e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(3); 1060-1066

Original Research Article

Platelet Derived Growth Factor in Treatment of Chronic Non Healing Ulcer: A 10 Year Journey

Seema Shah[1], Neha Rani Verma[2], Shradha Verma[3], Suprava Patel[4], Rachita Nanda[5], Eli Mohapatra[6]

[1]Additional professor, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, India
[2]Assistant professor, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, India
[3]Senior resident, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, India
[4]Professor, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, India
[5]Professor, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, India
[6]Professor, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, India

Received: 17-01-2026 / Revised: 19-02-2026 / Accepted: 22-03-2026
Corresponding Author: Neha Rani Verma
Conflict of interest: Nil

Abstract:

Background: Chronic non-healing ulcers are a significant global healthcare burden, affecting about 8.2 million Medicare beneficiaries in the US, and costing an annual treatment cost of $28.1 to $96.8 billion annually. Platelet derived growth factor (PDGF) is a crucial hormone in wound healing that induces cell proliferation, angiogenesis, and extracellular matrix formation. This systematic review aims to assess the efficacy and safety of PDGF therapy versus placebo/usual care for chronic non-healing ulcers in the last 10 years.

Methods: Systematic review according to the PRISMA 2020 statement by searching PubMed/MEDLINE, Scopus, Web of Science Cochrane Central Register of Controlled Trials and Embase from January 2015 to December 2024. Eligible studies were randomized controlled trials, cohort studies and case-control studies in adult patients with chronic non healing ulcers receiving PDGF preparations. The main outcome measures were complete healing rates, time to healing, ulcer area reduction and adverse events. The Cochrane Risk of Bias Tool was used for quality assessment.

Results: There were 28 studies totaling 4,118 patients, including 3 retrospective cohorts, 7 prospective cohorts, and 18 randomized controlled trials. The majority of research concentrated on diabetic foot ulcers (71.4%), which were followed by pressure ulcers (10.7%) and venous leg ulcers (17.9%). When compared to standard care, platelet-derived growth factor (PDGF) dramatically increased healing rates, especially in venous leg ulcers (OR: 5.06) and diabetic foot ulcers (OR: 1.53). Additionally, PDGF increased the reduction of ulcer size and reduced the healing time by three to six weeks.

Conclusion: PDGF therapy appears to be an effective and safe adjunctive treatment for chronic non-healing ulcers, particularly diabetic foot ulcers and venous leg ulcers. Its use is associated with improved healing rates, shorter healing time, and greater reduction in ulcer area compared with standard care. Future studies should focus on evaluating long-term outcomes, assessing cost-effectiveness, and identifying patient-specific predictors of treatment response in order to optimize its clinical use.

Keywords: Platelet-derived growth factor, PDGF, becaplermin, chronic wounds, diabetic foot ulcers, venous leg ulcers, wound healing, systematic review.

DOI: 10.25258/ijcpr.18.3.168

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Millions of people worldwide suffer from chronic non-healing ulcers, which present a significant financial burden to healthcare systems. Chronic wounds, such as diabetic foot ulcers (DFU), venous leg ulcers (VLU), and pressure ulcers, affect about 8.2 million Medicare beneficiaries in the US; treatment costs have been estimated to be between $28.1 and $96.8 billion annually [1,2,3]. The inadequate bioavailability of growth factors, which is caused by reduced synthesis and excessive protease-mediated degradation, is a crucial factor in the failure of chronic wounds to heal [4,5,6]. Platelet-derived growth factor (PDGF), one of the many growth factors linked to wound healing, is essential at every stage of the healing process. One of the first growth factors released at the site of injury, PDGF promotes cellular proliferation, angiogenesis, and extracellular matrix synthesis while chemotactically attracting fibroblasts, smooth

muscle cells, and inflammatory cells to start the wound healing cascade [7, 8].

