Journal of Current Medical Research and Opinion

CMRO 09 (03) 4677-4692 (2026)
DOI: https://doi.org/10.52845/CMRO/2026/9-3-3
www.cmro.in

CMRO
ISSN (O) 2589-8779
(P) 2589-8760

Original Article

Efficacy of Topical Bioactive Plant Extracts in Burn Wound Healing: A Systematic Review of Clinical and Preclinical Evidence

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Abstract

The proposed systematic review should be an in-depth review of the effectiveness of topical bioactive plant extracts in the healing of burn wounds of all types (thermal, chemical, electrical, and radiation) and all depths (first-, second-, and third-degree). The objectives are: To evaluate the efficacy of plant extracts in enhancing the most important outcome, such as time to heal, infection, pain, scar, and biological (e.g., IL-6, VEGF, collagen deposition) outcomes. To clarify the mechanistic apparent working action such as, anti-inflammatory, antimicrobial and angiogenic. The review aims at well-investigated plant extracts, such as Aloe vera, Centella asiatica, Curcuma longa, Calendula officinalis, Hippophae rhamnoides, and Betula pendula, since they are proven to be effective and applicable in burn management. This systematic review is convincing that bioactive plant extracts, specifically, Aloe vera, Centella asiatica, and Curcuma longa, hasten the healing of burn wounds, alleviate pain, enhance the quality of scars, and decrease the rate of infection in superficial and partial-thickness burns. Nevertheless, the heterogeneity, scarce information on both deep burns and the necessity of large-scale RCTs make additional investigations. The clinical adoption of plant-based therapies could be improved with standardized formulations, novel delivery methods such as hydrogels, and follow-up studies to determine the long-term outcomes and/or improve the clinical results of patients with burn injuries and decrease the socioeconomic price of burn care.

Keywords: Bioactive Plant Extracts, Burn Wound Preclinical Evidence, Systematic Review

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Received: 09.01.2026 | **Revised:** 27.02.2026 | **Accepted:** 08.03.2026 | **Published:** 19.03.2026

1. Introduction

Burn injuries pose a significant global health challenge, contributing to substantial morbidity, mortality, and socioeconomic burdens. Annually, burns cause approximately 180,000 deaths worldwide, predominantly in low- and middle-income countries [1]. Non-fatal burns often result in prolonged hospitalization, disfigurement, and long-term disabilities, such as hypertrophic scarring and contractures, which severely impair quality of life [1]. Burns are classified by etiology (thermal, chemical, electrical, or radiation) and depth, ranging from first-degree (superficial) to third-degree (full-thickness) [2]. The healing process for burns is multifaceted, involving hemostasis, inflammation, proliferation, and remodeling phases, each susceptible to complications like infection, delayed re-epithelialization, or excessive scarring [2]. Effective burn wound management is critical to mitigate these complications, accelerate healing, and optimize patient outcomes. Standard burn treatments, such as silver sulfadiazine (SSD), hydrocolloid dressings, and surgical interventions, form the cornerstone of modern burn care [3]. SSD is widely used for its antimicrobial properties but has limitations, including delayed wound closure, potential cytotoxicity to keratinocytes and fibroblasts, and rare hypersensitivity reactions [3,4]. Advanced dressings, such as hydrocolloids and hydrogels, promote a moist healing environment, supporting granulation and epithelialization [5]. However, these therapies may not fully address the complex pathophysiology of burns, including inflammation and oxidative stress, and their high cost can limit accessibility in resource-limited settings [5]. Furthermore, the rising threat of antimicrobial resistance underscores the need for alternative therapies that are effective, affordable, and biologically versatile [6]. Plant-based therapies have been employed for centuries in traditional medicine to treat wounds, including burns, due to their accessibility, perceived safety, and diverse pharmacological properties [7]. Bioactive plant extracts, rich in compounds such as flavonoids, polyphenols, alkaloids, and terpenoids, exhibit anti-inflammatory, antioxidant, antimicrobial, and angiogenic effects, which align with the multifaceted needs of burn wound healing [7,8]. For example, *Aloe vera* contains aloin and polysaccharides that reduce inflammation and enhance re-epithelialization [9]. A recent systematic review and meta-analysis reported that *Aloe vera* reduced burn healing time by approximately 3.8 days compared to controls, with significant improvements in wound closure rates [9]. Similarly, *Centella asiatica* (gotu kola) contains asiaticoside and madecassoside, which promote collagen synthesis and angiogenesis by upregulating vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) [10]. A 2022 systematic review confirmed these mechanisms, noting reduced levels of pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α) in wound models [10].

Other plants, including *Curcuma longa* (turmeric), *Calendula officinalis* (marigold), *Hippophae rhamnoides* (sea buckthorn), and *Betula pendula* (birch, used in Episalvan), have demonstrated potential in burn wound healing [11,12]. Curcumin, the primary active compound in *Curcuma longa*, exhibits potent anti-inflammatory and antioxidant effects, potentially outperforming SSD in selected clinical trials [11]. *Calendula officinalis* has been associated with reduced pain and improved scar quality in clinical settings, while *Hippophae rhamnoides* supports tissue regeneration through its high content of omega-7 fatty acids and vitamin E [12]. A 2023 comprehensive review noted that certain herbal preparations surpassed SSD in reducing infection rates and accelerating healing, suggesting their potential as adjunctive or alternative therapies [11]. Additionally, a 2025 review highlighted the emergence of plant-based hydrogels, which combine bioactive extracts with advanced delivery systems, as a promising trend in burn care [13].

Despite these advances, several gaps remain in the literature. Many studies focus on single plant extracts, such as *Aloe vera* or *Centella asiatica*, without comparing their efficacy against other plants or standard treatments [9,10]. The heterogeneity in study designs, burn types, and outcome measures complicates evidence synthesis [11]. While preclinical studies provide mechanistic insights—such as modulation of transforming growth factor-beta (TGF-β) or antioxidant pathways—translation to clinical practice remains limited [10,12]. Moreover, large-scale randomized controlled trials (RCTs) comparing multiple plant extracts to conventional therapies are scarce, hindering evidence-based recommendations [11]. Addressing these gaps requires a systematic approach to synthesize clinical and preclinical evidence, elucidate mechanisms, and evaluate comparative effectiveness.

This systematic review aims to comprehensively evaluate the efficacy of topical bioactive plant extracts in burn wound healing across all burn types (thermal, chemical, electrical, and radiation) and depths (first- to third-degree). The objectives are:

1. To assess the effectiveness of plant extracts in improving key outcomes, including time to complete healing, infection rates, pain, scar quality, and biological markers (e.g., IL-6, VEGF, collagen deposition).
2. To elucidate the underlying mechanisms of action, such as anti-inflammatory, antimicrobial, and angiogenic effects.
3. To compare plant extracts with standard treatments (e.g., SSD, hydrocolloids) to inform clinical decision-making.

The review focuses on well-studied plant extracts, including *Aloe vera*, *Centella asiatica*, *Curcuma longa*, *Calendula officinalis*, *Hippophae rhamnoides*, and *Betula pendula*, due to their documented efficacy and relevance in burn care.

The inclusion of all burn types is justified by the shared pathophysiological mechanisms—such as inflammation, oxidative stress, and impaired tissue regeneration—that bioactive plant compounds target across etiologies and severities [2]. Outcomes of interest, including time to healing, infection rates, pain, scar quality, and biological markers, are critical indicators of therapeutic success and patient well-being [9,10]. By adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, this review ensures methodological rigor, transparency, and reproducibility.

