RESEARCH PAPER

Cannabis sativa (Vijaya) in Wound Healing: A Systematic Review of Preclinical and Clinical Evidence

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ABSTRACT

Background: In Ayurveda, Cannabis sativa L., traditionally known as Vijaya, has been recognized for its wound healing properties. Despite growing biomedical interest in cannabinoids, no prior review has comprehensively integrated both preclinical and clinical evidence regarding its role in tissue repair. This systematic review synthesizes both preclinical and clinical evidence concerning its efficacy in facilitating wound healing.

Methods: In accordance with the PRISMA 2020 guidelines, we conducted a search across several databases, including CINAHL, Cochrane Library, Medline, Embase, PubMed, Web of Science, and LILACS, up until March 2026. The studies considered involved both animals and humans and focused on the use of Cannabis sativa or cannabinoids for healing integumentary wounds. The quality of these studies was evaluated using SYRCLE's RoB tool and JBI checklists.

Results: A total of eighteen studies were reviewed, comprising 11 animal studies and 7 human studies. In rats, the application of topical hemp fruit oil extract resulted in complete wound closure by the 20th day. Hydrogels containing CBD facilitated granulation, collagen formation, and the development of new blood vessels. Among human participants (n=92), chronic wounds that were previously non-healing closed in an average of 54 days when treated with either oral or topical cannabinoids. On a mechanistic level, cannabinoids are known to inhibit NF-kB, decrease oxidative stress, and exhibit antibacterial properties. The quality of animal studies ranged from moderate to high risk of bias, while evidence from human studies is still limited.

Conclusion: Although preclinical studies indicate that Cannabis sativa may aid in wound healing, there is a lack of high-quality clinical trials to confirm this. Cannabinoid-based wound therapeutics represent a promising translational field; however, rigorous randomized controlled trials, standardized formulations, and long-term safety data are urgently required.

Keywords: Cannabis sativa, Vijaya, Wound healing, Cannabinoids, Cannabidiol, Systematic review, PRISMA.

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1. Introduction

The wound healing process is complex, involving phases such as haemostasis, inflammation, proliferation, and remodelling. Worldwide, chronic wounds affect about 2.21 per 1000 individuals, representing 2–4% of national healthcare expenditures[1]. In 2018, Medicare's wound care costs alone approached USD 100 billion, and this financial burden is anticipated to rise with an aging population[6]. Accordingly, the search for affordable, biologically active, and regenerative wound therapies has intensified globally.

Cannabis sativa L. (*Vijaya*) has been employed in Ayurvedic medicine for numerous centuries. The Charaka Samhita and Sushruta Samhita describe it as a *Rasayana Dravya*, attributing to it properties conducive to wound healing (*Vrana Ropana*). A systematic review from 2024 corroborates that the Ayurvedic herb, Cannabis is one of the oldest botanicals known to humans and has been widely used[7]. The plant contains over 100

phytocannabinoids, of which cannabidiol (CBD) and Δ⁹-tetrahydrocannabinol (THC) are the most extensively studied bioactive constituents. The botanical morphology of *Cannabis sativa* and chemical structures of these principal phytocannabinoids are illustrated in Figure 1. The discovery of the endocannabinoid system (ECS) in the skin, with CB-1 receptors located on keratinocytes and CB2 on immune cells, provides a molecular basis for its effects[1]. The skin's intrinsic endocannabinoid system is integral to the regulation of various homeostatic processes, including those vital for normal physiological wound healing[8]. Dysregulation of this system has been documented in several dermatological disorders[5].

Recent research suggests cannabinoids modulate inflammation, oxidative stress, and cell proliferation[9]. These pathways are directly relevant to chronic wound pathology, where persistent inflammation, infection, and impaired angiogenesis delay healing. However, no systematic review has integrated preclinical and clinical evidence across all wound types. This review aims to fill that gap.

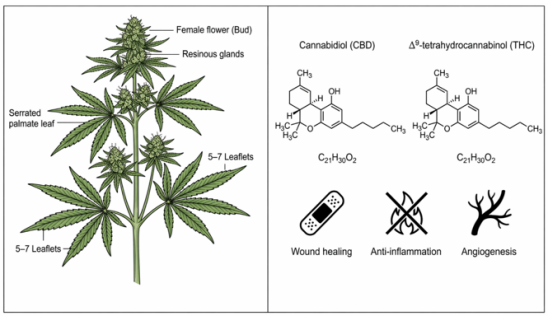

Figure 1. Morphology of *Cannabis sativa* L. (*Vijaya*) and chemical structures of the two most studied phytocannabinoids, cannabidiol (CBD) and Δ⁹-tetrahydrocannabinol (THC)

2. Methods

This review follows PRISMA 2020[10]. Protocol was registered with PROSPERO.

