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# The usefulness of platelet-rich plasma to manage skin wounds: A meta-analysis

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**Abstract**

A meta-analysis investigation to measure the usefulness of platelet-rich plasma (PRP) to manage skin wounds (SWs). A comprehensive literature inspection till February 2023 was applied and 1349 interrelated investigations were reviewed. The 22 chosen investigations enclosed animals' SWs were in the chosen investigations' starting point, 3348 of them were treated with PRP, and 2259 were control. Odds ratio (OR) in addition to 95% confidence intervals (CIs) were used to compute the value of the usefulness of PRP to manage SWs by the dichotomous and continuous approaches and a fixed or random model. PRP significantly higher percent of decreases in open wound area (OWA) (MD, 10.07; 95% CI, 6.55-13.59, $P < 0.001$), and lower healing time (HT) (MD, −6.31; 95% CI, −10.69 to −1.93, $P = 0.005$) compared to control in animals' SWs. PRP had a significantly higher percent of decreases in OWA and lower HT compared to control in animals' SWs. However, caused of the small sample sizes of several chosen investigations for this meta-analysis, care must be exercised when dealing with its values.

**KEYWORDS**

decrease in open wound area, healing time, platelet-rich plasma, skin wounds

**Key Messages**

- a meta-analysis investigation to measure the usefulness of platelet-rich plasma (PRP) to manage skin wounds (SWs)
- PRP had a significantly higher SWs percentage of decreases in open wound area and lower healing time compared to control in animals' SWs
- however, caused of the small sample sizes of several chosen investigations for this meta-analysis, care must be exercised when dealing with its values

## 1 | INTRODUCTION

The three main phases of wound healing are the inflammatory phase, the proliferative phase, and tissue remodelling (WH). A complex combination of molecular signals involving mediators, particularly cytokines and growth factors (GFs), controls these actions. The main cellular functions involved in the healing procedure are stimulated and modulated by GFs. Healing challenges develop in chronic wounds

because the usual course is slowed down and disturbed.[1] In the procedure of skin wound (SW) healing, platelets are crucial. During the proliferation phase, the platelet-derived GFs are essential for attracting mesenchymal cells and producing extracellular matrix (fibroplasia, reepithelialization, and neovascularization).[1] Platelets release the GFs found in the alpha granules following spontaneous or induced activation.[2] Activated platelet concentration known as platelet-rich plasma (PRP) is applied locally at the location of the lesion. Several preparation methods and activation agents have been suggested in recent years.[3] Two forms of PRP can be produced using various preparation techniques: PRP containing leukocytes and pure PRP devoid of leukocytes.[4] PRP has been shown to improve healing in a variety of human medical procedures in orthopaedic surgery and bone reconstruction, skin ulcers, plastic reconstructive and cosmetic surgery, oral-maxillofacial surgery, cartilage.[5] Despite the increased interest, there is still a dearth of randomised clinical trials (RCTs) in veterinary medicine, according to the scientific literature.[6] To determine whether PRP can be used to experimentally treat produced animals' wounds, it is necessary to evaluate the literature before performing clinical research on large human and animal populations with spontaneous disease. The study's goal was to analyse the available research to ascertain whether topical treatment of PRP helps animals with experimentally produced full-thickness SWs heal more quickly. The idea was that using PRP as an adjuvant would promote WH as compared to using a placebo or other therapies. Hence the aim of the present meta-analysis was to usefulness of PRP to manage SWs.

## 2 | METHODS

### 2.1 | Eligibility criteria

For the purpose of creating a summary, the investigations demonstrating the connection between PRP and SWs were chosen.[7]

### 2.2 | Information sources

Figure 1 represents the whole investigation. The kinds of literature were incorporated into the investigation when the inclusion criteria were met:

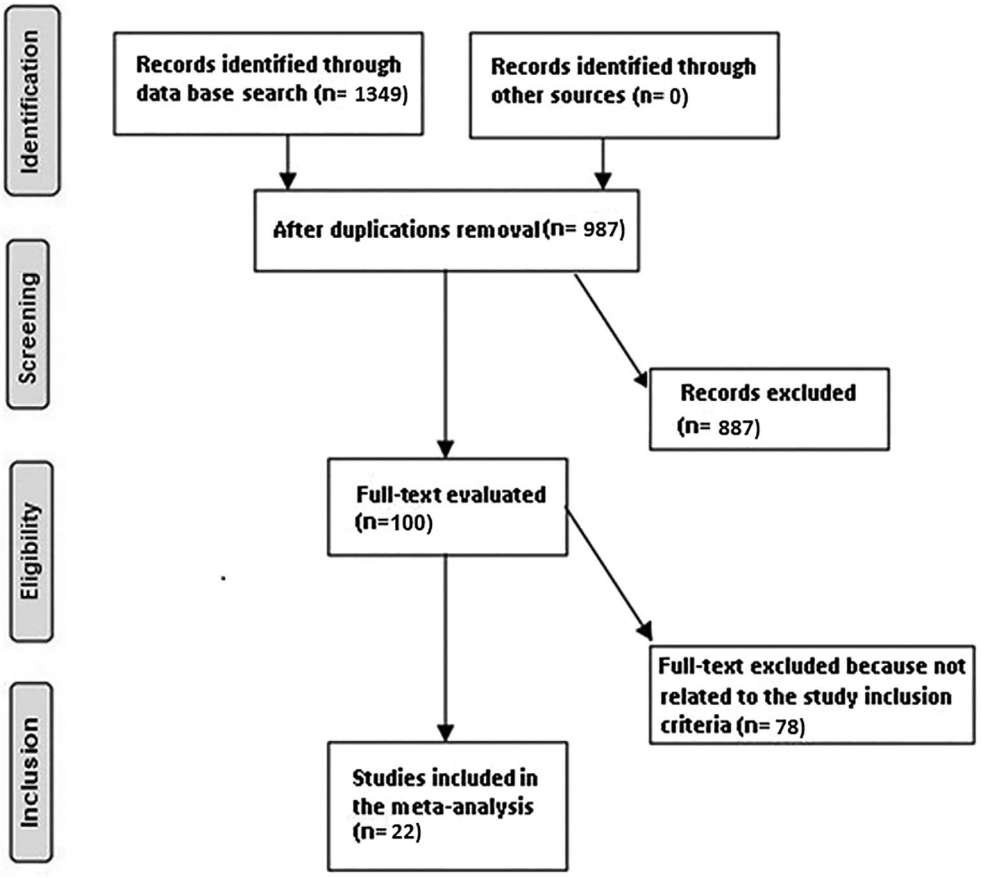


FIGURE 1 Flowchart of the investigation process.

1. The research was either an observational, prospective, retrospective or RCT investigation.
2. Animal models with SWs were the investigation chosen subjects.
3. The intervention incorporated PRP.
4. The investigation distinguished the usefulness of PRP to manage SWs.

The research that was excluded included persons where the significance of the comparison was not emphasised in it, investigations that did not inspect the characteristics of the usefulness of PRP to manage SWs, and investigations on SWs Animals without PRP.

## 2.3 | Search strategy

A search protocol procedures were recognised depending on the PICOS opinion, and we characterised it as next: topics for animal models with SWs, P; PRP is the "intervention" or "exposure," while the "comparison" was PRP compared to control; decrease in the open wound area (OWA) % and healing time (HT) were the "outcome" and last of all, the proposed investigation had no restrictions.[8]

We have searched Google Scholar, Embase, the Cochrane Library, PubMed, and OVID exhaustively. databases till February 2023 using an organisation of keywords and accompanying terms for the decrease in OWA; HT; SWs; and PRP as shown in Table 1. To avoid research that failed to establish a link between the outcomes of the usefulness of PRP to manage SWs, replications were removed from the papers, they were combined into one EndNote file, and the titles and abstracts were tested over.

## 2.4 | Selection process

Following the epidemiological declaration, a process was formed, which was then organised and analysed in the procedure of a meta-analysis.