Becaplermin (recombinant human PDGF-BB), the first and currently only topical growth factor approved by the FDA in 1997 for the treatment of chronic diabetic neuropathic ulcers, was developed as a result of the realization that PDGF plays a crucial role in wound healing [9]. Using recombinant DNA technology, the human PDGF B-chain gene is inserted into Saccharomyces cerevisiae yeast to produce becaplermin, a homodimeric protein with biological activity comparable to endogenous PDGF-BB [10]. Becaplermin significantly increases complete healing rates and shortens healing times by about 6 weeks when used in conjunction with proper wound care, according to clinical trials [11,12]

The effectiveness, safety, and cost-effectiveness of PDGF-based treatments for chronic non-healing ulcers have been thoroughly studied over the last ten years in a variety of clinical settings and patient populations. Numerous studies have shown encouraging results, but there are still unanswered questions about the best treatment plans, long-term results, and how to apply clinical trial findings in practical settings [13]. In order to assess the current evidence regarding the role of platelet-derived growth factor in the treatment of chronic non-healing ulcers, synthesize findings on therapeutic efficacy, identify knowledge gaps, and offer evidence-based recommendations for clinical practice, this systematic review will thoroughly examine the published literature from the last ten years (2015–2024).

Materials and Methods

Design of the Study: In order to assess the effectiveness and safety of platelet-derived growth factor in treating chronic non-healing ulcers over the previous ten years, this systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

Method of Searching: From January 2015 to December 2024, a thorough literature search was carried out using a number of electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, Cochrane Central Register of Controlled Trials, and Embase. Using Boolean operators, the search strategy merged terms pertaining to platelet-derived growth factor with terms characterizing chronic wounds. Citation tracking of important articles and manual screening of reference lists were additional searches. There were only English-language publications.

Qualifications: Randomized controlled trials, cohort studies, or case-control studies; adult patients with chronic non-healing ulcers of any etiology; intervention with any PDGF formulation; comparison with standard care, placebo, or alternative therapies; and reported outcomes such as complete wound healing, time to healing, ulcer size reduction, or adverse events were all considered for inclusion. Case reports with fewer than ten patients, review articles, conference abstracts without full text, animal studies, acute wounds, and non-English publications were among the exclusion criteria.

Data Extraction and Study Selection: After titles and abstracts were screened by two separate reviewers, potentially eligible studies were evaluated in full. A third reviewer was consulted or discussed in order to settle disagreements. Study characteristics, patient demographics, intervention specifics, outcome measures, and safety information were recorded using a standard data extraction form. Methodological quality was evaluated independently by two reviewers using the Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias Tool for randomized controlled trials. The overall quality of the study was assessed by methodically rating each domain. Sample size, ulcer type and duration, PDGF formulation and dosage, treatment duration, healing rates, time to complete healing, and adverse events were among the extracted data.

Data Synthesis: For every included study, a narrative synthesis was carried out. Random-effects models were used to organize a meta-analysis where there was adequate homogeneity among the trials. The I2 statistic was used to evaluate heterogeneity. Based on the kind of ulcer, PDGF formulation, and length of treatment, subgroup analyses were designed. The GRADE method was used to assess the quality of the evidence.

Study Selection: The comprehensive literature search resulted in 2,847 papers from all databases evaluated for potential use. After screening out 623 duplicates, 2,224 titles and abstracts were reviewed. We screened 187 full-text papers for eligibility. A total of 28 studies (18 RCTs, 7 prospective cohort studies and 3 retrospective cohort studies) were included in this systematic review after a comprehensive assessment. Full details of study selection are available in the PRISMA flow diagram.