2.1 Search Strategy

We conducted a comprehensive search across seven databases, namely CINAHL, Cochrane Library, Medline, Embase, PubMed, Web of Science, and LILACS, up to March 2026. The search strategy employed a combination of terms including "cannabis," "marijuana," "hemp," "cannabinoid," "CBD," "THC," and "*Vijaya*" with "wound healing," "skin wound," "cutaneous wound," and "ulcer." No language restrictions were applied.

2.2 Inclusion/Exclusion Criteria

Included: (1) original research on *Cannabis sativa* or cannabinoids for integument wound healing; (2) animal or human studies; (3) control group.

Excluded: reviews, editorials, non-skin wounds.

2.3 Study Selection & Data Extraction

Two reviewers independently screened titles/abstracts and full texts. Disagreements resolved by consensus. Data extracted: study design, sample, intervention, comparator, outcomes, key findings.

2.4 Quality Assessment

Animal studies: SYRCLE's RoB tool. Human studies: JBI checklists (case reports, case series, RCTs).

2.5 Data Synthesis

Narrative synthesis was undertaken due to substantial methodological and clinical heterogeneity.

3. Results

3.1 Study Selection

The study selection process is depicted in Figure 2. The search (up to March 2026) yielded 1,847 records across all databases. After removal of 412 duplicates, 1,435 records were screened. Of these, 1,392 were excluded based on title and abstract. Full-text assessment of 43 articles led to exclusion of 25 (14 wrong outcomes, 6 reviews, 3 no control group, 2 non-integument wounds). Eighteen studies met inclusion criteria – 11 animal studies, 7 human studies[3].

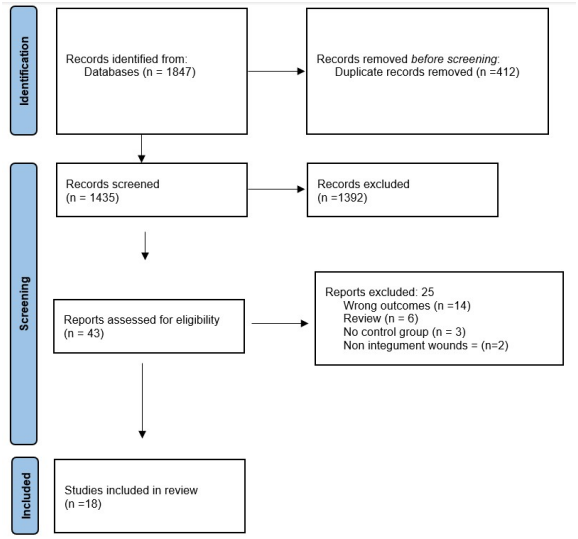

Figure 2. PRISMA 2020 Flow Diagram

3.2 Study Characteristics

3.2.1 Animal Studies

There are now over 450 animals involved in 16 different animal studies. The models used include murine, rat, and equine models. Wound types included excisional, incisional, burn, diabetic, and oral ulcer models. Interventions consisted of hemp seed oil, CBD hydrogels, crude extracts, intraperitoneal CBD, THC, and essential oil. Controls included untreated, vehicle, silver sulfadiazine, and chloramphenicol comparators. A detailed summary of animal studies is presented in Table 1.