## 2.5 | Data collection process

Among the criteria used to collect data were the name of the primary author, the investigation date, the year of the investigation, the country or area, the population type, the medical and therapy physiognomies, categories, the qualitative and quantitative estimate process, the data source, the consequence estimate, and statistical analysis.[9]

**TABLE 1** Search strategy for each database.

| Database | Search strategy |
|---|---|
| Pubmed | #1 "platelet-rich plasma"[MeSH Terms] OR "healing time"[All Fields] [All Fields]<br>#2 "skin wounds"[MeSH Terms] OR "decrease in open wound area"[MeSH Terms] [All Fields]<br>#3 #1 AND #2 |
| Embase | 'platelet-rich plasma'/exp OR 'healing time'<br>#2 'skin wounds'/exp OR 'decrease in open wound area'<br>#3 #1 AND #2 |
| Cochrane library | (platelet-rich plasma):ti,ab,kw (healing time): ti,ab,kw (Word variations have been searched)<br>#2 (skin wounds):ti,ab,kw OR (decrease in open wound area): ti,ab,kw (Word variations have been searched)<br>#3 #1 AND #2 |

## 2.6 | Data items

Whenever an investigation had variable values, we separately acquired the data based on an evaluation of the usefulness of PRP to manage SWs.

## 2.7 | Investigation risk of bias assessment

Two authors independently estimated the procedure of the selected publications to see whether there was a possibility that each investigation may have been biased. The procedural quality was estimated using the "risk of bias instrument" from the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. After being categorised by the appraisal criteria, each investigation was assigned one of the bias risks indicated below: low: An investigation was categorised as having a low bias risk if all of the quality criteria were met; an investigation was categorised as having a medium bias risk if one or more requirements were not met or were not encompassed. The investigation was deemed to have a significant bias risk if one or more quality needs were either completely or just partially met.

## 2.8 | Effect measures

Sensitivity analyses were only carried out on research that assessed and documented the usefulness of PRP to manage SWs. To compare PRP in SWs compared to control sensitivity, a subclass analysis was used.

## 2.9 | Synthesis methods

A random- or fixed-effect model was used to generate the odds ratio (OR) and a 95% confidence interval (CI) using dichotomous or continuous approaches. Between 0% and 100%, the I2 index was determined. The values at 0%, 25%, 50%, and 75%, respectively, presented no, low, moderate, and high heterogeneity.[10] Other features that show a strong degree of resemblance among the related research were also analysed to make sure the correct model was being used. The random effect was utilised if I2 was ≥50%; if I2 was <50% the possibility of utilising fixed-effect rose.[10] A subclass analysis was completed by stratifying the initial estimation by the aforementioned consequence groups. A *P*-value of <0.05 was utilised in the analysis to specify the statistical significance of differences between subcategories.

## 2.10 | Reporting bias assessment

Investigations bias was measured statistically and qualitatively using the Egger regression test and funnel plots that exhibit the logarithm of the ORs versus their standard errors (investigations bias was deemed present if $P \geq 0.05$).[11]

## 2.11 | Certainty assessment

Two-tailed testing was used to investigate each *P*-value. Using Reviewer Manager Version 5.3, graphs and statistical analyses were produced (The Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark).

# 3 | RESULTS

22 publications from a total of 1349 connected investigations that were examined that met the inclusion criteria and were published between 2008 and 2022 were chosen and included in the investigation.[12-26] The results of these researches are presented in Table 2. 6707 animals' SWs were in the chosen investigations' starting point, 3348 of them were treated with PRP, and 2259 were control. The sample size was between 6 and 537 animals' SWs.