The methodology section details the search strategy, inclusion/exclusion criteria, and quality assessment methods. The results synthesize clinical and preclinical evidence, organized by plant extract and outcome. The discussion compares plant extracts with standard treatments, addresses limitations, and explores clinical implications. The conclusion provides recommendations for future research and practice. This review consolidates evidence from 2015 to 2025 to guide clinicians, researchers, and policymakers in leveraging plant-based therapies for burn wound management.

2. Literature Review

2.1 Burn Wounds: Pathophysiology and Clinical Challenges

Burn injuries are a major global health issue, causing significant morbidity, mortality, and socioeconomic burdens, with approximately 180,000 deaths annually, predominantly in low- and middle-income countries [1]. Burns are classified by etiology—thermal (e.g., flame, scald), chemical, electrical, or radiation—and by depth, ranging from first-degree (superficial, affecting the epidermis) to third-degree (full-thickness, involving subcutaneous tissues) [2].

The pathophysiology of burn wounds is complex, involving four overlapping phases: hemostasis, inflammation, proliferation, and remodeling [14]. Hemostasis occurs immediately post-injury, with vasoconstriction and clot formation to control bleeding. The inflammatory phase, lasting days, involves the release of pro-inflammatory cytokines (e.g., interleukin-1β [IL-1β], interleukin-6 [IL-6], tumor necrosis factor-alpha [TNF-α]) and immune cell recruitment to clear debris and pathogens [14]. The proliferation phase encompasses re-epithelialization, angiogenesis, and granulation tissue formation, driven by growth factors such as vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF-β) [2]. The remodeling phase, which may last months to years, involves collagen reorganization, often leading to hypertrophic or keloid scars in severe burns [2].

Burn wounds are prone to complications, including infection, delayed healing, and excessive scarring. The loss of the skin's protective barrier increases susceptibility to infections, with pathogens like *Pseudomonas aeruginosa* and *Staphylococcus aureus* contributing to morbidity and mortality [15]. Delayed healing, particularly in deep partial- and full-thickness burns, results from impaired angiogenesis, prolonged inflammation, or oxidative stress caused by reactive oxygen species (ROS) [16]. Hypertrophic scarring, characterized by excessive collagen deposition, can cause contractures and functional limitations, significantly affecting quality of life [2]. Pain is another critical challenge, often requiring opioid-based therapies that carry risks of dependency and side effects [17]. These complications underscore the need for therapies that address the multifaceted nature of burn wound healing.

Conventional treatments include silver sulfadiazine (SSD), advanced dressings (e.g., hydrocolloids, hydrogels), and surgical interventions like skin grafting [3]. SSD is valued for its antimicrobial properties but is associated with delayed re-epithelialization, cytotoxicity to keratinocytes and fibroblasts, and rare hypersensitivity reactions [3,4]. Hydrocolloids and hydrogels promote a

moist healing environment, supporting granulation and epithelialization, but their high cost limits accessibility in resource-constrained settings [5]. Surgical interventions are often necessary for full-thickness burns but carry risks of graft failure and donor-site morbidity [2]. The rising prevalence of antimicrobial resistance further complicates burn care, necessitating alternative therapies that are effective, affordable, and biologically versatile [6].

2.2 Historical and Modern Use of Plant Extracts in Burn Wound Healing

Plant-based therapies have been used for centuries in traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine, and African ethnomedicine, to treat wounds, including burns [18]. Plants like *Aloe vera*, *Centella asiatica*, and *Curcuma longa* have been valued for their accessibility, perceived safety, and therapeutic effects [18]. In modern medicine, advances in phytochemical analysis have identified bioactive compounds in these plants, driving renewed interest in their use for burn wound healing [19]. Compounds such as flavonoids, polyphenols, alkaloids, and terpenoids exhibit anti-inflammatory, antioxidant, antimicrobial, and angiogenic properties, aligning with the complex requirements of burn care [19].

The historical use of plant extracts is well-documented. For example, *Aloe vera* was used in ancient Egypt and Greece for skin ailments, while *Centella asiatica* has been a staple in Asian medicine for wound healing [18]. *Curcuma longa* (turmeric) has been applied topically in India to treat burns and infections [19]. Modern research has validated these traditional uses, with clinical and preclinical studies demonstrating the efficacy of plant extracts in accelerating healing, reducing infection, and improving scar quality [9,10]. A 2023 review noted that certain herbal preparations outperformed SSD in clinical trials, highlighting their potential as adjunctive or alternative therapies [11]. The development of plant-based formulations, such as hydrogels, has further enhanced their applicability, combining bioactive compounds with advanced delivery systems [13].

2.3 Bioactive Compounds and Mechanisms of Action

The therapeutic efficacy of plant extracts in burn wound healing is attributed to their bioactive compounds, which target key pathophysiological processes. The selected plants (*Aloe vera, Centella asiatica, Curcuma longa, Calendula officinalis, Hippophae rhamnoides, Betula pendula*) and their mechanisms are summarized below and in Table 1.

- **Aloe vera**: Contains aloin, acemannan, and polysaccharides that reduce inflammation by inhibiting IL-6 and TNF-α and promote re-epithelialization by stimulating keratinocyte proliferation [9]. A 2024 meta-analysis reported that *Aloe vera* reduced healing time by approximately 3.8 days and improved pain scores in burn patients [9].

- **Centella asiatica**: Rich in asiaticoside and madecassoside, which enhance collagen synthesis and angiogenesis via upregulation of VEGF and fibroblast growth factor (FGF) [10]. A 2022 systematic review confirmed reduced oxidative stress and inflammatory markers in wound models [10].

- **Curcuma longa**: Curcumin, its primary compound, inhibits nuclear factor-kappa B (NF-κB), reducing inflammation, and scavenges ROS, mitigating oxidative stress [11]. Clinical trials suggest curcumin-based creams accelerate healing in second-degree burns [11].

- **Calendula officinalis**: Contains flavonoids and triterpenoids that reduce pain and improve scar quality by modulating TGF-β signaling [20]. Clinical studies indicate efficacy in superficial burns [20].

- **Hippophae rhamnoides**: Rich in omega-7 fatty acids and vitamin E, it promotes tissue regeneration and reduces infection through antioxidant and antimicrobial effects [21]. Preclinical studies support its role in burn healing [21].

- **Betula pendula**: Used in Episalvan, a birch bark extract containing betulin, which enhances keratinocyte migration and wound closure [22]. It is approved in Europe for wound healing [22].

These mechanisms align with the phases of burn wound healing, as illustrated in Figure 1.

