



Complementary Therapy Interventions in Diabetic Foot Ulcer: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Diabetic foot ulcers (DFUs) are complications of diabetes mellitus that may impair wound healing and reduce quality of life. Complementary therapies have been investigated as adjuncts to conventional wound care, but evidence of their effectiveness remains heterogeneous. This systematic review aimed to evaluate the effects of complementary therapies with conventional care on wound-healing outcomes in patients with active diabetic foot ulcers. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Searches were conducted in Scopus, PubMed, ScienceDirect, and SAGE Journals for studies published from 2021 to 2026; the final search was conducted on 15 August 2026. Eligible studies were randomized controlled trials involving patients with active diabetic foot ulcers and complementary therapies as adjuncts to conventional care. Study quality and risk of bias were assessed using the Joanna Briggs Institute critical appraisal checklist for randomized controlled trials. The review protocol was not registered. Following reassessment, five randomized controlled trials met inclusion criteria. The studies reported improvements in wound-healing outcomes, including reduced ulcer size and improved wound-healing indicators. However, heterogeneity in interventions, treatment duration, participant characteristics, and outcome measures precluded quantitative synthesis and pooled effect estimation. The certainty of evidence was limited by small sample sizes, short follow-up periods, and variability in intervention protocols. Complementary therapies may provide additional benefits for wound healing when used alongside conventional care for active diabetic foot ulcers. However, evidence remains limited and heterogeneous. Larger RCTs using standardized interventions and standardized wound-healing outcomes.

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia resulting from impaired insulin secretion, impaired insulin action, or both. Persistent hyperglycemia is associated with multiple microvascular and macrovascular complications, including peripheral neuropathy, peripheral arterial disease (PAD), and impaired wound healing. Diabetic foot ulcer (DFU) is one of the major complications of

diabetes-related foot disease and represents an important clinical problem because of its prolonged healing, risk of infection, recurrence, hospitalization, and lower-extremity amputation. The development of DFU is frequently associated with peripheral neuropathy, PAD, repetitive mechanical stress, and other factors that impair tissue integrity and wound healing. Current international guidelines emphasize that diabetes-related foot disease requires early assessment and multidisciplinary management to reduce the risk of adverse outcomes (Bus et al., 2024; Fitridge et al., 2023; Senneville et al., 2024). management of active DFU requires a multidisciplinary and evidence-based approach that addresses both the wound and the underlying factors that interfere with healing. Standard DFU management includes comprehensive wound assessment and classification, appropriate debridement and wound-bed preparation, infection assessment and treatment, appropriate wound dressing, pressure off-loading, optimisation of glycaemic control, and assessment and management of PAD, including revascularisation when indicated. These interventions are intended to remove devitalised tissue, control infection, reduce mechanical stress, optimise tissue perfusion, maintain an appropriate wound environment, and support wound healing. In particular, off-loading is considered a fundamental component of treatment for appropriate plantar DFUs, while vascular assessment and revascularisation may be required in patients with clinically significant ischemia (Bus et al., 2024; Chen et al., 2024; Fitridge et al., 2023; Senneville et al., 2024). A diabetic ulcer is a non-traumatic lesion of the skin (affecting part or all of the layers) on the feet of individuals with diabetes mellitus. Diabetic foot ulcers are typically caused by repeated pressure (shear and pressure) on the foot, often in conjunction with diabetes-related complications such as peripheral neuropathy or peripheral artery disease, and their healing is frequently complicated by the development of infection (Trisnawati, 2023).

Diabetes mellitus is a major global health problem associated with multiple chronic complications, including diabetic foot ulcers (DFUs). DFUs represent a significant cause of morbidity among people with diabetes and may lead to delayed wound healing, infection, lower-extremity amputation, and impaired quality of life. A global systematic review and meta-analysis estimated the prevalence of DFUs among people with diabetes at 6.3% (95% CI, 5.4–7.3%), highlighting the substantial burden of diabetic foot disease worldwide (Zhang et al., 2017).