**TABLE 2** Characteristics of the selected investigations for the meta-analysis.

| Study | Country | Total | Platelet-rich plasma | Controls |
|---|---|---|---|---|
| Lee[31] | UK | 527 | 261 | 266 |
| Blanton[32] | USA | 501 | 248 | 253 |
| Monteiro[33] | France | 525 | 260 | 265 |
| Nisbet[34] | Turkey | 519 | 257 | 262 |
| Vermeulen[35] | Belgium | 528 | 264 | 264 |
| Sardari[36] | Iran | 519 | 257 | 262 |
| Yang[37] | Korea | 535 | 265 | 270 |
| Al-Bayati[38] | Iraq | 509 | 252 | 257 |
| Dionyssiou[39] | Greece | 76 | 38 | 38 |
| Abegão[40] | Brazil | 537 | 266 | 271 |
| Barrionuevo[41] | Brazil | 537 | 266 | 271 |
| Souza[42] | Brazil | 132 | 88 | 44 |
| Karayannopoulou[43] | Greece | 513 | 254 | 259 |
| Notodihardjo[44] | Japan | 369 | 182 | 187 |
| Farghali[45] | Egypt | 6 | 3 | 3 |
| Hamed[46] | Egypt | 48 | 24 | 24 |
| Tetila[47] | Brazil | 16 | 8 | 8 |
| Liu[48] | China | 40 | 20 | 20 |
| Xu[49] | China | 80 | 40 | 40 |
| Huang[50] | China | 36 | 18 | 18 |
| Sultana[51] | Bangladesh | 144 | 72 | 72 |
| Ramos-Gonzalez[52] | Venezuela | 10 | 5 | 5 |
| | Total | 6707 | 3348 | 3359 |

PRP significantly higher percent of decreases in OWA (MD, 10.07; 95% CI, 6.55-13.59, $P < 0.001$) with high heterogeneity ($I^2 = 100\%$), and lower HT (MD, −6.31; 95% CI, −10.69 to −1.93, $P = 0.005$) with high heterogeneity ($I^2 = 99\%$) compared to control in animals' SWs as shown in Figures 2 and 3.

The lack of data prevented stratified models from being used to inspect the effects of particular factors, such as gender, and age, on comparison outcomes. No evidence of investigation bias was found ($P = 0.87$) using the quantitative Egger regression test and the visual interpretation of the funnel plot in Figures 4 and 5. The majority of the implicated RCTs, however, were found to have poor methodological quality and no bias in selective reporting.

## 4 | DISCUSSION

In investigations that were considered for the meta-analysis, animals' SWs were in the chosen investigations' starting point, 3348 of them were treated with PRP, and 2259 were control.[12-26] PRP significantly higher percent of decreases in OWA, and lower HT compared to control in animals' SWs. Though precautions must be exercised when dealing with its values since some of the selected investigations for this meta-analysis were with a low sample size (8 out of 22 were ≤100 individuals).

The number of research taken into account in this and other systematic reviews (85-90) shows that PRP use has significantly increased in recent years. This review looked at experimentally generated skin lesions in animals. Given that these wounds are nearly matching from a morphological and qualitative perspective at the beginning of the study and throughout the study, preserving the same situations of groups' homogeneity throughout the follow-up, this situation unquestionably shows a high level of experimental indication. They are, however, artificially produced in healthy animals. Thus, they must be viewed as acute wounds on an ideal substrate with normal healing capacity, which means that the benefit of PRP in clinical practice may be quite constrained. According to the literature, patients with wounds that are challenging to heal may benefit from the clinical usage of PRP. Individuals with persistent wounds that have a poor propensity to heal (such as sores, pressure ulcers, diabetic, and vascular ulcers), which are frequently characterised by an ongoing inflammatory state and a lack of GFs,[27] may profit even more from management with PRP, despite the fact that this type of wound was not the focus of this meta-analysis.[28] Clinical research on dogs with spontaneous persistent decubital wounds is in some ways consistent with this idea. The researchers discovered that wounds older than 14 weeks experienced a larger decrease in wound size following PRP therapy than wounds younger than 14 weeks. They did not discover any appreciable differences in full WH, but.[28] A systematic review concluded that there is a need for well-designed and sufficiently powered clinical trials because the current evidence for the use of autologous PRP in treating chronic human wounds is of low quality and is based on a few RCTs with a high or unclear risk of bias.[29]