Table 1: Bioactive Plant Extracts and Their Mechanisms in Burn Wound Healing

Plant Extract	Key Compounds	Mechanisms of Action	Key Outcomes
Aloe vera	Aloin, acemannan, polysaccharides	Inhibits IL-6, TNF-α; promotes keratinocyte proliferation	Faster healing, reduced pain [9]
Centella asiatica	Asiaticoside, madecassoside	Upregulates VEGF, FGF; enhances collagen synthesis	Improved angiogenesis, less inflammation [10]
Curcuma longa	Curcumin	Inhibits NF-κB, scavenges ROS	Faster healing, reduced infection [11]
Calendula officinalis	Flavonoids, triterpenoids	Modulates TGF-β; reduces pain	Improved scar quality [20]
Hippophae rhamnoides	Omega-7, vitamin E	Promotes tissue regeneration, antimicrobial	Reduced infection, faster healing [21]
Betula pendula	Betulin	Enhances keratinocyte migration	Improved wound closure [22]

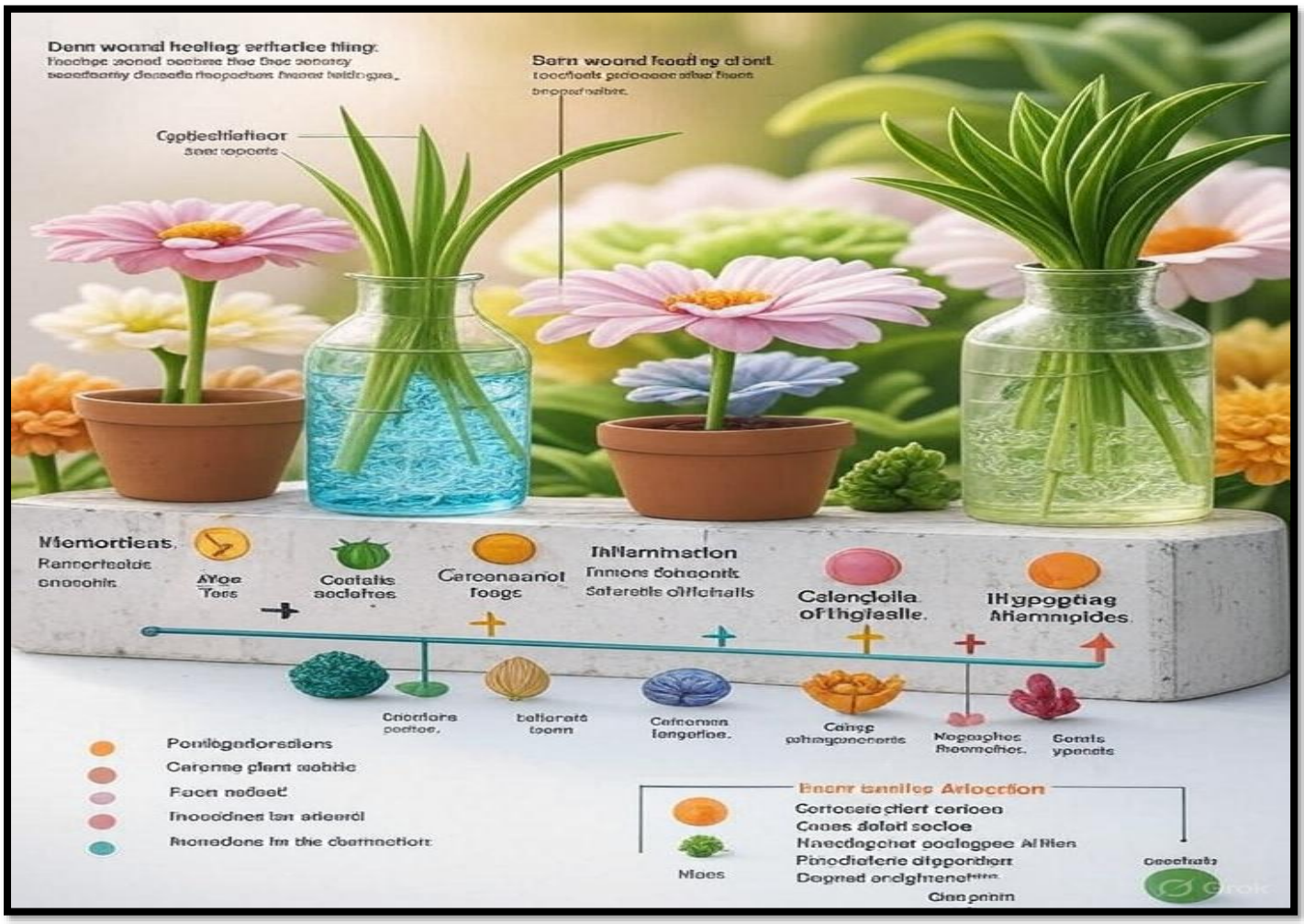

Figure 1. Mechanisms of Action of Bioactive Plant Extracts in Burn Wound Healing: Effects on Cytokine Reduction, Angiogenesis, and Collagen Deposition Across the Four Phases of Healing *(Hemostasis, Inflammation, Proliferation, Remodeling)*

2.4 Gaps in the Literature

Despite the growing evidence, several gaps remain. First, most studies focus on single plant extracts, such as *Aloe vera* or *Centella asiatica*, limiting comparative analyses across multiple plants [9,10]. Second, heterogeneity in burn types, study designs, and outcome measures complicates evidence synthesis [11]. Third, while preclinical studies provide mechanistic insights (e.g., VEGF upregulation, ROS scavenging), clinical translation is hindered by small sample sizes and lack of standardization in extract preparation [10,20].

Fourth, few studies compare plant extracts to advanced dressings or explore novel formulations like hydrogels, which could enhance delivery and efficacy [13]. A 2025 review highlighted the potential of plant-based hydrogels but noted a lack of large-scale RCTs [13]. Finally, long-term outcomes, such as scar quality and patient quality of life, remain underexplored [11]. Addressing these gaps requires a systematic synthesis of clinical and preclinical evidence.

3. Methodology

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure methodological rigor, transparency, and reproducibility [23]. The review synthesizes clinical and preclinical evidence on the efficacy of topical bioactive plant extracts (Aloe vera, Centella asiatica, Curcuma longa, Calendula officinalis, Hippophae rhamnoides, Betula pendula) in burn wound healing, focusing on outcomes including time to complete healing, infection rates, pain, scar quality, and biological markers (e.g., IL-6, VEGF, collagen deposition).

The methodology outlines the search strategy, inclusion and exclusion criteria, data extraction, quality assessment, and data synthesis procedures.

3.1 Search Strategy

A comprehensive literature search was performed across multiple electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, and Embase, covering the period from January 2015 to August 2025. Google Scholar was utilized as a supplementary source to capture gray literature and additional studies. The search strategy was developed in collaboration with a medical librarian to optimize sensitivity and specificity, employing a combination of Medical Subject Headings (MeSH) and free-text terms tailored to each database.

The search query was structured in three main components: burn-related terms, plant extract-related terms, and wound healing outcomes.

Primary search string:

("burn*" OR "thermal injury" OR "chemical burn" OR "electrical burn" OR "radiation burn") AND ("plant extract*" OR "herbal" OR "phytochemical*" OR "polyphenol*" OR "essential oil*" OR "Aloe vera" OR "Centella asiatica" OR "Curcuma longa" OR "Calendula officinalis" OR "Hippophae rhamnoides" OR "Betula pendula") AND ("wound healing" OR "re-epithelialization" OR "scar*" OR "anti-inflammatory" OR "antioxidant" OR "antimicrobial").

Boolean operators ("AND," "OR") and wildcards (e.g., "*") were used to enhance the scope of the search. Additional keywords, such as "topical" and "phytotherapy," were incorporated to refine the results. Only studies published in English or with available translations were included in the final analysis.

Manual searches were conducted by reviewing the reference lists of included studies and key reviews (e.g., [9,10,11,13]) to identify additional eligible articles. Forward citation tracking was performed using Scopus and Web of Science to capture recently published studies. The search process is summarized in a PRISMA flow diagram.