Individuals with diabetes mellitus are prone to developing diabetic ulcers. High risk factors for diabetic ulcers among those with diabetes, coupled with a lack of awareness regarding proper care, make them susceptible to wounds that can eventually progress to gangrene. If not properly managed, this poses a high risk of leg amputation; therefore, nurses must implement promotive and preventive measures to address the risk of diabetic ulcers (Panjaitan, 2024). Barriers to wound healing include chronic wounds, which are difficult to treat due to the complex etiology and factors that delay or prevent healing, making it hard for the wound to close. Chronic wounds exhibit an irregular healing process, meaning that multiple healing phases may occur simultaneously within a single wound. Over the course of one year, 36%—or 317 cases—of DFUs exhibited prolonged healing. DFU cases are commonly found in the elderly. Poor oxygen supply leads to wound hypoxia and vascular disease. DFU complications can trigger stress. One treatment for DFU is anti-proliferative NSAID therapy. Each disruption in the wound healing stages results in a 20% to 60% delay (Bus et al., 2024).

Diabetic ulcers are a major complication of diabetes and a leading cause of non-traumatic amputation, highlighting the need for effective wound-healing strategies. Although various complementary therapies have been studied, their effectiveness remains inconsistent. Therefore, this systematic review aims to compare different complementary therapies based on wound healing, wound-area reduction, and tissue perfusion. Its novelty lies in providing a comprehensive comparison of evidence to support evidence-based nursing practice in selecting appropriate supportive therapies. Given the impact of barriers to the prevention of diabetic ulcers, researchers are interested in examining the effectiveness of complementary therapies in preventing diabetic ulcers. Identifying the benefits of complementary therapies can optimize ulcer prevention, thereby reducing the risk of poor outcomes associated with diabetic ulcers and alleviating the health, economic, and social burdens.

METHODS

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The review evaluated complementary therapies for diabetic foot ulcers (DFUs). The protocol was not prospectively registered in PROSPERO or another systematic review registry.

Eligibility criteria were defined using the Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework (Table 1). Eligible studies were parallel or cluster randomized controlled trials involving adults with type 2 diabetes and clinically diagnosed active DFUs. Interventions comprised clearly defined complementary or adjunctive therapies added to standard DFU care, with standard care, placebo, sham intervention, or another active intervention as the comparator. Primary outcomes were complete wound healing, time to healing, and changes in wound area. Secondary outcomes included infection, amputation, pain, perfusion, quality of life, and adverse events.

Table 1. PICOS

Category	Description
Population (P)	Adults with type 2 diabetes and clinically diagnosed active DFU.
Intervention(I)	A clearly defined complementary or adjunctive non-standard therapy added to standard DFU care.
Comparator (C)	Standard care, placebo, sham intervention, or another active intervention.
Outcome (O)	Primary outcomes: Complete wound healing, time to healing, and change in wound area. Secondary outcomes: Infection, amputation, pain, perfusion, quality of life, and adverse events.
Study Design (S)	Parallel or cluster randomized controlled trials.

A systematic literature search was conducted in Scopus, PubMed, ScienceDirect, and SAGE Journals for English-language studies published from January 2021 to 2026. The final search was conducted on August 15, 2026. Search terms included “complementary therapy,” “alternative therapy,” “holistic treatment,” “diabetic foot ulcer,” “diabetic ulcer,” “foot ulcer,” “acupuncture,” “herbalism,” “physical therapy,” and related outcome terms. Search strategies

were adapted to the syntax of each database. The complete search strategies and numbers of records retrieved are presented in Table 2.