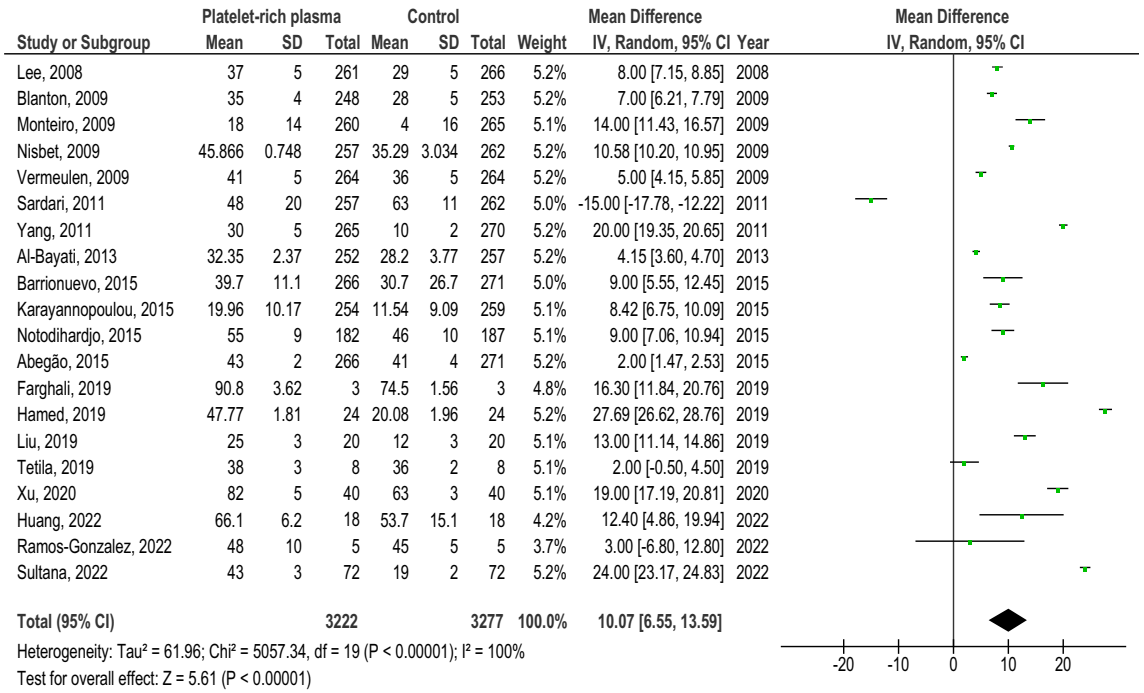


FIGURE 2 The effect's forest plot of the effect of PRP on the percent of decreases in OWA in animal models of SWs.