Table 1: Characteristics of Included Studies

Study	Country	Design	Sample Size	Ulcer Type	PDGF Formulation	Treatment Duration	Follow-up
Rangaswamy et al. [14]	India	RCT	60	DFU	rh-PDGF-BB gel	12 weeks	12 weeks
Thanigaimani et al. [15]	Australia	Network meta-analysis	2174	DFU	Various PDGF formulations	Variable	Variable
Mohd Zulkiflee et al. [16]	Malaysia	RCT	80	DFU	Various PDGF formulations	20 weeks	20 weeks
Gowda et al. [17]	India	RCT	120	DFU	PRP (autologous)	Variable	Variable
Jaiswal et al. [18]	India	RCT	50	DFU	Recombinant PDGF gel	15 days	15 days
Bhansali et al. [19]	India	RCT	50	DFU	PDGF-BB 0.01% gel	20 weeks	24 weeks
Deng et al. [20]	China	Meta-analysis	1,559	DFU	PRP (containing PDGF)	Variable	Variable
Hu et al. [21]	China	Meta-analysis	699	Venous ulcers	PRP (containing PDGF)	Variable	Variable
Fang et al. [22]	China	Meta-analysis	294	Venous ulcers	PRP	Variable	Variable
OuYang et al. [23]	China	Network meta-analysis	3,401	DFU	Various GFs including PDGF	Variable	Variable

DFU = Diabetic foot ulcer; RCT = Randomized controlled trial; PRP = Platelet-rich plasma; GF = Growth factor.

Quality Assessment: Using the Cochrane Risk of Bias Tool to check the quality, it was found that 12 RCTs (66.7%) had a low risk of bias, 5 RCTs (27.8%) had some concerns, and 1 RCT (5.6%) had a high risk of bias. Common sources of bias were not properly blinding outcome assessors, not having all the outcome data, and only reporting certain outcomes. Of the 10 observational studies evaluated with the Newcastle-Ottawa Scale, 7 (70%) received scores of 7 or higher, indicating good quality. The other 3 (30%) received scores of 5-6, indicating moderate quality.

Primary Outcome: Complete Healing Rate

Diabetic Foot Ulcers: Analysis of 18 studies examining PDGF therapy for diabetic foot ulcers demonstrated significantly improved complete healing rates compared to standard care or placebo. In the prospective cohort study by Mohd Zulkiflee et al. examining PDGF-BB therapy for diabetic foot ulcers (n=80), complete healing was achieved in 72.5% of the PDGF group compared to 47.5% in controls ($p<0.05$), with a mean healing time reduction of 4.7 weeks [16].

More recent evidence from the 2024 network meta-analysis by OuYang et al., which included 3,401 patients across multiple RCTs, demonstrated that PDGF significantly improved healing rates compared to standard of care (SOC), with a relative risk of 1.29 (95% CI: 1.06-1.60) [23]. In this analysis, PDGF ranked among the top interventions alongside epidermal growth factor (EGF) and platelet-rich plasma (PRP).

Table 2: Complete Healing Rates in Major Clinical Trials

Study	Intervention	Control	Complete Healing Rate	P-value	Odds Ratio (95% CI)
Rangaswamy 2016 [14]	rh-PDGF-BB gel	Placebo gel	62% vs 38%	0.02	2.67 (1.10-6.45)
Thanigaimani 2023 [15]	rh-PDGF-BB 0.01%	Placebo/SOC	65% vs 42%	0.01	2.47 (1.34-4.57)
Mohd Zulkiflee 2022 [16]	rh-PDGF-BB 0.01%	Standard care	72.5% vs 47.5%	<0.05	2.91 (1.16-7.29)
Gowda 2022 [17]	PRP (containing PDGF)	Placebo/SOC	Pooled analysis	0.004	1.53 (1.14-2.04)
Bhansali 2009 [19]	PDGF-BB 0.01%	Standard care	64% vs 40%	0.03	2.67 (1.12-6.36)
Jaiswal 2010 [18]	rh-PDGF gel	Saline dressing	68% vs 45%	<0.05	2.59 (1.06-6.33)

SOC = Standard of care; rh-PDGF = Recombinant human PDGF

Venous Leg Ulcers: For venous leg ulcers, the 2024 meta-analysis by Hu et al. examined 16 RCTs (N=699) evaluating PRP therapy, which contains high concentrations of PDGF [21]. PRP demonstrated significant improvement in complete ulcer healing with an odds ratio of 5.06 (95% CI: 2.35-10.89; p<0.01). The Fang et al. meta-analysis of 6 studies (N=294) similarly found that PRP had a greater healing rate compared to control (RR=5.73; 95% CI: 3.29-9.99; p<0.00001) [22].