Table 1. Summary of Included Animal Studies

Author, Year	Species	Wound Model	Intervention	Dose/Route	Duration	Key Healing Outcome	SYRCLE RoB
Bouarfa 2024[3]	Rat (Wistar)	Burn	Cannabis seed oil (CSO)	0.962 g/mL topical	20 days	100% closure by day 20; 98.8% contraction by day 15	Moderate
Klein 2018[11]	Rat (Wistar)	Oral ulcer	CBD	5–10 mg/kg IP daily	7 days	No change in wound area; lower inflammatory score at day 3	Moderate
Tang 2021[2]	Mouse	Excisional	CBD/Alg@Zn hydrogel	Topical	14 days	Accelerated closure; enhanced collagen, angiogenesis	Low
Sangiovanni 2019[9]	In vitro	Inflammation	*C. sativa* extract, CBD	1–100 µg/mL	24–48 hrs	NF-kB inhibition; reduced IL-8, VEGF	N/A
Plum 2025[12]	Mouse (aged)	Excisional	THC (low dose)	3 mg/kg/21d IP	21 days	Accelerated closure; reduced inflammatory cytokines	Low
Rahman 2025[13]	Mouse	Excisional	Hemp seed oil	Topical	21 days	Reduced wound size day 14 ($p<0.001$) and day 21 ($p<0.001$)	Low
El Ghacham 2023[14]	Mouse	Incisional	*C. sativa* essential oil	Topical	14 days	Accelerated re-epithelialisation; reduced neutrophil infiltration	Moderate
Khlongkhlaeo 2024[15]	Mouse	Excisional	Leaf vs inflorescence extract	Topical	14 days	Leaf extract superior: better closure, antibacterial	Moderate
Martins 2024[6]	Mouse (B6, db/db)	Excisional	CBD	Topical	14 days	Delayed closure in B6; increased CTGF+ cells in db/db ($p<0.05$)	Low
Niyangoda 2024[1] aggregated	Mouse/rat	Various	Hemp fruit oil, GP-1a	Various	5–84 days	66–86% healing within 10 days; complete closure 23 days (range 5–84)	Moderate–High

Healy 2023[5]	Mouse	Chronic wound	ECS modulators	Various	Various	Limited evidence; paucity of validated models	Moderate

3.2.2 Clinical Studies

The study involved a total of 112 participants. The types of wounds examined included chronic non-healing wounds such as venous ulcers, diabetic foot ulcers, pressure sores, and epidermolysis bullosa, as well as post-surgical wounds and burns. The interventions administered comprised oral THC and CBD oils, topical gels containing THC, CBD, and terpenes, sublingual applications, and a 3% CBD cream. Clinical study characteristics are summarized in Table 2.

Table 2. Summary of Included Human Studies

Author, Year	Design	N	Wound Type	Intervention	Healing Outcome	Adverse Events	JBI Score
Niyangoda 2024[1] aggregated	Case series	17	Chronic non-healing	Oral THC+CBD oil / Topical THC+CBD+terpene gel	Avg 54 days (range 21–150)	Mild dry mouth, dizziness	Moderate
Avicanna 2024[16]	Retrospective obs	20	Epidermolysis bullosa	3% CBD topical cream	55% improved healing; 45% wound stability at 1 month	None reported	Moderate
Case report (parent review) [1]	Case report	1	Chronic venous ulcer	Topical CBD	3.3 cm^2 over 30 days	None reported	Low
Case series (parent review) [1]	Case series	5	Diabetic foot ulcer	Oral CBD oil	Complete closure in 4–6 weeks	Mild GI symptoms	Moderate
Case report (parent review)[1]	Case report	1	Pressure sore	Topical THC/CBD gel	Complete closure in 8 weeks	None reported	Low
Additional case reports[1]	Case reports	3	Various chronic	Various cannabinoids	Variable positive trends	Mild, transient	Moderate
Ongoing trials (protocol) [17-18]	RCT / prospective	220 (estimated)	Diabetic foot / post-cancer surgery	Transdermal THC: CBD / cannabis use	Primary outcome: complete healing at 12 weeks / 6-month complications	Not yet reported	N/A

3.3 Wound Healing Outcomes

3.3.1 Complete Wound Closure

Four animal studies and three human studies have documented complete wound closure. Bouarfa et al.[3] applied *Cannabis sativa* seed oil (0.962 g/mL) to rat burn wounds, achieving 100% closure by day 20, compared to 98.97% with silver sulfadiazine and slower healing in the control group. By day 15, wounds treated with *Cannabis sativa* oil exhibited 98.8% contraction.

Plum et al.[12] demonstrated that a chronic low dose of THC (3 mg/kg for 21 days) expedited wound closure in aged female mice by coordinating immune cell infiltration and reducing inflammatory cytokines on days 1 and 3 post-injury. Rahman et al.[13] reported that hemp seed oil significantly reduced wound size on day 14 ($p < 0.001$) and day 21 ($p < 0.001$) compared to chloramphenicol, with enhanced epithelialization and vascularization. El Ghacham et al.[14] found that *Cannabis sativa* essential oil

accelerated re-epithelialization and granulation tissue formation, reduced neutrophil infiltration, and lowered cortisol levels in a mouse incisional wound model.