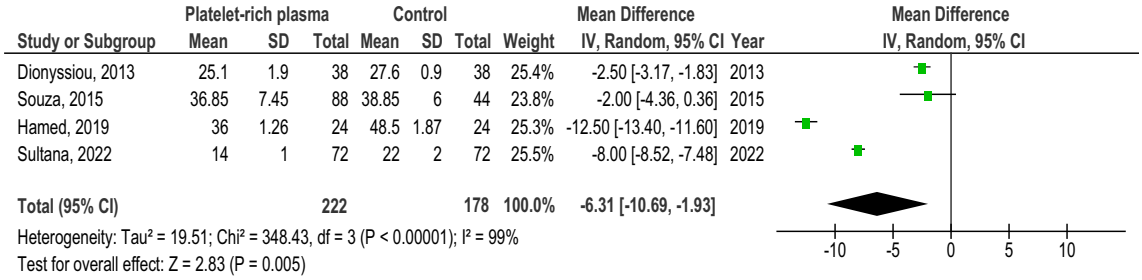


**FIGURE 3** The effect's forest plot of the effect of PRP on HT in animal models of SWs.

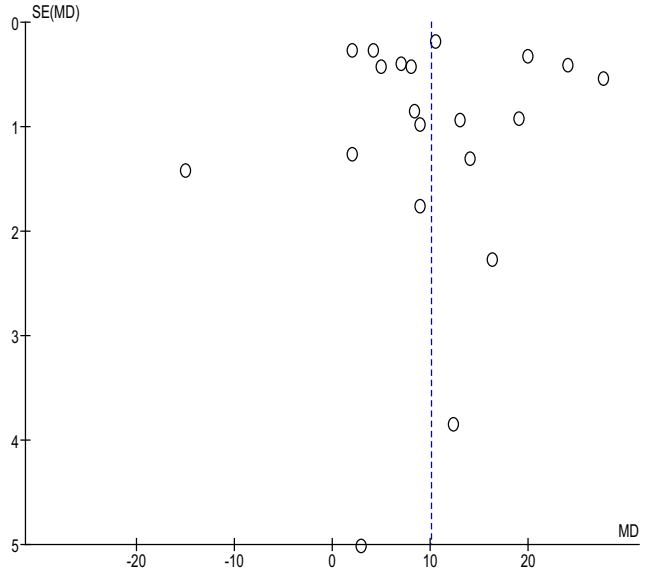


**FIGURE 4** The outcome's funnel plot of the effect of PRP on the percent of decreases in OWA in animal models of SWs.

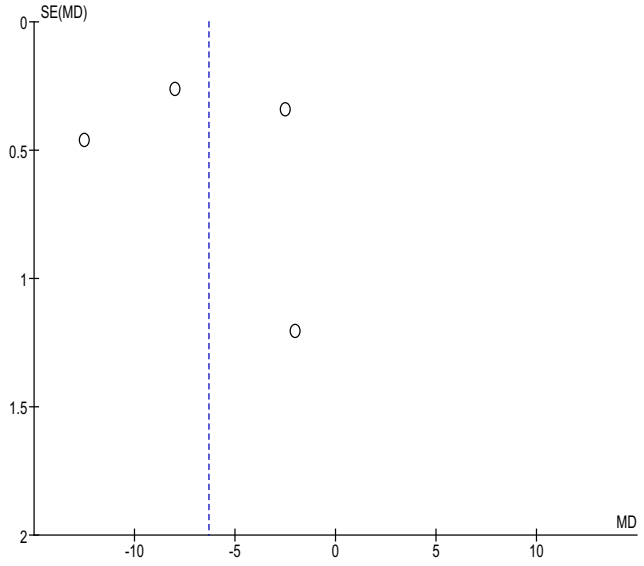


**FIGURE 5** The outcome's funnel plot of the effect of PRP on HT in animal models of SWs.

This meta-analysis confirmed the usefulness of PRP to manage SWs. More inspection is still desirable to clarify these feasible influences. For this investigation, larger, more homogeneous samples are required. This was also noted in earlier studies that employed a similar meta-analysis technique and discovered comparable values of the influence.[30] Although the meta-analysis was incapable to discover if differences in these characteristics are related to the outcomes being researched, properly-led RCTs are vital to consider these aspects as well as the mixture of different ages, and genders of patients. In conclusion, PRP had a significantly higher percentage of decreases in OWA, and lower HT compared to control in animals' SWs.

## 4.1 | Limitations

Since some of the investigations involved in the meta-analysis were not included, there might have been selection bias. The animals in the studies are not the same however, it was the same within each study. That could be the reason for the high heterogeneity in the meta-analysis. The omitted investigations, however, did not fulfil the necessities for inclusion in the meta-analysis. Also, we lacked the expertise to determine whether factors like age and gender influenced results. The drive of the investigation was to measure the usefulness of PRP to manage SWs. Bias may have grown because incomplete or incorrect data from earlier research were included. Possible sources of bias involved the individuals' nutritional status in addition to their ages, and genders. Unwantedly, incomplete data and certain unpublished work may distort the value that is being examined.

## 5 | CONCLUSIONS

PRP had a significantly higher percent of decreases in OWA and lower HT compared to control in animals'

SWs. Though precautions must be exercised when dealing with its values since some of the selected investigations for this meta-analysis were with a low sample size (8 out of 22 were ≤100 individuals).

## DATA AVAILABILITY STATEMENT

On request, the corresponding author is required to provide access to the meta-analysis database.

## ORCID

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