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Medicinal Plants As Promising Agents In Wound Healing: Phytochemical Mechanisms, Evidence, And Challenges

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Abstract

Wound healing remains challenging due to chronic delays, high costs, and antibiotic resistance in conventional therapies. Medicinal plants offer potent, natural alternatives rich in phytochemicals (flavonoids, tannins, alkaloids, terpenoids, saponins) that drive antimicrobial, antioxidant, anti-inflammatory, collagen synthesis, and angiogenic actions. Proven species like Aloe vera, Curcuma longa (curcumin), Centella asiatica, and Calendula officinalis accelerate tissue regeneration and reduce scarring. Supported by robust in vitro, in vivo, and growing clinical evidence, advanced formulations (gels, nanoparticles, films) and synergistic polyherbal blends enhance efficacy. Overcoming standardization, toxicity, and regulatory hurdles will unlock sustainable, cost-effective wound care solutions globally.

Key words: Medicinal plants, Wound healing, Phytochemicals, Formulations, Clinical evidence

Introduction

Wound healing is a complex and essential process in clinical practice, as it restores the integrity of the skin barrier, prevents infections, and maintains overall physiological homeostasis.[1] Proper wound management is critical for reducing morbidity, especially in chronic conditions like diabetes, where impaired healing can lead to severe complications such as amputations.[2] Nutrition plays a key role in optimizing wound healing outcomes, with deficiencies potentially delaying recovery and increasing healthcare burdens.[3] Effective wound care also minimizes scarring and improves quality of life for patients across various medical specialties.

Limitations of conventional therapies: Conventional wound healing therapies, such as dressings, antibiotics, and debridement, often face challenges including delayed healing in chronic wounds, high treatment costs, risks of antibiotic resistance, and failure to address underlying issues like poor vascularization

or persistent inflammation.[4][5] These approaches may lead to incomplete recovery, recurrence, and limited efficacy in accelerating tissue regeneration, highlighting the need for advanced alternatives.[6]

Rationale for exploring medicinal plants: Medicinal plants offer a promising alternative for wound healing due to their natural bioactive compounds, which exhibit anti-inflammatory, antimicrobial, antioxidant, and regenerative properties with generally fewer side effects compared to synthetic drugs.[7][8] Traditional and evidence-based use of herbs has demonstrated efficacy in promoting faster wound closure, reducing infection risks, and supporting tissue repair through multiple mechanisms.[9][10] Exploring these plants is particularly rational in resource-limited settings, where they provide cost-effective, accessible options to overcome the shortcomings of conventional methods.

Physiology of Wound Healing

The wound healing process is a complex, dynamic, and highly orchestrated physiological response to tissue injury, aimed at restoring skin integrity and function.[11][12] It involves overlapping phases: hemostasis, inflammation, proliferation, and remodeling.[13][14] These phases are mediated by intricate interactions among various cell types, growth factors, cytokines, chemokines, and the extracellular matrix (ECM).[15][16]

Stages of Wound Healing

Hemostasis (Immediate, minutes to hours)

This initial phase stops bleeding and forms a provisional matrix.[11][14] Vasoconstriction occurs, followed by platelet aggregation and activation, leading to the formation of a fibrin clot. Platelets degranulate, releasing growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), which initiate recruitment of inflammatory cells.[19]

Inflammation (Days 1–4, peaking at 2–3 days): The clot provides a scaffold for immune cell infiltration.[12][13] Neutrophils arrive first to clear debris and bacteria via phagocytosis and reactive oxygen species (ROS) production. Macrophages follow, shifting from pro-inflammatory (M1) to anti-inflammatory (M2) phenotypes, clearing apoptotic neutrophils, and releasing cytokines to transition to the proliferative phase.[20] This phase prevents infection but prolonged inflammation can delay healing.[15]

Proliferation (Days 4–21)

Granulation tissue forms, characterized by fibroblast proliferation, angiogenesis, and re-epithelialization.[16][17] Fibroblasts produce ECM components (e.g., collagen type III). Endothelial cells form new blood vessels via angiogenesis (driven by VEGF).[18] Keratinocytes migrate and proliferate to re-epithelialize the wound surface. Myofibroblasts contribute to wound contraction.[15]

Remodeling (Maturation; Weeks to years, starting around day 21)