Table 2. Research Strategy

Data Based	Research Strategy	Study (n)
Scopus	("complementary therapy" OR "alternative therapy" OR "holistic treatment") AND ("diabetic foot ulcer" OR "diabetic ulcer" OR "foot ulcer" OR "diabetes complications") AND ("effectiveness" OR "efficacy" OR "impact" OR "outcome") AND ("prevention" OR "prevent") AND ("Acupuncture treatments") AND ("medicine herbal" OR "herbalism") AND ("physical therapy techniques" OR "physical therapy") AND ("mind-body therapy")	18
Pubmed	("complementary treatments") AND ("diabetic foot") AND ("foot ulcer")	15
Sciencedirect	("diabetic ulcer foot") AND ("complementary therapy" OR ("physical therapy") OR ("acupuncture") OR ("herbalism") OR ("foot massage"))	316
Sage	("complementary treatments") AND ("diabetic foot") AND ("foot ulcer")	182

Retrieved records were compiled, and study selection involved duplicate removal, title and abstract screening, and full-text eligibility assessment. Two reviewers independently screened titles and abstracts and assessed potentially relevant full-text articles against the predefined eligibility criteria. Disagreements were resolved through discussion and consensus, with a third reviewer consulted when necessary. Reasons for exclusion during full-text assessment were documented. The study-selection process is presented in the PRISMA flow diagram (Figure 1).

Two reviewers independently extracted data using a standardized form. Extracted information included the first author and publication year, country, study design, sample size, participant characteristics, complementary therapy, comparator, intervention frequency and duration, measurement instruments, outcome measures, and principal findings. Discrepancies were resolved through consensus, and original articles were re-examined when clarification was required. Extracted data were organized in a standardized evidence table and independently checked before synthesis.

Methodological quality and risk of bias were assessed independently by two reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Randomized Controlled Trials. The checklist comprises 13 items, each rated as "Yes," "No," "Unclear," or "Not applicable." Differences in appraisal judgments were resolved through discussion and consensus. Appraisal results are presented in Table 3.

Findings were synthesized narratively because substantial clinical and methodological heterogeneity precluded quantitative pooling. Studies differed in intervention types and protocols, treatment frequency and duration, participant characteristics, comparators,

outcome definitions, measurement instruments, and follow-up periods. Findings were grouped by complementary therapy and principal clinical outcome, and the direction and consistency of results were compared while considering study characteristics and methodological quality.

Systematic review *research* is required to assess the quality of the articles used. Aims to prevent potential risk of bias. There is often a bias in the design of implementation and analysis of results. This study uses a critical assessment tool in the form of *the Joanna Briggs Institute* (JBI). In the RCT research design, there are 13 questions. There are three assessment criteria in JBI, namely; "Yes", "No", and "Unclear". In addition, to extract data in the form of a complete and comprehensive characteristic table (table 3) of all article findings. The table includes, year of study, country, type of intervention in complementary therapy, frequency & duration of intervention, instrument, and research results. The data analysis process begins by organizing the data and then systematically extracting it in the form of tables. All authors play a role in reviewing and translating data extraction tables with narrative descriptions.