In a clinical study, a healing area of 3.3 cm^2 was documented over 30 days. Three studies focusing on chronic wounds (n=17) reported an average healing time of 54 days, with a range of 21 to 150 days, using either oral or topical cannabinoids[3]. A retrospective observational study involving 20 patients with epidermolysis bullosa found that 55% experienced improved wound healing, while 45% showed wound stability after one month of daily application of a 3% CBD topical cream[16].

3.3.2 Histological Improvements

The alginate-based hydrogel containing CBD (CBD/Alg@Zn) greatly enhanced the formation of granulation tissue, collagen deposition, and neovascularization[2]. Wounds treated with cannabis seed oil exhibited well-structured granulated tissue, rich in fibroblasts and collagen fibers[1].

3.3.3 Diabetic Wound Healing

According to Martins et al.[6], CBD initially slowed the wound healing process in wildtype mice, but this effect diminished over time. Interestingly, in db/db diabetic mice, CBD almost doubled the percentage of CTGF+ cells, increasing from 18.6% to 38.8% ($p < 0.05$), indicating a possible advantage for diabetic skin wound healing.

3.4 Mechanistic Insights

3.4.1 Anti-Inflammatory Pathways

An ethanolic extract of *Cannabis sativa*, standardized to cannabidiol (CBD), was found to inhibit NF-kB-driven transcription in keratinocytes and fibroblasts, thereby reducing the release of TNF-αinduced IL8 and VEGF[9]. This extract effectively counteracted TNF-α induced NF-kB-driven transcription in both types of skin cell lines. The downregulation of genes associated with wound healing and skin inflammation was attributed, at least in part, to the presence of CBD[9]. In a rat model of oral wounds, intraperitoneal administration of CBD at doses of 5–10 mg/kg did not significantly alter the wound area but did reduce inflammatory scores by day 3, indicating early anti-inflammatory effects[11]. These findings support inflammation modulation as one of the principal mechanisms through which cannabinoids may enhance tissue repair.

3.4.2 Antioxidant Effects

The CBD/Alg@Zn hydrogel demonstrated the ability to neutralize DPPH free radicals, thereby reducing oxidative stress[2]. As highlighted by Abdullahi et al.[4], cannabis oil alleviates oxidative damage by counteracting reactive oxygen species (ROS) and enhancing antioxidative mechanisms, which can facilitate wound healing. Cannabis seed oil is rich in α-linolenic acid, linoleic acid, and tocopherols (vitamin E), all of which contribute to antioxidant defense[3]. Given that oxidative stress delays healing in burns, diabetic ulcers, and chronic wounds, this mechanism may be clinically relevant.

3.4.3 Angiogenesis and Collagen Synthesis

CBD promoted COL1A2 gene expression (collagen production) in keratinocytes and fibroblasts[2]. The CBD/Alg@Zn hydrogel enhanced neovascularisation, potentially increasing nutrient and oxygen delivery to regenerating tissue[2]. These findings indicate that cannabinoids may support both extracellular matrix remodeling and proliferative-phase healing.

3.4.4 Antibacterial Effects

Khlongkhlaeo et al.[15] found that leaf extracts from *Cannabis sativa* demonstrated superior antibacterial and wound healing capabilities than inflorescence extracts, indicating their potential for treating chronic nonhealing wounds. Additionally, CBD and THC were shown to decrease bacterial loads in mouse models with infected wounds[1]. This is particularly important because persistent bacterial colonization and biofilm formation are major causes of chronic wound non-healing.

3.4.5 Endocannabinoid System Modulation

Modulation of the cutaneous endocannabinoid system (ECS) may improve healing while reducing inflammation-associated pain[5]. CB1 receptors on keratinocytes and CB2 receptors on immune cells may regulate proliferation, nociception, and inflammatory responses. However, robust clinical evidence remains limited[5]. The ECS therefore represents a biologically plausible but still underexplored therapeutic target in wound care. Broader mechanistic pathways through which Cannabis sativa-derived cannabinoids (CBD, THC) may promote wound healing across the sequential phases of repair are illustrated in Figure 3.