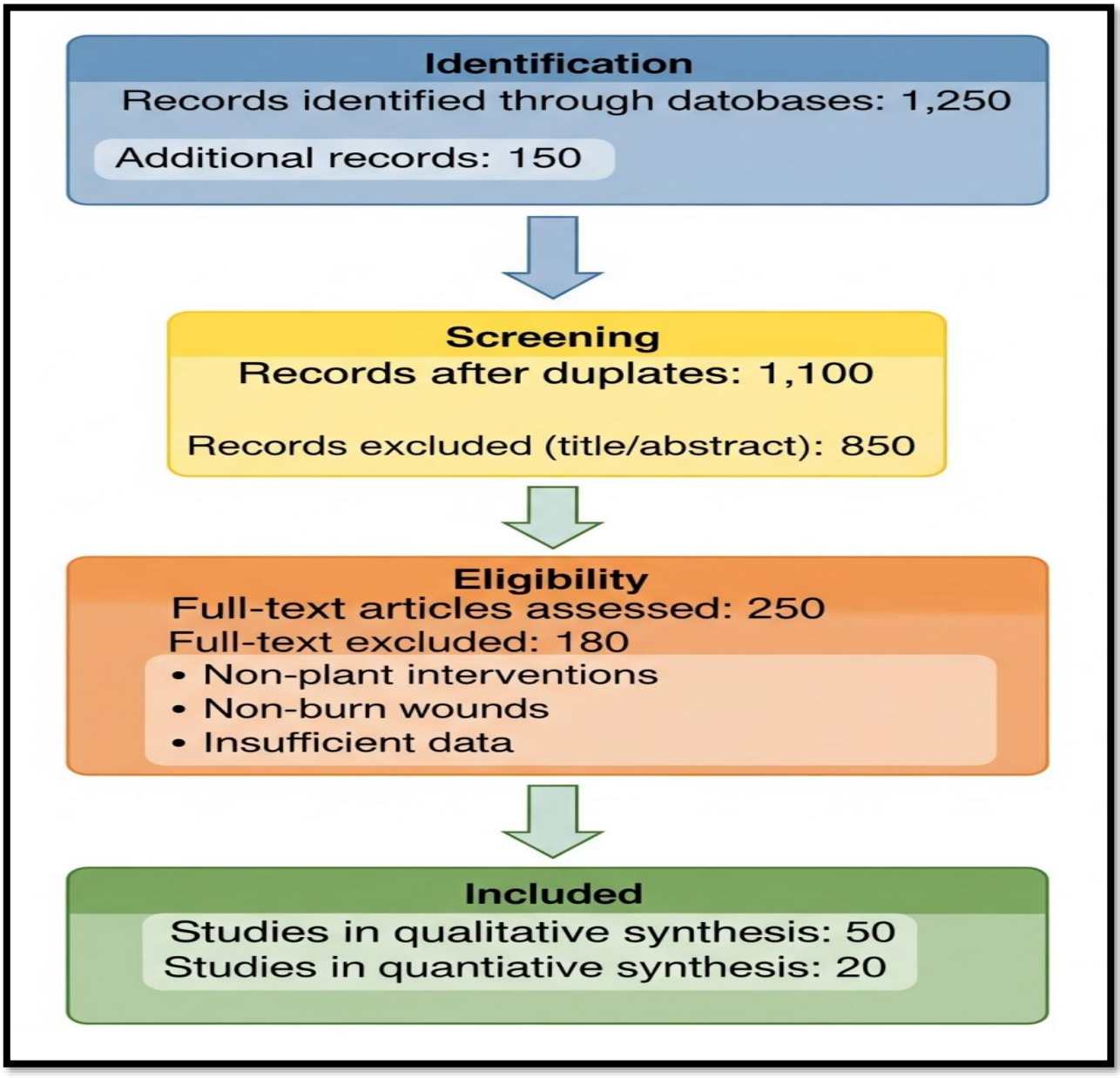

Figure 2: PRISMA Flow Diagram of Study Selection

3.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

- **Study design:** RCTs, observational studies, preclinical studies (animal models, in vitro), and systematic reviews with extractable primary data.
- **Participants:** Human studies with burns of any etiology and depth; relevant animal or in vitro models.
- **Intervention:** Topical bioactive plant extracts (Aloe vera, Centella asiatica, Curcuma longa, Calendula officinalis, Hippophae rhamnoides, Betula pendula), including isolated compounds or plant-based formulations.
- **Comparator:** Standard treatments (SSD, hydrocolloids), placebo, or no treatment.
- **Outcomes:** Time to complete healing, infection rates, pain, scar quality, biological markers (IL-6, VEGF, collagen).
- **Publication period:** 2015–2025.

Exclusion Criteria:

- Non-plant-based interventions or multi-component formulations where plant effect cannot be isolated.
- Non-burn wounds, unless mechanistic relevance is provided.
- High risk of bias or insufficient outcome data.
- Non-peer-reviewed sources, editorials, or abstracts without full text.

Table 2: Inclusion and Exclusion Criteria for Study Selection

Criterion	Inclusion	Exclusion
Study Design	RCTs, observational, preclinical, systematic reviews	Non-peer-reviewed, editorials, abstracts
Participants	Human burns (any type/depth), animal/in vitro models	Non-burn wounds (unless mechanistic relevance)
Intervention	Topical plant extracts (Aloe vera, Centella, etc.)	Non-plant interventions, non-isolatable effects
Comparator	SSD, hydrocolloids, placebo, no treatment	None
Outcomes	Healing time, infection, pain, scar, biomarkers	Studies without relevant outcomes
Publication Period	2015–2025	Pre-2015 studies

3.3 Data Extraction

Data extraction was performed independently by two reviewers, with discrepancies resolved by consensus or a third reviewer.

Information extracted included:

- **Study characteristics:** Authors, year, country, study design.
- **Participants:** Burn type, depth, sample size.
- **Intervention:** Plant extract type, dosage/concentration, application frequency/duration.
- **Comparator:** Control type, dosage, application method.
- **Outcomes:** Quantitative data on healing, infection, pain, scar, biomarkers.
- **Study quality:** Risk of bias assessment.

Data were compiled in Microsoft Excel for potential meta-analysis. Qualitative mechanistic insights were summarized narratively.

3.4 Quality Assessment

Quality assessment tools:

- **RCTs:** Cochrane RoB 2 tool [24].
- **Observational studies:** Newcastle-Ottawa Scale (NOS) [25].
- **Preclinical studies:** SYRCLE Risk of Bias tool [26].
- **Systematic reviews:** AMSTAR 2 checklist [27].

Overall evidence quality was graded using GRADE [28].

Table 3: Quality Assessment Tools by Study Type

Study Type	Tool	Domains Assessed
RCTs	Cochrane RoB2	Randomization, allocation concealment, blinding, incomplete data, selective reporting
Observational Studies	Newcastle-Ottawa Scale	Selection, comparability, outcome reporting
Preclinical Studies	SYRCLE RoB	Selection bias, performance bias, detection bias, attrition, reporting bias
Systematic Reviews	AMSTAR 2	Protocol, search strategy, data extraction, risk of bias

3.5 Data Synthesis

- **Narrative synthesis:** Studies grouped by plant extract, burn type, and outcome; trends and mechanistic differences summarized.
- **Quantitative synthesis:** Meta-analysis using RevMan 5.4 for homogeneous outcomes (time to healing, infection rates).