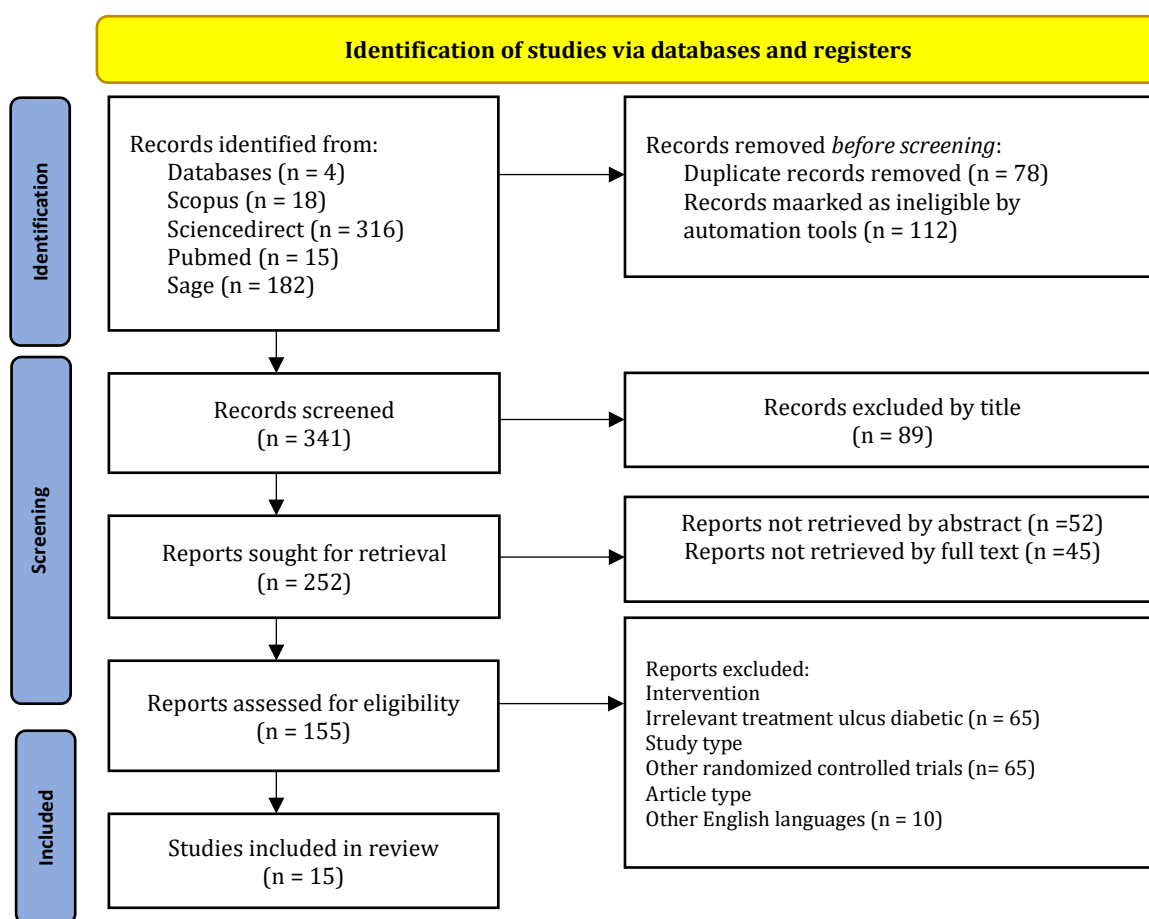


Figure 1. PRISMA

RESULTS

The database search identified 531 records: 18 from Scopus, 15 from PubMed, 316 from ScienceDirect, and 182 from SAGE Journals. After removing 78 duplicates and 112 records marked as ineligible by an automation tool, 341 records underwent title and abstract screening. Of these, 89 were excluded, leaving 252 reports sought for retrieval. Ninety-seven reports were not retrieved, and 155 underwent full-text assessment. A further 140 reports were excluded

because of irrelevant interventions ($n = 65$), inappropriate study designs ($n = 65$), or inappropriate article or language types ($n = 10$). Fifteen randomized controlled trials were included, as shown in Figure 1.

The methodological quality of the included trials was assessed using the 13-item Joanna Briggs Institute (JBI) checklist. The appraisal results are presented in Table 3.

Table 3. Critical Appraisal Joanna Briggs Institute (JBI)

No	Authors, Year	Study Design	JBI (%) critical Appraisal
1.	(Sanpinit <i>et al.</i> , 2024)	RCT	11/13 (84.6%)
2.	(Gyurova-kancheva <i>et al.</i> , 2026)	RCT	12/13 (92.3%)
3.	(Apaydin & Hintistan, 2025)	RCT	11/13 (84.6%)
4.	(Mohammadalinia <i>et al.</i> , 2025)	RCT	13/13 (100%)
5.	(Gündüz-oruç & Yilmaz-karabulutlu, 2025)	RCT	12/13 (92.3%)
6.	(Amiri <i>et al.</i> , 2025)	RCT	11/13 (84.6%)
7.	(Nese <i>et al.</i> , 2025)	RCT	11/13 (84.6%)
8.	(Aslan <i>et al.</i> , 2025)	RCT	12/13 (92.3%)
9.	(Nittur <i>et al.</i> , 2023)	RCT	11/13 (84.6%)
10.	(Glonek <i>et al.</i> , 2022)	RCT	13/13 (100%)
11.	(Ghanadian <i>et al.</i> , 2024)	RCT	11/13 (84.6%)
12.	(He <i>et al.</i> , 2021)	RCT	12/13 (92.3%)
13.	(Zellers <i>et al.</i> , 2026)	RCT	11/13(84.6%)
14.	(Ahmadvash <i>et al.</i> , 2025)	RCT	13/13 (100%)
15.	(Ajith <i>et al.</i> , 2025)	RCT	11/13 (84.6%)

Eight trials scored 11/13 (84.6%), four scored 12/13 (92.3%), and three scored 13/13 (100%). All trials were classified as having good methodological quality in the manuscript.