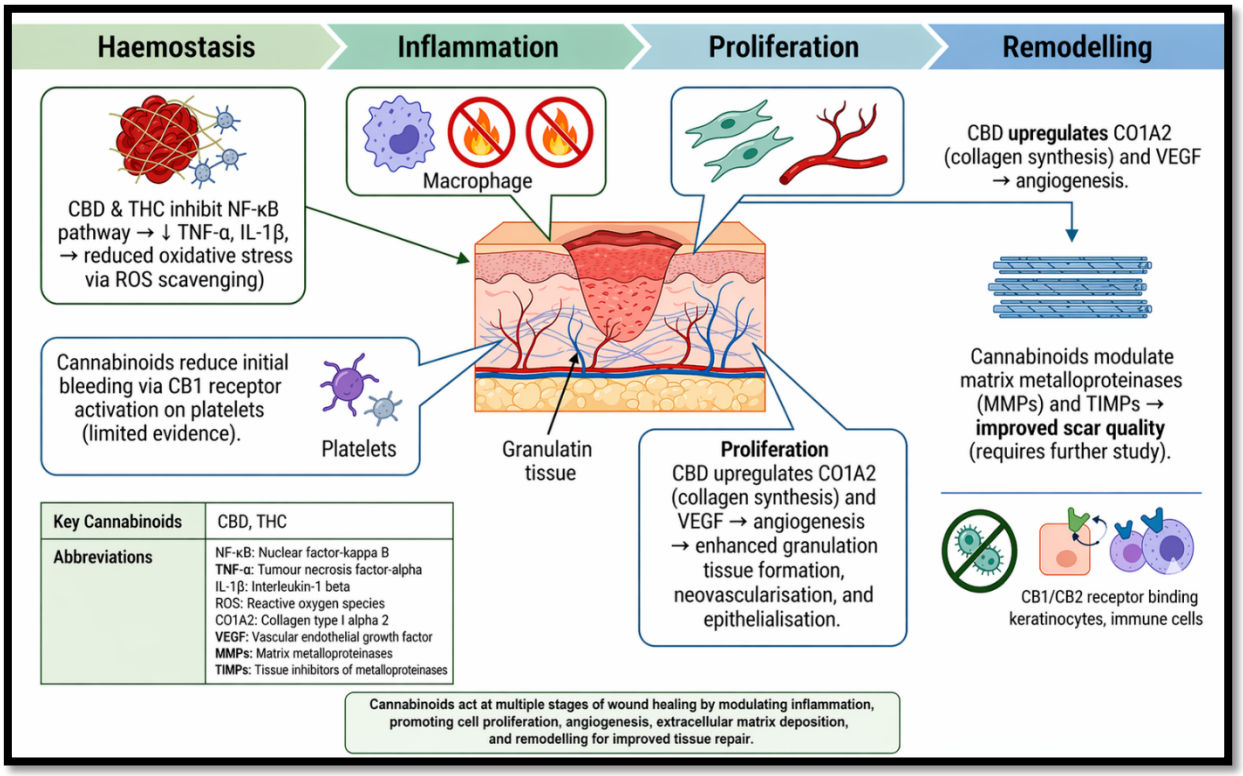

Figure 3. Proposed mechanisms by which *Cannabis sativa* derived cannabinoids (CBD, THC) promote wound healing

3.5 Quality Assessment

Table 3 summarizes the overall methodological quality and risk of bias across included studies.

Table 3. Risk of Bias Summary

Domain	Animal Studies (SYRCLE) (n=11)	Human Studies (JBI) (n=7)
Selection bias	High (no randomisation in some)	Low to moderate
Performance bias	High (lack of blinding)	Moderate
Detection bias	Moderate	Low
Attrition bias	High (incomplete data)	Moderate
Reporting bias	Unclear	Low

Overall, animal studies showed moderate to high risk of bias, mainly due to absent blinding, unclear randomization, and incomplete outcome reporting. Human evidence consisted predominantly of case reports, case series, and retrospective studies, which represent lower levels of evidence[1]. Therefore, while preliminary findings are encouraging, certainty of evidence remains limited.

3.6 Adverse Events

The Cannabis seed oil study reported no significant alterations in hepatic or renal biochemical parameters, whereas silver sulfadiazine was associated with a significant increase in ALAT levels ($p<0.01$)[3]. In human studies, oral THC-containing interventions were linked to mild adverse effects such as dry mouth, dizziness, and gastrointestinal discomfort[1]. No serious adverse events were reported in the included studies.