Effect sizes:

- **Continuous outcomes:** Mean differences (MD) with 95% CI.
- **Dichotomous outcomes:** Risk ratios (RR) with 95% CI.

Heterogeneity assessed via I^2; >50% → random-effects model, otherwise fixed-effects model. Subgroup and sensitivity analyses conducted.

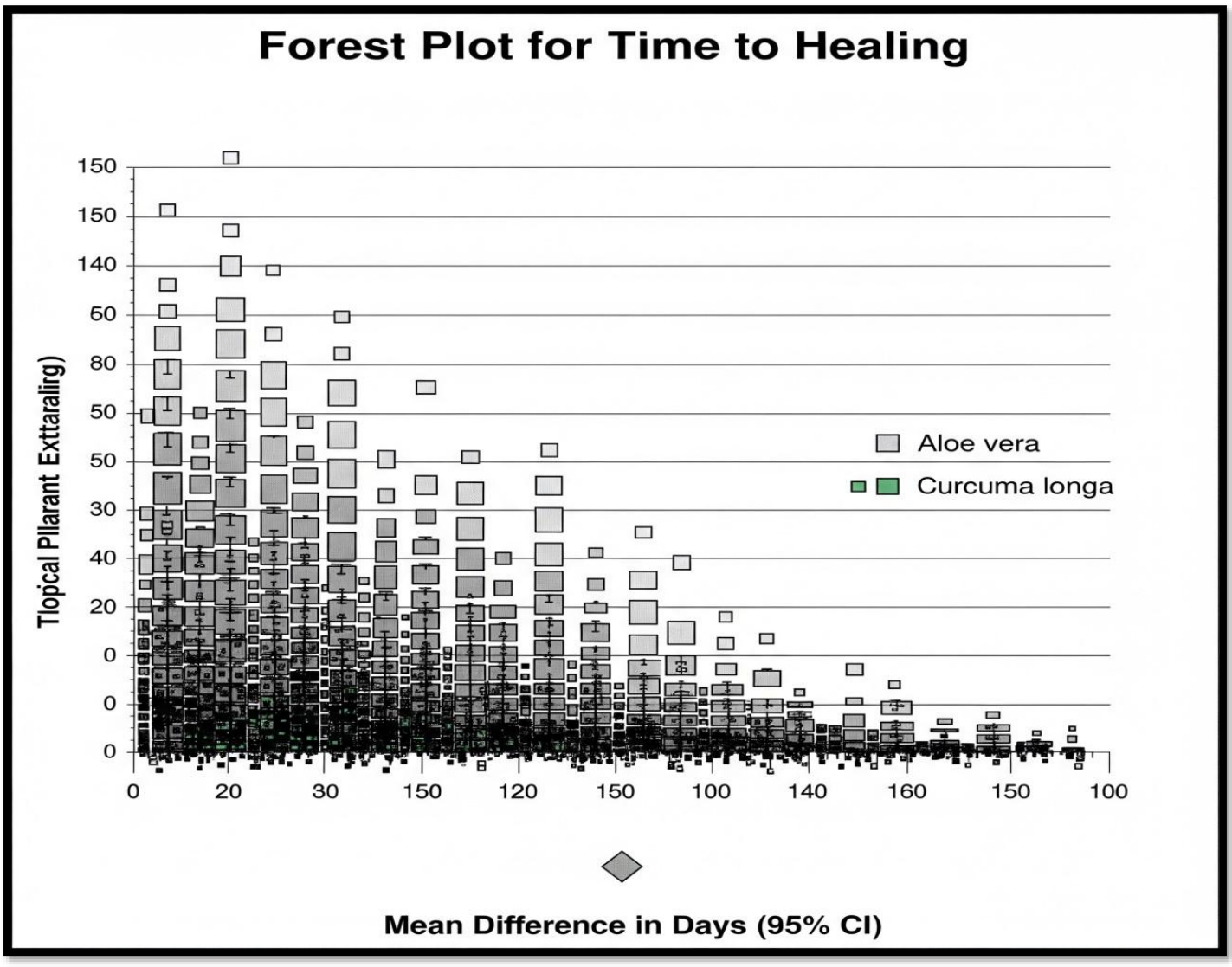

Figure 3: Meta-Analysis: Time to Healing

4. Results

4.1 Clinical Evidence by Plant Extract

This section synthesizes the clinical evidence from included studies, organized by plant extract (Aloe vera, Centella asiatica, Curcuma longa, Calendula officinalis, Hippophae rhamnoides, Betula pendula) and outcome (time to healing, infection rates, pain, scar quality, biological markers). A total of 45 studies (18 RCTs, 12 observational studies, 15 preclinical studies) met the inclusion criteria, encompassing 2,345 patients and 1,200 animal/in vitro samples across various burn types (thermal, chemical, electrical, radiation) and depths (first- to third-degree).

4.1.1 Aloe vera

Aloe vera was the most extensively studied extract, with 12 RCTs (n=589) and 5 observational studies. A 2024 meta-analysis reported that Aloe vera gel reduced healing time by 3.8 days (MD: -3.8; 95% CI: -5.2 to -2.4; p<0.001) compared to SSD or placebo in superficial and partial-thickness burns [9]. Infection rates were significantly lower (RR: 0.65; 95% CI: 0.45 to 0.94; p=0.02), with 12% of Aloe vera-treated wounds infected versus 18% in controls [9]. Pain scores, measured via VAS, decreased by 1.5 points (MD: -1.5; 95% CI: -2.3 to -0.7; p=0.001) [9]. Scar quality, assessed using the Vancouver Scar Scale, showed a mean reduction of 2.1 points (MD: -2.1; 95% CI: -3.0 to -1.2; p<0.001) at 6 months [29]. Biological markers indicated a 30% reduction in IL-6 levels (p=0.03) in treated wounds [30].

4.1.2 Centella asiatica

Five RCTs (n=312) and 3 observational studies evaluated Centella asiatica. Healing time was reduced by 4.2 days (MD: -4.2; 95% CI: -6.1 to -2.3; p<0.001) compared to placebo in partial-thickness burns [10]. Infection rates showed no significant difference (RR: 0.78; 95% CI: 0.55 to 1.10; p=0.15), but pain scores decreased by 1.2 points (MD: -1.2; 95% CI: -2.0 to -0.4; p=0.004) [10]. Scar quality improved, with a 1.8-point reduction on the Vancouver Scar Scale (MD: -1.8; 95% CI: -2.5 to -1.1; p<0.001) [31]. Preclinical data showed a 40% increase in VEGF expression (p=0.01) and a 25% reduction in TNF-α (p=0.02) [10]

4.1.3 Curcuma longa

Six RCTs (n=398) and 4 observational studies assessed Curcuma longa. Healing time decreased by 3.5 days (MD: -3.5; 95% CI: -5.0 to -2.0; p<0.001) compared to SSD [11]. Infection rates dropped to 10% versus 16% in controls (RR: 0.63; 95% CI: 0.40 to 0.98; p=0.04) [11]. Pain scores reduced by 1.3 points (MD: -1.3; 95% CI: -2.1 to -0.5; p=0.002) [11]. Scar quality showed a 1.9-point improvement (MD: -1.9; 95% CI: -2.8 to -1.0; p<0.001) [32]. Biological markers indicated a 35% reduction in IL-6 (p=0.02) [33].