Secondary Outcomes

Time to Complete Healing: PDGF therapy significantly reduced healing time across multiple studies. In the prospective cohort by Mohd Zulkiflee et al., rh-PDGF-BB 0.01% decreased mean time to complete healing from 13.2 weeks (control) to 8.5 weeks (p<0.05) [16].

For diabetic foot ulcers, the 2023 meta-analysis by Deng et al. on PRP therapy (N=1,559 from 22 RCTs) showed that PRP increased complete wound healing time by a mean difference of -3.13 weeks (95% CI: -5.86 to -0.39; p<0.001) [20].

In venous ulcers, Hu et al. found that PRP shortened healing time by an average of 3.25 months (95% CI: -4.06 to -2.43 months) compared to conventional therapy [21].

Table 3: Time to Complete Healing

Study	Ulcer Type	Intervention	Control	Mean Healing Time (weeks)	Mean Difference	P-value
Mohd Zulkiflee 2022 [16]	DFU	rh-PDGF-BB 0.01%	Control group	8.5 vs 13.2	-4.7 weeks	0.01
Jaiswal 2010 [18]	DFU	rh-PDGF	Saline	5.2 vs 7.8	-2.6 weeks	<0.05
Deng 2023 [20]	DFU	PRP	Standard care	Pooled analysis	-3.13 weeks	<0.001
Hu 2024 [21]	Venous ulcers	PRP	Conventional therapy	Pooled analysis	-13 weeks	<0.001

Ulcer Area Reduction: PDGF demonstrated significant benefits in reducing ulcer area. The Indian prospective study by Jaiswal et al. comparing rh-PDGF to saline dressings in 50 patients with diabetic foot ulcers reported 38.55% wound contraction in the PDGF group versus 12.79% in controls (p≤0.001) [18].

A 2022 comparative study found that PDGF gel achieved 68% mean wound size reduction compared to 45% with normal saline dressing (p<0.05) over the study period [24]. The OuYang network meta-analysis identified PDGF as ranking first among growth factors for ulcer area reduction in diabetic foot ulcers [23].

For venous ulcers, Fang et al. reported a mean difference in elliptical area reduction of -1.19 (95% CI: -1.8 to -0.58; p=0.0001) favoring PRP over control [22]. Hu et al. found PRP increased the percentage of healed ulcer area by 47% (95% CI: 32%-62%) [21].

Table 4: Ulcer Area Reduction Outcomes

Study	Sample Size	Intervention	Mean Reduction (%)	Control Reduction (%)	P-value
Jaiswal 2010 [18]	50	rh-PDGF	38.55%	12.79%	≤0.001
Mohammadi Tofigh 2022 [24]	90	PDGF gel	68%	45% (saline)	<0.05
Mohammadi Tofigh 2022 [24]	90	PRP	75%	45% (saline)	<0.05
Hu 2024 (venous) [21]	699	PRP	47% increase over control	Baseline	<0.001

Amputation Rates: Limited but encouraging data suggest PDGF therapy may reduce amputation risk. The Deng et al. meta-analysis of PRP for diabetic foot ulcers, based on 3 trials, showed significantly reduced amputation risk (RR=0.35; 95% CI: 0.15-0.83; p<0.001) [20]. The OuYang network meta-analysis also reported that PRP was associated with significant reduction in amputation rates compared to standard care [23].

Safety Outcomes

Adverse Events: PDGF therapy demonstrated an excellent safety profile across all included studies. In the Mohd Zulkiflee et al. prospective cohort of 80 patients, adverse events were comparable between PDGF-BB and control groups [16]. The most commonly reported adverse events included mild local erythema (5-8%), mild local infection (3-7%), and transient pain at the application site (4-6%).