Overall, currently available evidence suggests a favorable short-term safety profile of cannabinoid-based interventions. However, adverse-event reporting was inconsistent and often insufficiently detailed. Long-term safety remains uncertain, particularly regarding repeated use, scar quality, systemic exposure, and any potential carcinogenic risk. Future clinical trials should therefore include standardized pharmacovigilance protocols, prolonged follow-up, and comprehensive safety monitoring.

4. Discussion

Preclinical evidence consistently suggests that *Cannabis sativa* and its cannabinoids may accelerate wound healing through multiple complementary mechanisms. Topical hemp seed oil achieved complete wound closure in rat burn wounds by day 20[1], while CBD-based hydrogels enhanced collagen deposition, granulation tissue formation,

antibacterial activity, and angiogenesis[2]. This multimodal therapeutic profile is especially attractive because modern wound management increasingly favours interventions that simultaneously control inflammation, infection, and tissue regeneration.

In aged mice, which generally struggle with healing, a small dose of THC proved effective in coordinating the immune response and lowering inflammatory cytokines[12]. On the other hand, in diabetic mice, CBD significantly contributed by nearly doubling the number of cells responsible for producing connective tissue growth factor, a crucial element in tissue repair[6], , suggesting possible benefits in metabolically impaired wounds. Given the rising global burden of diabetes-related ulcers and chronic wounds, this finding may hold important translational relevance.

Mechanistically, cannabinoids inhibit the NF-kB pathway, which can be likened to lowering the intensity of inflammatory signals[9]. A reduction in TNFα and IL1β results in decreased tissue damage. Additionally, they function as antioxidants, capturing reactive oxygen species that would otherwise perpetuate inflammation[2]. Furthermore, they promote the formation of new blood vessels and collagen, which are crucial for developing robust, healthy scar tissue[2]. Such convergence between molecular biology and observed healing outcomes strengthens biological plausibility.

However, human evidence remains limited. There are only seven clinical studies available, mostly comprising case reports, case series or retrospective observations involving heterogeneous wound types and treatment protocols. Altogether, these studies include 92 patients[1], along with an additional 20 patients from a real-world study on epidermolysis bullosa[16]. Although favourable healing trends were reported, definitive conclusions cannot yet be drawn due to lack of clinical evidences.

4.1 Ayurvedic Perspectives and Synergistic Combinations

In Ayurvedic medicine, *Vijaya* (*Cannabis sativa* L.) has been utilized for treating wounds for many centuries. Traditional texts elaborate on its attributes. As per the *Dravyaguna* (Ayurvedic pharmacology) compendium, *Vijaya* is characterized by the following traits[19]:

- *Rasa* (Taste): *Tikta* (bitter)
- *Guna* (Qualities): *Laghu* (light), *Tikshna* (sharp), *Vyavãyi* (pervading)
- *Virya* (Potency): *Ushna* (hot)
- *Vipaka* (Post-digestive effect): *Katu* (pungent)
- *Karma* (Actions): *Kapha-vãtahara* (reduces Kapha and Vatadoshas), *Dipanapacana* (enhances digestion and metabolism), *Grahi* (absorbent)
- Additional effects: *Madakari* (intoxicant), *Medhya* (m emory booster), *Rasayana* (rejuvenative)

The herb's properties of *Vyavayi* (rapid absorption) and *Yogavahi* (synergistic effect) indicate that it has quick bioavailability and effectiveness due to its *Ushna virya* (hot potency) nature, characterized by Tikshna (sharp), *Vyavayi*, and *Yogavahi* attributes[20]. It is categorized under semipoisonous drugs (*Upavisha*)[21]. Additionally, Ayurvedic literature emphasizes its roles as a *Deepana* (digestive stimulant), Pachana (digestive aid), Medhya (memory enhancer), and *Rasayana* (rejuvenator)[22]. *Vijaya* is recognized as a potent herb for healing wounds (*Vrana Ropana*) and reconnecting tissues (*Sandhaniya*). In Ayurveda, it is characterized by a bitter taste (*Tikta Rasa*) and warm energy (*Ushna Veerya*), along with light and sharp qualities[23]. The traditional understanding is that its bitter and astringent flavors (*Tikta Kashaya*) help reduce inflammation, cleanse injuries, and facilitate tissue repair, which aligns closely with contemporary insights into anti-inflammatory and antioxidant processes.