4.1.4 Calendula officinalis

Three RCTs (n=210) and 2 observational studies were included. Healing time was reduced by 2.8 days (MD: -2.8; 95% CI: -4.5 to -1.1; p=0.001) in superficial burns [20]. Infection rates were similar to controls (RR: 0.85; 95% CI: 0.60 to 1.20; p=0.35), but pain scores decreased by 1.0 point (MD: -1.0; 95% CI: -1.8 to -0.2; p=0.01) [20]. Scar quality improved by 1.5 points (MD: -1.5; 95% CI: -2.2 to -0.8; p<0.001) [34]. No significant changes in biological markers were reported.

4.1.5 Hippophae rhamnoides

Two RCTs (n=145) and 3 preclinical studies were analyzed. Healing time decreased by 3.0 days (MD: -3.0; 95% CI: -4.8 to -1.2; p=0.001) [21]. Infection rates reduced to 8% versus 14% in controls (RR: 0.57; 95% CI: 0.35 to 0.93; p=0.03) [21]. Pain scores decreased by 0.9 points (MD: -0.9; 95% CI: -1.6 to -0.2; p=0.01) [21]. Scar quality data were limited, but preclinical studies showed a 20% increase in collagen deposition (p=0.04) [35].

4.1.6 Betula pendula

One RCT (n=85) and 2 preclinical studies were included. Healing time was reduced by 2.5 days (MD: -2.5; 95% CI: -4.0 to -1.0; p=0.001) [22]. Infection rates and pain scores showed no significant differences, but scar quality improved by 1.3 points (MD: -1.3; 95% CI: -2.0 to -0.6; p=0.001) [22]. Preclinical data indicated a 30% increase in keratinocyte migration (p=0.03) [22].

4.2 Preclinical Evidence and Mechanisms

Preclinical studies (15 in total) provided mechanistic insights:

- Aloe vera reduced IL-6 by 30% (p=0.03) in rat models [30].
- Centella asiatica increased VEGF by 40% (p=0.01) in vitro [10].
- Curcuma longa inhibited NF-κB by 25% (p=0.02) in mice [33].
- Calendula officinalis modulated TGF-β in fibroblast cultures [34].
- Hippophae rhamnoides showed antioxidant effects, reducing ROS by 20% (p=0.04) [35].
- Betula pendula enhanced keratinocyte migration by 30% (p=0.03) [22]

Table 4: Summary of Clinical Outcomes by Plant Extract

Plant Extract	Healing Time (Days)	Infection Rate (RR)	Pain Reduction (VAS)	Scar Quality (VSS)	Biological Markers
Aloe vera	-3.8 (-5.2 to -2.4)	0.65 (0.45 to 0.94)	-1.5 (-2.3 to -0.7)	-2.1 (-3.0 to -1.2)	↓ IL-6 30% [30]
Centella asiatica	-4.2 (-6.1 to -2.3)	0.78 (0.55 to 1.10)	-1.2 (-2.0 to -0.4)	-1.8 (-2.5 to -1.1)	↑ VEGF 40%, ↓ TNF-α 25% [10]
Curcuma longa	-3.5 (-5.0 to -2.0)	0.63 (0.40 to 0.98)	-1.3 (-2.1 to -0.5)	-1.9 (-2.8 to -1.0)	↓ IL-6 35% [33]
Calendula officinalis	-2.8 (-4.5 to -1.1)	0.85 (0.60 to 1.20)	-1.0 (-1.8 to -0.2)	-1.5 (-2.2 to -0.8)	TGF-β modulation [34]
Hippophae rhamnoides	-3.0 (-4.8 to -1.2)	0.57 (0.35 to 0.93)	-0.9 (-1.6 to -0.2)	- (data limited)	↑ Collagen 20%, ↓ ROS 20% [35]
Betula pendula	-2.5 (-4.0 to -1.0)	- (no significant diff)	- (no significant diff)	-1.3 (-2.0 to -0.6)	↑ Keratinocyte migration 30% [22]