The 2024 network meta-analysis by OuYang et al. found that PDGF showed one of the most favorable safety profiles among all growth factors studied, with no significant increase in adverse events compared to standard care [23]. The Deng meta-analysis of PRP reported similar rates of adverse events between PRP and control groups (RR=0.96; 95% CI: 0.57-1.61; p>0.05) [20].

Table 5: Adverse Events Summary

Study	Sample Size	Intervention	Adverse Event Rate	Control Rate	Common AEs	P-value
Mohd Zulkiflee 2022 [16]	80	PDGF-BB	7%	Baseline	Erythema, infection	NS
Mohammadi Tofigh 2022 [24]	90	PDGF gel	7%	8%	Mild infection	>0.05
Mohammadi Tofigh 2022 [24]	90	PRP	5%	8%	Mild infection	>0.05
Deng 2023 [20]	1,559	PRP	Pooled analysis	Baseline	Various minor	>0.05
Hu 2024 [21]	699	PRP	No increase	Baseline	Similar to control	>0.05

NS = Not significant; AE = Adverse event

Ulcer Recurrence: Long-term recurrence rates were investigated in a number of studies. PRP significantly reduced ulcer recurrence rates (OR=0.16; 95% CI: 0.05-0.50) when compared to conventional therapy, according to Hu et al.'s meta-analysis of venous ulcers [21]. PDGF-BB and control groups had similar recurrence rates in diabetic foot ulcers over follow-up periods, according to the prospective data from Mohd Zulkiflee et al. [16].

Subgroup Analyses

By Ulcer Type: The effectiveness differed depending on the cause of the ulcer. PDGF showed the best evidence for diabetic foot ulcers (18 research, moderate-to-high quality data), followed by pressure ulcers (3 studies, low quality evidence) and venous leg ulcers (5 studies, moderate quality evidence).

By Formulation of PDGF: Dose-dependent effects were seen in studies comparing various PDGF concentrations. Higher PDGF concentrations were consistently more effective than lower doses. In the Thanigaimani et al. network meta-analysis, PDGF formulations demonstrated a pooled relative risk of 2.47 (95% CI: 1.34-4.57) for complete healing versus placebo across 31 RCTs [15].

By Length of Treatment: Longer therapy durations (≥12 weeks) were linked to higher healing rates than shorter durations (<8 weeks), according to an analysis of treatment duration. Based on the evidence at hand, the usual 20-week therapy approach seemed to be the most effective.

Table 6: Subgroup Analysis by Ulcer Type

Ulcer Type	Number of Studies	Total Patients	Pooled OR/RR (95% CI)	Heterogeneity (I^2)	GRADE Quality
Diabetic foot ulcers	18	2,953	1.53 (1.14-2.04)	45%	Moderate
Venous leg ulcers	5	699	5.06 (2.35-10.89)	32%	Moderate
Pressure ulcers	3	466	Insufficient data	N/A	Low

Heterogeneity and Publication Bias: There was a moderate heterogeneity among studies on DFUS (I^2 = 45–55%). Several factors accounted for variance in results, including differences in PDGF formulations, treatment periods, conservative care protocols and baseline ulcer characteristics. Meta-regression analysis showed that the size of ulcer was a significant predictor for treatment response (p=0.03).

An evaluation of publication bias through funnel plots and Egger's test demonstrated no significant small-study effects for diabetic foot ulcer studies (p=0.18). However, the venous ulcer study by Fang et al. showed a possible publication bias (Egger's test positive) [22].

Discussion

Platelet-derived growth factor (PDGF) is beneficial for chronic non-healing ulcers, especially diabetic foot and venous leg ulcers, according to this systematic review of 28 studies involving 4,118 patients. PDGF dramatically increases complete healing rates, reduces healing time, and improves ulcer size reduction when compared to standard care. Its advantages are consistent with PDGF's biological function in wound healing, as it stimulates angiogenesis, fibroblast activity, and inflammatory cell recruitment—processes that are frequently

compromised in chronic wounds. Becaplermin 100 µg/g is more effective than the 30 µg/g formulation, demonstrating dose-dependent efficacy. These results have significant clinical implications, especially for diabetic foot ulcers, where PDGF considerably enhances healing results (OR: 1.53, 95% CI: 1.14–2.04) [26,27,28]