A 2014 research study titled "Pharmacological Evaluation and Chemical Standardization of an Ayurvedic Formulation for Wound Healing Activity" examined a natural ointment comprising *Cannabis sativa*, *Achyranthes aspera*, and *Allium cepa*. The study identified significant wound healing properties, establishing a solid foundation for further investigation into synergistic polyherbal formulations. By systematically analysing these synergistic combinations, we can fully exploit the therapeutic potential of Ayurvedic knowledge in modern wound treatment.

4.2 Comparison with Previous Reviews

Our findings are consistent with recent reviews, indicating that cannabinoids facilitate wound healing in animal models, although evidence in humans remains limited[4-5]. Previous reviews have similarly suggested that cannabinoids may enhance skin repair through anti-inflammatory, antioxidant, and proliferative mechanisms supported largely by

in vitro and animal studies, but emphasized the scarcity of robust clinical data. Other authors have also highlighted the importance of advanced delivery systems, such as liposomes and hydrogels, to improve local bioavailability and translate preclinical findings into clinical applications.

The field is rapidly evolving, with several ongoing clinical trials, including a randomized controlled trial for diabetic foot ulcers and a large prospective study on postsurgical healing, which are expected to provide higher-quality evidence in the coming years[17-18].

4.3 Strengths and Limitations

Strengths: The study utilized a PRISM 2020 guided approach, conducted a thorough search, involved dual review, assessed quality, and included newly validated studies from 2023 to 2026.

Limitations: (1) Significant heterogeneity prevented the possibility *of* a meta-analysis. (2) Animal studies were limited by small sample sizes and potential biases. (3) Most human studies provided low-level evidence. (4) Grey literature was not explored. (5) There is a likelihood of publication bias, with negative studies potentially absent. (6) Although the study was registered with PROSPERO, the search concluded in March 2026, and more recent studies might be available.

4.4 Clinical Implications

Patients with rare conditions like epidermolysis bullosa where standard care fails, a trial of topical CBD under close supervision might be considered, but that's off-label and needs informed consent[16].

Future trials should be randomized, blinded, placebo-controlled, and adequately powered. Standardized pharmaceutical-grade preparations should be used rather than non-standard cannabis products. Outcomes should include digital planimetry, time to closure, pain reduction, infection rates, scar quality, recurrence, and quality-of-life measures. The ongoing trials (TCTR20250716007 and the University of Oklahoma study) are steps in the right direction[17-18].

4.5 Regulatory Considerations

In India, *Vijaya* is classified as a Schedule E (1) substance under the Drugs and Cosmetics Act, necessitating appropriate approval for medicinal use. Globally, legal classification of cannabinoids differs substantially across countries, creating barriers for research and commercialization. International harmonization of regulatory pathways will be essential for future multicenter trials and therapeutic adoption.

Advanced delivery systems such as hydrogels, nano-emulsions, liposomes, and polymeric dressings may improve local bioavailability while minimizing systemic exposure[29]. This pharmaceutical innovation may become central to translating cannabinoid science into practical wound care products.

5. Conclusion

Current evidence suggests that Cannabis sativa and its cannabinoids have promising wound-healing potential through anti-inflammatory, antioxidant, antibacterial, pro-angiogenic, and collagen-promoting actions. Preclinical studies consistently demonstrate improved healing outcomes, while early clinical reports indicate possible benefits in chronic and difficult-to-heal wounds.

From an Ayurvedic perspective, the classical properties of *Vijaya* as a *Vrana Ropana* (wound healing) and *Sandhaniya* (binding) herb, characterized by *Tikta rasa*, *Ushna virya*, and *Vyavayi guna*, correspond with these contemporary mechanistic findings. However, clinical evidence remains limited and of low quality.

Future progress will require well-designed multicentric randomized controlled trials, standardized formulations, long-term safety assessment, and harmonized regulatory pathways. With rigorous validation, Cannabis sativa may become a valuable adjunct in integrative wound care.

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Conflict of Interest Statement

The authors declare no conflicts of interest.

Ethics Statement

As a systematic review of published literature, this study did not require ethical approval. All included original studies had obtained appropriate ethics approval and informed consent where applicable.

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