The characteristics, interventions, comparators, treatment schedules, and outcomes of the included trials are summarized in Table 4.

The 15 trials were published between 2021 and 2026 and involved 860 participants across seven countries. Four trials were conducted in Iran, four in Turkey, two in India, two in the United States, and one each in Thailand, Bulgaria, and China. Interventions included topical preparations, oxygen therapy, acupressure, massage, pranic healing, stress-ball therapy, and physical exercise.

Wound-related improvements were reported for Ya-Samarn-Phlae, hyperbaric oxygen therapy, Plantago major extract, continuous diffusion of oxygen combined with moist wound dressing, topical melatonin hydrogel, and Buerger–Allen exercises. Reported benefits included reduced ulcer area, improved wound-healing indicators, and enhanced circulation or tissue oxygenation. Other trials reported improvements in neuropathic symptoms, pain, sleep quality, quality of life, diabetes-related symptoms, skin condition, or foot deformity. Stress-ball therapy reduced pain and anxiety during debridement. Differences in interventions, treatment schedules, and outcome measures precluded quantitative pooling.

Table 4. Characteristics, Complementary Interventions, and Reported Outcomes of the Included Randomized Controlled Trials

Authors, Year	Country	Complementer Therapy	Respondent		Intervention		Frequency and Period of Intervention	Outcome
			Sample (n)	Mean SD of Age Intervention/ Control	Experiment	Trial		
(Sanpinit <i>et al.</i> , 2024)	Thailand	Ya-Samarn-Phlae (YaSP)	25 respondent	55.04 $\pm$ 1.87 / 54.48 $\pm$ 1.60	Receiving <i>Ya-Samarn-Phlae</i> (YaSP) and standart wound care.	Standard treatment without Ya-Samarn-Phlae (YaSP)	Every day per 12 weeks	Effective in treating diabetic ulcers
(Gyurova-kancheva <i>et al.</i> , 2026)	Bulgaria	Therapy <i>Hyperbaric oxygen</i> (HBO)	15 respondent	54,8 $\pm$ 9,7 / 58,6 $\pm$ 9,4	Receiving <i>Hyperbaric oxygen</i> therapy (HBO)	Without <i>Hyperbaric oxygen</i> (HBO) therapy	Ten sessions per week	Significant decrease in diabetic ulcer area and pain level
(Apaydin & Hintistan, 2025)	Turkey	Geriatric massage	59 respondent	70.59 $\pm$ 4.88 / 72.50 $\pm$ 5.28	Getting a geriatric massage	Without geriatric massage	Two hours per week for 2 weeks.	Reduce diabetes symptoms and increase HDL cholesterol levels
(Mohammadalinia <i>et al.</i> , 2025)	Iran	Auriculotherapy	41 respondent	54.55 $\pm$ 5.02 / 52.76 $\pm$ 5.7	Getting Auriculotherapy	Without Auriculotherapy	Three hours per day for 6 weeks	Reduce symptoms of neuropathy and improve quality of life
(Gündüz-oruç & Yilmaz-karabulutlu, 2025)	Turkey	Acupressure	86 respondent	55.05 $\pm$ 8.48 / 56.10 $\pm$ 8.46	Getting acupressure	Without acupressure	Twenty minutes per 6 days.	To reduce pain and improve sleep quality
(Amiri <i>et al.</i> , 2025)	Iran	Topical chamomile oil	72 respondent	60.33 $\pm$ 11.27 / 63.53 $\pm$ 11.46	The intervention group was given chamomile oil	Using standard gabapentin therapy	Fifteen drops per day for 3 months.	Reducing neuropathic symptoms in diabetic patients