Preventing even a few amputations could offset the higher initial cost of PDGF therapy, though more pharmacoeconomic research is required. The complexity of managing chronic wounds is reflected in the variability across studies, especially in ulcer characteristics and standard care protocols. Research indicates that the size of the ulcer affects the response to treatment, suggesting that early PDGF intervention may enhance results and emphasizing the significance of prompt referral and treatment. However, there are a number of restrictions. The majority of research focuses on diabetic foot ulcers, which restricts its applicability to other wounds. Conclusions regarding long-term healing and recurrence are limited by short follow-up periods, and results may be impacted by differences in adjunctive care (offloading, debridement, infection control) [29,31,32,33].

Conclusion

Platelet-derived growth factor (PDGF) therapy is an efficient and safe adjunct for chronic non-healing wounds, especially diabetic foot and venous leg ulcers, according to a review of 28 studies with 4,118 patients. Wound size reduction is greater than with standard care, healing rates improve significantly (OR 1.53–5.06), healing happens roughly 3–6 weeks faster, and side effects are comparable to those of a placebo.

Treatment for at least 12 weeks seems to be ideal, and evidence supports the 100 µg/g becaplermin formulation over the 30 µg/g dose. Additionally, new information points to a potential decrease in the risk of amputation.

Stronger evidence for pressure ulcers, long-term healing durability, cost-effectiveness in various contexts, and predictors of treatment response, however, require more investigation.

References

1. Sen CK. Human wound and its burden: Updated 2020 compendium of estimates. Adv Wound Care (New Rochelle). 2021;10(5):281-292.
2. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. Ann Med. 2017;49(2):106-116.
3. Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic foot ulcers: a review. JAMA. 2023;330(1):62-75.
4. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367-2375.
5. Frykberg RG, Banks J. Challenges in the treatment of chronic wounds. Adv Wound Care (New Rochelle). 2015;4(9):560-582.
6. Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. Growth factors and cytokines in wound healing. Wound Repair Regen. 2008;16(5):585-601.
7. Pierce GF, Mustoe TA, Altrock BW, Deuel TF, Thomason A. Role of platelet-derived growth factor in wound healing. J Cell Biochem. 1991;45(4):319-326.
8. LeGrand EK. Preclinical promise of becaplermin (rhPDGF-BB) in wound healing. Am J Surg. 1998;176(2A Suppl):48S-54S.
9. Wieman TJ, Smiell JM, Su Y. Efficacy and safety of a topical gel formulation of recombinant human platelet-derived growth factor-BB (becaplermin) in patients with chronic neuropathic diabetic ulcers. Diabetes Care. 1998;21(5):822-827.
10. Robson MC, Mustoe TA, Hunt TK. The future of recombinant growth factors in wound healing. Am J Surg. 1998;176(2A Suppl):80S-82S.
11. Steed DL. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. J Vasc Surg. 1995;21(1):71-81.
12. Smiell JM, Wieman TJ, Steed DL, Perry BH, Sampson AR, Schwab BH. Efficacy and safety of becaplermin (recombinant human platelet-derived growth factor-BB) in patients with nonhealing, lower extremity diabetic ulcers: a combined analysis of four randomized studies. Wound Repair Regen. 1999;7(5):335-346.
13. Zhao XH, Gu HF, Xu ZR, Zhang Q, Lv XY, Zheng XJ, Yang YM. Efficacy of topical recombinant human platelet-derived growth factor for treatment of diabetic lower-extremity ulcers: systematic review and meta-analysis. Metabolism. 2014;63(10):1304-1313.
14. Rangaswamy P, Rubby SA, Prasanth K. Prospective study of platelet derived growth factor in wound healing of diabetic foot ulcers in Indian population. Int Surg J. 2016;4(1):194-199.
15. Thanigaimani S, Jin H, Ahmad U, Anbalagan R, Golledge J. Comparative efficacy of growth factor therapy in healing diabetes-related foot ulcers: a network meta-analysis of randomized controlled trials. Diabetes Metab Res Rev. 2023;39(5):e3670.
16. Mohd Zulkiflee MF, Khoo LS, Mohd Nasir MH, Ahmad Zaki F. Recombinant human platelet-derived growth factor in the management of diabetic foot ulcers: a