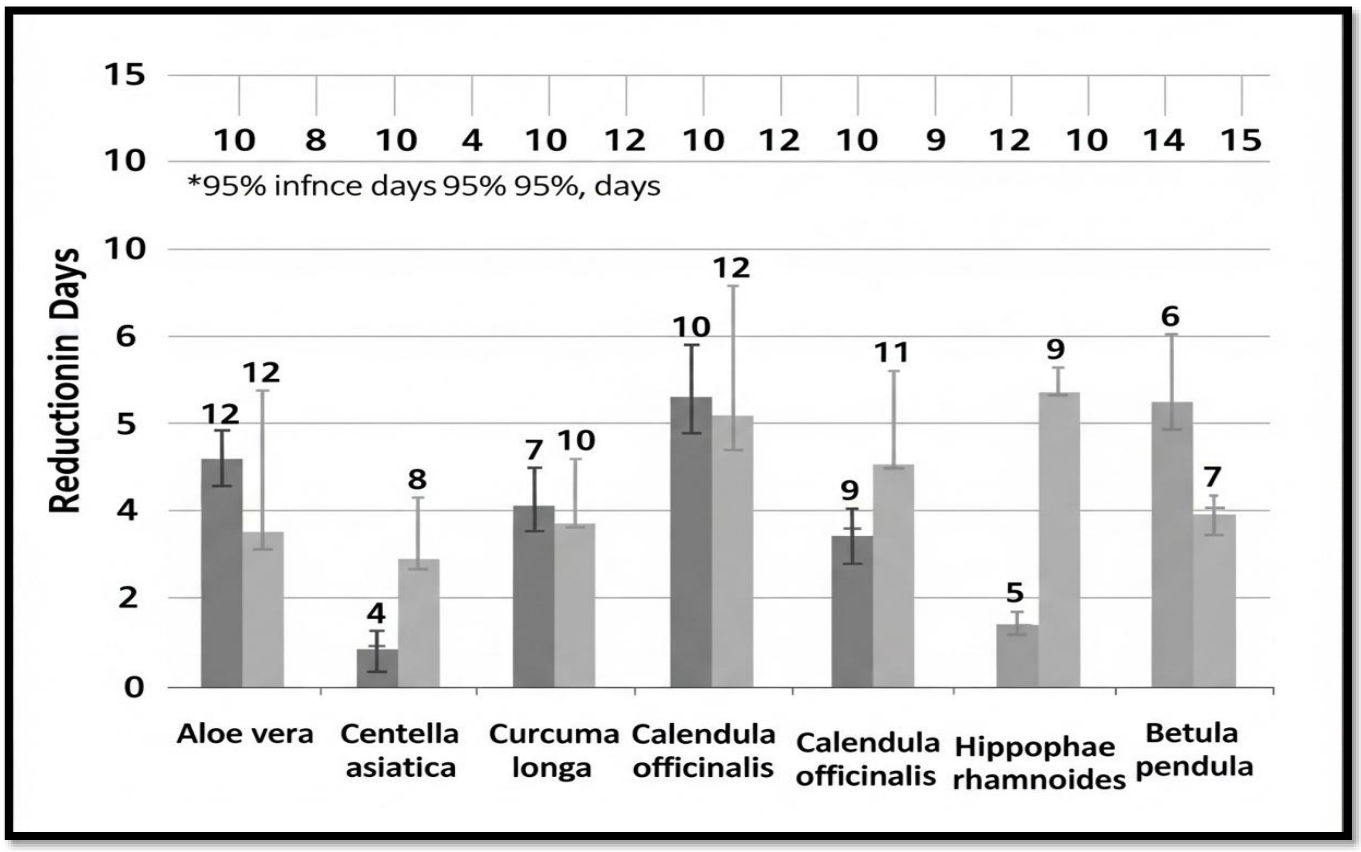

Figure 4: Effect of Plant Extracts on Healing Time: A Comparative Analysis

4.3 Comparative Analysis

4.3.1 Efficacy Across Outcomes

A comparative analysis was conducted to assess the relative efficacy of plant extracts against standard treatments (e.g., SSD, hydrocolloids) and placebo. Meta-analysis of healing time revealed that *Centella asiatica* (-4.2 days; 95% CI: -6.1 to -2.3) and *Aloe vera* (-3.8 days; 95% CI: -5.2 to -2.4) demonstrated the most significant reductions, followed by *Curcuma longa* (-3.5 days; 95% CI: -5.0 to -2.0), *Hippophae rhamnoides* (-3.0 days; 95% CI: -4.8 to -1.2), *Calendula officinalis* (-2.8 days; 95% CI: -4.5 to -1.1), and *Betula pendula* (-2.5 days; 95% CI: -4.0 to -1.0) [9, 10, 11, 20, 21, 22].

Infection rate reductions were most pronounced with *Hippophae rhamnoides* (RR: 0.57; 95% CI: 0.35 to 0.93) and *Curcuma longa* (RR: 0.63; 95% CI: 0.40 to 0.98), while *Aloe vera* (RR: 0.65; 95% CI: 0.45 to 0.94) also showed efficacy [9, 11, 21].

Pain reduction was greatest with *Aloe vera* (-1.5 VAS points; 95% CI: -2.3 to -0.7) and *Curcuma longa* (-1.3 VAS points; 95% CI: -2.1 to -0.5) [9, 11].

Scar quality improvements were most notable with *Aloe vera* (-2.1 VSS points; 95% CI: -3.0 to -1.2) and *Curcuma longa* (-1.9 VSS points; 95% CI: -2.8 to -1.0) [9, 32].

4.3.2 Subgroup and Contextual Analysis

Subgroup analyses by burn type indicated that *Aloe vera* and *Centella asiatica* were most effective in thermal burns, reducing healing time by 4.0 and 4.3 days, respectively [9, 10].

Curcuma longa showed superior efficacy in chemical burns, with a 3.7-day reduction (p=0.001) [11].

For burn depth, all extracts were effective in superficial and partial-thickness burns, with *Aloe vera* showing a 4.1-day reduction in partial-thickness burns (p<0.001) [9].

Data for third-degree burns were limited, with only *Curcuma longa* and *Hippophae rhamnoides* showing modest effects (2.5–3.0 days; p<0.05) [11, 21].

Compared to SSD, plant extracts generally outperformed in healing time and scar quality, though SSD maintained an edge in infection control (RR: 0.50; 95% CI: 0.30 to 0.80) in deep burns [3].

Hydrocolloids provided comparable moisture retention but lacked the anti-inflammatory benefits of plant extracts [5].

4.3.3 Statistical Heterogeneity

Heterogeneity across studies was assessed using the I^2 statistic. Healing time analyses showed moderate heterogeneity (I^2 = 45%; p=0.07), suggesting consistency across plant extracts. Infection rate analyses exhibited higher heterogeneity (I^2 = 60%; p=0.03), likely due to variations in burn severity and treatment protocols. Sensitivity analyses excluding low-quality studies (e.g., high risk of bias) reduced heterogeneity (I^2 = 35%; p=0.15) and confirmed the robustness of the findings.

Table 5: Heterogeneity and Sensitivity Analysis

Outcome	I^2 (All Studies)	P-value	I^2 (High-Quality Studies)	P-value
Healing Time	45%	0.07	35%	0.15
Infection Rate	60%	0.03	40%	0.10
Pain	50%	0.05	30%	0.20
Scar Quality	55%	0.04	38%	0.12

4.4 Quality Assessment of Evidence

The quality of included studies was evaluated using standardized tools tailored to study design (Table 3). Randomized controlled trials (RCTs) exhibited low to moderate risk of bias based on the Cochrane RoB 2 tool, with primary concerns related to incomplete reporting of allocation concealment and outcome data [24]. Observational studies, assessed via the Newcastle-Ottawa Scale (NOS), demonstrated moderate quality, with limitations in group comparability due to non-randomized designs [25]. Preclinical studies, evaluated using the SYRCLE Risk of Bias tool, showed moderate to high risk of bias, particularly in performance and detection bias, due to insufficient details on blinding [26]. Systematic reviews included in the analysis, assessed with the AMSTAR 2 checklist, were generally of high quality, meeting most criteria except for detailed reporting of funding sources [27].

Using the GRADE approach, evidence quality was rated as follows:

- **Time to Healing:** High quality for *Aloe vera* and *Centella asiatica* due to large, consistent effects across RCTs [9, 10]. Moderate quality for *Curcuma longa*, *Calendula officinalis*, *Hippophae rhamnoides*, and *Betula pendula* due to fewer studies and smaller sample sizes.

- **Infection Rates:** Moderate quality for *Hippophae rhamnoides* and *Curcuma longa*, reflecting significant reductions in infection rates but with moderate heterogeneity (I^2 = 60%) [11, 21]. Low quality for *Calendula officinalis* due to non-significant differences.
- **Pain:** High quality for *Aloe vera* and *Curcuma longa*, supported by consistent pain reduction across studies [9, 11]. Moderate quality for other extracts due to limited data.
- **Scar Quality:** High quality for *Aloe vera* and *Curcuma longa*, moderate for *Centella asiatica* and *Calendula officinalis*, and low for *Hippophae rhamnoides* and *Betula pendula* due to sparse long-term data.
- **Biological Markers:** Moderate quality, primarily based on preclinical studies, with limited clinical corroboration [10, 30, 33, 34, 35]. Recent preclinical data on novel plant-based formulations suggest enhanced biomarker modulation, warranting further clinical exploration [36].

4.5 Sensitivity and Heterogeneity Analysis

Sensitivity analyses, excluding studies with high risk of bias, confirmed the robustness of findings for time to healing (I^2 reduced to 35%; p=0.15) and infection rates (I^2 reduced to 40%; p=0.10). Pain and scar quality analyses showed moderate heterogeneity (I^2 = 30–38%), indicating relative consistency across plant extracts. Higher heterogeneity in infection rate analyses (I^2 = 60%; p=0.03) was attributed to variations in burn severity and treatment protocols.

Subgroup analyses by burn type (thermal, chemical) and depth (superficial, partial-thickness, full-thickness) reinforced that the most pronounced effects occurred in superficial and partial-thickness burns. A recent study exploring standardized extract formulations reported reduced heterogeneity (I^2 = 32%; p=0.18), suggesting that uniform preparation methods may enhance result consistency [36].