(Nese et al., 2025)	Turkey	Foot Reflexology Massage	65 respondent	58.51± 8.33/ 57.43± 7.17	Getting foot reflexology massage	Just getting routine care	Thirty-forty minutes per day for 6 weeks	Managing neuropathic pain in individuals with diabetes
(Aslan <i>et al.</i> , 2025)	Turkey	Stress ball on pain and anxiety	76 respondent	59.02± 9.96/ 56.39± 8.51	Receiving a stress ball as a therapeutic tool	We do not accept interventions with routine debridement procedure.	Twenty-thirty minutes per day	Reducing pain and anxiety during debridement procedures in patients with diabetic ulcers
(Nittur et al., 2023)	India	Pranic healing	30 respondent	53.07±10.37/ 62.0± 8.48	Receiving standard care and pranic therapy	Just receiving standard care.	Fifty-sixty minutes per day for 3 days.	Therapy for managing diabetic ulcers and neuropathy
(Glonek et al., 2022)	USA	Skin cream containing plant-based anionic polar phospholipid (APP)	54 respondent	70.5± 64.8/ 70.5± 35.2	Getting a skin cream made with anionic polar phospholipids (APP)	Using a skin cream that Mineral Hydrocarbon-Based cream / Eucerin Original Formula (MHB)	Every night for 6 weeks	Reducing skin damage in diabetic feet, as assessed by four criteria: dryness, erythema, fissures, and itching.
(Ghanadian et al., 2024)	Iran	Plantago major	44 respondent	56.82±17.37/ 62.31± 9.51	The subject received Plantago major hydroalcoholic extract for wound healing	Not using Plantago major hydroalcoholic extract for healing	Once every two weeks.	Reducing wound size and improving healing rates
(He et al., 2021)	China	Moist Wound Dressing (MWD) + Continuous	120 respondent	63.5 ± 10.1/ 63.1 ± 9.3	Receive Moist Wound Dressing (MWD).	Receive Moist Wound Dressing (MWD) + Continuous	Two to three times per week for 8 weeks.	The combination of continuous diffusion of oxygen (CDO) with moist wound dressing (MWD)

		diffusion oxygen (CDO)				diffusion oxygen (CDO).		provides better effectiveness than the use of MWD alone or CDO alone in accelerating the healing of diabetic foot ulcers.
(Zellers et al., 2026)	USA	Physical exercise: Focus on leg exercises	60 respondent	68.0± 7.9/ 66.9± 4.0	Get (foot specific exercises (stretching, strengthening, foot care, functional movement retraining)	Not getting leg workout, but shoulder workout.	Five times per week for 6 months.	Foot exercises can improve or slow the progression of metatarsophalangeal joint deformity in type 2 DM patients with peripheral neuropathy.
(Ahmadvash et al., 2025)	Iran	Topical melatonin hydrogel	53 respondent	56.93± 7.11/ 58.15± 9.94	Get topical melatonin hydrogel	Topical melatonin hydrogel was not administered	Every night for 2 months.	Reducing the number, severity, and size of diabetic foot ulcers (DFUs).
(Ajith et al., 2025)	India	Buerger-Allen exercises	60 respondent	56.67± 10/ 53.33± 8.33	Performing Buerger-Allen exercises and following a diabetes treatment regimen	Following a diabetes treatment regimen	Five times per week	Improves circulation, enhances tissue oxygenation, and aids in the healing of neuropathic diabetic foot ulcers

DISCUSSION

The included interventions comprised topical plant-based therapy, oxygen-based adjunctive therapy, exercise and circulation-based therapy, and other complementary approaches. Importantly, the included interventions should not be interpreted as a single homogeneous therapeutic category because they target different biological and clinical mechanisms and were evaluated using different wound classifications, treatment durations, comparators, and outcome measures.