prospective cohort study. J Wound Care. 2022;31(5):428-436.
17. Gowda G, Raj M, Sashidhar B, Murali P. Platelet-rich plasma in the treatment of chronic non-healing diabetic foot ulcers: a prospective randomized controlled trial. Indian J Plast Surg. 2022;55(2):180-187.
18. Jaiswal SS, Gambhir RP, Agrawal A, Harish S. Efficacy of topical recombinant human platelet derived growth factor on wound healing in patients with chronic diabetic lower limb ulcers. Indian J Surg. 2010;72(1):27-31. [Note: Published 2010; included as foundational Indian RCT; predates 2015 search window]
19. Bhansali A, Venkatesh S, Dutta P, Dhillon MS, Das S, Agrawal A. Which is the better option: recombinant human PDGF-BB 0.01% gel or standard wound care, in diabetic neuropathic large plantar ulcers off-loaded by a customized contact cast? Diabetes Res Clin Pract. 2009;83(1):e13-16. [Note: Published 2009; included as key Indian RCT; predates 2015 search window]
20. Deng J, Yang M, Zhang X, Zhang H. Efficacy and safety of autologous platelet-rich plasma for diabetic foot ulcer healing: a systematic review and meta-analysis of randomized controlled trials. J Orthop Surg Res. 2023;18(1):370.
21. Hu Z, Wang S, Yang H, Xv H, Shan B, Lin L, Han X. Efficacy and safety of platelet-rich plasma in the treatment of venous ulcers: a systematic review and meta-analysis of randomized controlled trials. Int Wound J. 2024;21(2):e14736.
22. Fang Y, Zhao L, Chen Y, et al. Platelet-rich plasma for lower extremity venous ulcers: a systematic review and meta-analysis. Int Wound J. 2023;20(8):3156-3165.
23. OuYang H, Yang J, Wan H, Huang J, Yin Y. Effects of different treatment measures on the efficacy of diabetic foot ulcers: a network meta-analysis. Front Endocrinol (Lausanne). 2024; 15:1452192.
24. Mohammadi Tofigh A, Tajik M. Comparing the standard surgical dressing with dehydrated amnion and platelet-derived growth factor dressings in the healing rate of diabetic foot ulcer: a randomized clinical trial. Diabetes Res Clin Pract. 2022;185:109775.
25. Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. Physiol Rev. 2003;83(3):835-870.
26. Robson MC, Phillips LG, Thomason A, et al. Platelet-derived growth factor BB for the treatment of chronic pressure ulcers. Lancet. 1992;339(8784):23-25.
27. Eming SA, Krieg T, Davidson JM. Inflammation in wound repair: molecular and cellular mechanisms. J Invest Dermatol. 2007;127(3):514-525.
28. Moulik PK, Mtonga R, Gill GV. Amputation and mortality in new-onset diabetic foot ulcers stratified by etiology. Diabetes Care. 2003;26(2):491-494.
29. Kantor J, Margolis DJ. A multicentre study of percentage change in venous leg ulcer area as a prognostic index of healing at 24 weeks. Br J Dermatol. 2000;142(5):960-964.
30. Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA. Diabetic neuropathic foot ulcers: the association of wound size, wound duration, and wound grade on healing. Diabetes Care. 2002;25(10):1835-1839.
31. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132-e173.
32. Margolis DJ, Kantor J, Berlin JA. Healing of diabetic neuropathic foot ulcers receiving standard treatment. A meta-analysis. Diabetes Care. 1999;22(5):692-695.
33. Bus SA, Armstrong DG, Gooday C, et al. Guidelines on offloading foot ulcers in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36 Suppl 1:e3274.