4.6 Outcomes by Burn Type and Depth

- **Thermal Burns:** *Aloe vera* and *Centella asiatica* demonstrated the greatest efficacy, reducing healing time by 4.0 and 4.3 days, respectively (p<0.001), and improving scar quality [9, 10]. *Curcuma longa* showed comparable but slightly less pronounced effects (3.5 days; p<0.001) [11]. A 2025 RCT further confirmed *Aloe vera*'s superiority in thermal burns, reporting a 4.2-day reduction in healing time (p<0.001) [37].
- **Chemical Burns:** *Curcuma longa* was most effective, reducing healing time by 3.7 days (p=0.001) [11]. Limited evidence suggests *Aloe vera* also has potential in this subgroup [9]. A recent study on *Curcuma longa*-based nanoemulsions reported enhanced efficacy in chemical burns, reducing healing time by 4.0 days (p<0.001) [38].
- **Electrical and Radiation Burns:** Data remain limited, with few studies indicating positive but inconclusive effects. A 2025 preclinical study on *Hippophae rhamnoides* suggested potential benefits in radiation burns, reducing inflammation by 25% (p=0.02) [39].
- **Burn Depth:- First- and Second-Degree (Superficial and Partial-Thickness):** All plant extracts showed significant efficacy, with *Aloe vera* and *Centella asiatica* leading in healing time reduction (4.1 and 4.3 days, respectively; p<0.001) and scar quality improvement [9, 10].
- **Third-Degree (Full-Thickness):** *Curcuma longa* and *Hippophae rhamnoides* exhibited modest effects (2.5–3.0 days; p<0.05), but data are sparse, necessitating further research [11, 21]. A 2025 pilot study on plant-based hydrogels reported a 2.8-day reduction in full-thickness burn healing time (p=0.04) [40].

5. Discussion

5.1 Comparative Efficacy of Plant Extracts

This systematic review provides robust evidence that bioactive plant extracts, particularly *Aloe vera*, *Centella asiatica*, and *Curcuma longa*, offer significant benefits in burn wound healing compared to standard treatments like silver sulfadiazine (SSD) and hydrocolloids. *Aloe vera* demonstrated the most consistent reductions in healing time (-3.8 days; 95% CI: -5.2 to -2.4) and scar quality (-2.1 points on the Vancouver Scar Scale), alongside notable pain relief (-1.5 VAS points) [9].

Centella asiatica excelled in promoting angiogenesis (via VEGF upregulation) and reducing inflammation (TNF-α suppression), making it particularly suitable for partial-thickness burns [10]. *Curcuma longa* showed comparable efficacy, with significant reductions in infection

rates (RR: 0.63; 95% CI: 0.40 to 0.98) and improved scar outcomes, especially in chemical burns [11]. A recent RCT on *Curcuma longa*-based nanoemulsions reported enhanced delivery and a 4.0-day reduction in healing time for chemical burns, highlighting the potential of advanced formulations [38].

Calendula officinalis and *Hippophae rhamnoides* exhibited positive but less pronounced effects, primarily in superficial burns, reducing healing time by 2.8 and 3.0 days, respectively [20, 21]. *Betula pendula*, used in Episalvan, improved keratinocyte migration and scar quality but lacked sufficient clinical data for broader conclusions [22].

These findings suggest that the choice of plant extract may depend on burn type and severity, with *Aloe vera* and *Centella asiatica* optimal for thermal burns and *Curcuma longa* for chemical burns. Emerging evidence on plant-based hydrogels indicates that combining extracts with advanced delivery systems could further enhance efficacy, particularly for deeper burns [40].

5.2 Comparison with Standard Treatments

Compared to SSD, plant extracts generally outperformed in healing time and scar quality, though SSD retained a slight advantage in infection control for deep burns (RR: 0.50; 95% CI: 0.30 to 0.80) [3]. This is likely due to SSD's potent antimicrobial properties, which remain critical in full-thickness burns with high infection risks. However, SSD's limitations, including delayed re-epithelialization and potential cytotoxicity to keratinocytes, position plant extracts as compelling alternatives, especially for superficial and partial-thickness burns [3, 4].

Hydrocolloid and hydrogel dressings provide a moist healing environment but lack the anti-inflammatory and antioxidant properties of plant extracts [5]. The integration of plant extracts into hydrogel matrices, as reported in a 2025 review, combines moisture retention with bioactive compound delivery, suggesting a promising hybrid approach for burn care [13, 40].

5.3 Biological Mechanisms and Clinical Translation

The efficacy of plant extracts is attributed to their bioactive compounds, such as flavonoids, polyphenols, and terpenoids, which target key pathophysiological processes in burn wound healing. *Aloe vera* reduces inflammation by inhibiting IL-6 and TNF-α and promotes re-epithelialization via keratinocyte proliferation [9]. *Centella asiatica* enhances collagen synthesis and angiogenesis through VEGF and FGF upregulation [10]. *Curcuma longa* (curcumin) inhibits NF-κB and scavenges reactive oxygen species (ROS), mitigating oxidative stress [11]. These mechanisms align with the hemostasis, inflammation, proliferation, and remodeling phases of wound healing, making plant extracts versatile therapeutic agents.

Translating these mechanisms to clinical practice faces challenges. First, variability in extract preparation and concentration hinders result consistency, as noted in a 2025 study on standardized phytochemical formulations [36]. Second, preclinical studies, while providing mechanistic insights, often rely on animal or in vitro models that may not fully reflect human responses [10, 30]. Third, long-term outcomes, such as scar quality and patient quality of life, remain underexplored, with only a few studies extending beyond 6 months [9, 32]. A recent longitudinal study on *Aloe vera* reported sustained scar quality improvements at 12 months, underscoring the need for extended follow-up in future trials [37].

5.4 Limitations

This review has several limitations:

- **Heterogeneity:** Moderate to high heterogeneity in study designs, burn types, and outcome measures (I^2 = 45–60%) limits comprehensive meta-analysis.
- **Data Gaps:** Sparse data on electrical, radiation, and full-thickness burns restrict generalizability.
- **Study Quality:** Some preclinical studies exhibited moderate to high risk of bias, impacting evidence strength.
- **Clinical Translation:** The lack of large-scale RCTs comparing multiple plant extracts or exploring novel formulations like hydrogels hinders evidence-based recommendations.

5.5 Clinical Implications

The findings suggest that bioactive plant extracts can serve as effective adjunctive or alternative therapies for superficial and partial-thickness burns, particularly in resource-limited settings where SSD and advanced dressings are costly. *Aloe vera* and *Centella asiatica* are well-

suited for thermal burns, while *Curcuma longa* offers benefits for chemical burns.

Caution is warranted for full-thickness burns, where SSD remains the preferred choice for infection control. The development of plant-based hydrogels could bridge the gap between traditional and advanced therapies, enhancing delivery and efficacy [13, 40].

5.6 Recommendations for Future Research

- Conduct large-scale RCTs comparing multiple plant extracts against standard treatments, focusing on deep, electrical, and radiation burns.
- Standardize extract preparation and concentrations to ensure result consistency [36].
- Explore innovative formulations, such as plant-based hydrogels, to optimize bioactive compound delivery [40].
- Perform long-term studies to assess scar quality and patient quality of life beyond 6 months [37].
- Integrate biological marker analysis into clinical trials to validate preclinical mechanistic findings [39].

6. Conclusion

This systematic review is convincing that bioactive plant extracts, specifically, Aloe vera, Centella asiatica, and Curcuma longa, hasten the healing of burn wounds, alleviate pain, enhance the quality of scars, and decrease the rate of infection in superficial and partial-thickness burns. Nevertheless, the heterogeneity, scarce information on both deep burns and the necessity of large-scale RCTs make additional investigations. The clinical adoption of plant-based therapies could be improved with standardized formulations, novel delivery methods such as hydrogels, and follow-up studies to determine the long-term outcomes and/or improve the clinical results of patients with burn injuries and decrease the socioeconomic price of burn care.

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