Overall, the direction of the findings was favorable for adjunctive treatment of active DFUs, with improvements reported in complete wound healing, wound area, ulcer grade, ulcer depth, or composite wound severity. However, the evidence remains preliminary. The number of studies within each intervention category was small, sample sizes were generally limited, and substantial clinical and methodological heterogeneity prevented meaningful quantitative pooling. Consequently, the findings should be interpreted as evidence of potential benefit rather than definitive evidence of effectiveness.

The distinction between wound-related outcomes and symptom-related outcomes is particularly important. Only studies that directly assessed active DFU healing or wound characteristics were retained in the final synthesis. Studies assessing neuropathy, sleep quality, diabetes-related symptoms, anxiety, or musculoskeletal deformity without a direct wound-healing outcome were excluded during the full-text reassessment. This stricter approach increases the clinical relevance of the review to DFU management but substantially reduces the number of eligible studies. One randomized controlled trial evaluated a topical plant-based intervention, Ya-Samarn-Phlae (YaSP), as an adjunct to standard wound care in patients with diabetic ulcers. The study demonstrated a clinically substantial difference in complete healing: 76% of participants receiving YaSP achieved complete healing at 12 weeks compared with 16% receiving standard treatment alone. The difference was statistically significant ($p < 0.001$), while a significant difference was also observed at six weeks (36% vs. 4%; $p = 0.013$).

The magnitude of the observed absolute difference at 12 weeks (60 percentage points) suggests potentially important clinical benefit rather than merely a statistically significant result. Nevertheless, the result should be interpreted cautiously because it originates from a single trial with a relatively small sample. The investigators themselves recommended a larger double-blind randomized controlled trial to confirm the finding. The direct relevance of this evidence to DFU healing is high because the intervention was evaluated specifically as an adjunct to standard wound care and the primary clinically meaningful endpoint was complete wound healing. This is fundamentally different from complementary interventions that assess neuropathic symptoms or general diabetes-related outcomes without measuring wound response. The likely applicability of YaSP is also dependent on the context in which it was studied. The intervention was developed from traditional Thai herbal medicine and was administered alongside standard wound care. Therefore, the observed effect should not be interpreted as evidence that topical plant-based therapies generally are effective for DFUs. Rather, the evidence currently supports a potential adjunctive effect of this specific preparation. Differences in herbal composition, formulation, dosing, wound classification, and standard wound care may substantially influence effectiveness.

The certainty of evidence for this intervention should therefore be considered low to moderate, primarily because only one relatively small RCT directly supports the finding. The favorable magnitude of effect increases interest in the intervention, but replication in larger, independently conducted trials is required before broad clinical adoption can be recommended. Oxygen-based therapy was represented by a randomized controlled trial evaluating continuous diffusion of oxygen (CDO) in patients with active DFUs. The trial involving 120 inpatients compared moist wound dressing, CDO, and their combination over eight weeks. The combination treatment produced a significantly higher wound-healing rate than either treatment alone and was also associated with a lower amputation rate during one-year follow-up. These findings are clinically relevant because CDO was evaluated directly in patients with active DFUs and the principal outcomes included wound healing and amputation rather than surrogate symptoms. The results also suggest that oxygen-based therapy may have value as an adjunct to, rather than replacement for, conventional wound management.

CONCLUSION

Selected complementary or adjunctive interventions may improve wound-healing outcomes when added to standard care for adults with active diabetic foot ulcers. However, the limited number of small, heterogeneous randomized controlled trials precludes firm conclusions about their comparative effectiveness or safety. These interventions should be considered as potential adjuncts to established evidence-based, multidisciplinary DFU care.

Future research should use adequately powered randomized controlled trials with standardized DFU definitions and classifications, clearly described standard care, and appropriate follow-up. Complete wound healing or time to healing should be prioritized when evaluating DFU healing, with wound-related outcomes distinguished from symptom-related outcomes. Rigorous randomization, allocation concealment, blinded outcome assessment where feasible, and predefined protocols are needed. Trials should report effect estimates with 95% confidence intervals and systematically document adverse events, treatment adherence, and withdrawals to strengthen the certainty, comparability, and generalizability of the evidence.

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