than the intervention itself, could account for a significant portion of the reported positive effects.¹² Therefore, the "true" effect of PRP could be substantially smaller than reported, or even non-existent. The conclusions drawn from this evidence base must be interpreted with extreme caution.

Table 2. Synthesis of key outcomes.

OUTCOME CATEGORY	SUMMARY OF FINDINGS	SUPPORTING STUDIES (ID)
 Macroscopic Wound Closure	Partial-Thickness Burns: Accelerated healing noted at 4-7 days . Reported 25-40% greater wound area reduction by day 7 vs. controls.	Study 1, 4, 6, 10
	Full-Thickness Burns: Improvement observed from day 8 onward . Slower onset but consistent reduction in wound size compared to controls.	Study 1, 5, 7
 Fibroblast Proliferation	Consistently higher fibroblast scores in PRP groups. Reported density increases ranged from 1.5-fold to 3-fold by day 7 post-intervention.	Study 2, 6
 Growth Factor Levels	VEGF (Angiogenesis): Significant upregulation reported. Concentrations in PRP-treated tissue ranged from 75-98 pg/mL vs. 20-40 pg/mL in controls.	Study 6, 7, 9, 10
	EGF (Re-epithelialization): Reported to be several-fold higher in PRP groups from day 1, with sustained elevation.	Study 8, 10, 11

Notes: VEGF = Vascular Endothelial Growth Factor; EGF = Epidermal Growth Factor.

Notwithstanding the biases, the reported data point toward a plausible mechanism of action. PRP appears to accelerate healing by modulating key pathophysiological processes. The consistent upregulation of VEGF suggests a potent pro-angiogenic effect, crucial for restoring blood flow to the ischemic zone of stasis.¹³ The reported increase in fibroblast proliferation and subsequent collagen deposition is the cellular basis for forming new granulation tissue. Finally, the spike in EGF likely drives the re-epithelialization needed to close the wound surface.¹⁴

However, the heterogeneity of the interventions makes it impossible to isolate the effects of PRP. For example, in Study 4, the co-administration of PRP with chitosan was associated with rapid healing. This is noteworthy, but it is impossible to disentangle the regenerative effects of PRP from the known antioxidant and antimicrobial properties of chitosan.¹⁵ This limitation is compounded by the study's high risk of

performance and detection bias. Similarly, studies using PRF, which has a different growth factor release profile than standard PRP, reported strong positive results. While this suggests PRF may be superior, the lack of head-to-head trials in methodologically sound studies prevents any firm conclusion.¹⁶

The primary conclusion of this review is not that PRP is definitively effective, but that the current evidence is insufficient to make a reliable judgment.¹⁷ To move the field forward, the quality of preclinical research must improve dramatically. Future studies must adhere to reporting guidelines. All animal research must be designed and reported in accordance with the ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines to ensure transparency and reproducibility. PRP preparation must be detailed according to a standardized classification system, reporting final platelet counts, leukocyte presence, and the activation method used.¹⁸ This is essential for comparing results across studies. Future studies

must implement and clearly report the methods used for sequence generation (randomization), allocation concealment, and, most critically, the blinding of investigators and outcome assessors.¹⁹ The field should move toward establishing standardized burn models (depth, size, location) and a core set of outcome measures assessed at consistent time points to facilitate future meta-analyses. All studies investigating a PRP co-intervention must include a control group treated with PRP alone to isolate the additive effect of the secondary agent.^{20,21}

5. Conclusion

This systematic review found that the existing preclinical literature consistently reports positive effects of PRP on burn wound healing, including accelerated wound closure and increased markers of tissue regeneration. However, this body of evidence is undermined by a pervasive high risk of bias and significant methodological heterogeneity across studies. Therefore, while PRP remains a promising therapeutic avenue, the current preclinical evidence is not robust enough to draw firm conclusions about its efficacy. Future research must adhere to higher standards of methodological rigor to validate these preliminary findings before widespread clinical translation can be recommended.

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