The scar matures as collagen type III is replaced by stronger type I collagen, organized along tension lines.[11][16] Matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) balance ECM degradation and deposition. Cellularity decreases via apoptosis, vessels regress, and tensile strength increases (up to ~80% of normal skin).[14]

Principal cellular and Molecular participants

Cellular participants

Platelets: Initiate hemostasis and release growth factors.[11][14]

Neutrophils: Early debris clearance and antimicrobial defense.[12]

Macrophages: Central orchestrators; polarize to regulate inflammation-to-proliferation transition and promote angiogenesis/ECM synthesis.[13][15]

Fibroblasts/Myofibroblasts: ECM production, contraction, and remodeling.[16]

Keratinocytes: Re-epithelialization and barrier restoration.[17]

Endothelial cells: Angiogenesis and neovascularization.[18]

Other: Lymphocytes (e.g., regulatory T cells for resolution), pericytes (vessel stabilization).

Molecular participants

Growth Factors: PDGF (fibroblast recruitment), TGF-β (fibrosis and contraction), VEGF (angiogenesis), EGF/FGF (keratinocyte proliferation).[19]

Cytokines/Chemokines: IL-1, TNF-α (pro-inflammatory), IL-10 (anti-inflammatory).[13]

ECM Components: Fibrin (provisional), collagen (types III → I), fibronectin.[16]

Enzymes: MMPs (remodeling), ROS (signaling and defense).[11]

Dysregulation (e.g., persistent inflammation or excessive TGF-β) can lead to chronic wounds or hypertrophic scarring.[20]

Medicinal Plants in Wound Healing

Medicinal plants have been widely utilized for wound healing due to their rich content of bioactive phytochemicals, which accelerate the repair process through multiple mechanisms.[21][22] These natural compounds offer advantages such as lower side effects and accessibility compared to synthetic alternatives.[23][24]

Involved Phytochemicals

The primary phytochemical classes contributing to wound healing include:

- **Flavonoids** (e.g., quercetin, rutin, kaempferol): Potent antioxidants and anti-inflammatory agents commonly found in many plants.[25][26]
- **Tannins**: Polyphenolic compounds with astringent properties that promote tissue contraction and reduce exudation.[22][27]
- **Alkaloids** (e.g., berberine): Nitrogen-containing compounds exhibiting antimicrobial and analgesic effects.[21][28]
- **Terpenoids** (e.g., triterpenoids like asiaticoside, 1,8-cineole): Diverse group promoting cell proliferation and matrix remodeling.[24][29]
- **Saponins** (e.g., asiaticoside, madecassoside): Glycosides that enhance granulation and epithelialization.[23][30]

These compounds often act synergistically, with many plants containing multiple classes (e.g., flavonoids alongside tannins and terpenoids).[21][22]

Mechanisms of Action

Phytochemicals from medicinal plants facilitate wound healing via several key mechanisms:

- **Antimicrobial**: Disrupt bacterial cell walls, inhibit biofilm formation, and prevent infections (prominent in alkaloids, tannins, and some terpenoids).[21][27][28]
- **Antioxidant**: Scavenge reactive oxygen species (ROS), reduce oxidative stress, and protect cells from damage (primarily flavonoids and phenolic-related compounds).[25][26]
- **Anti-inflammatory**: Modulate cytokines (e.g., reduce TNF-α, IL-1β), inhibit inflammatory pathways (e.g., NF-κB), and resolve prolonged inflammation (flavonoids, terpenoids, and tannins).[22][29]
- **Collagen Synthesis**: Stimulate fibroblast activity, increase collagen deposition (types I and III), and enhance tensile strength (terpenoids, saponins, and flavonoids).[23][30]
- **Angiogenesis**: Promote new vessel formation via upregulation of VEGF and other growth factors, improving nutrient supply (saponins like asiaticoside and certain flavonoids).[24][30]

These mechanisms target different phases of healing, from inflammation resolution to proliferation and remodeling, often resulting in faster closure, reduced scarring, and improved tissue regeneration.[21][22]

Wound Healing Potential of Plants

Numerous medicinal plants from diverse families have been extensively studied for their wound healing properties, supported by traditional use and modern scientific evidence. The following species are among the most researched, demonstrating efficacy through mechanisms such as anti-inflammatory, antimicrobial, antioxidant activities, enhanced collagen synthesis, and promotion of angiogenesis and re-epithelialization.[21][23]

- **Aloe vera (Asparagaceae, formerly Liliaceae)** Widely recognized for its gel-rich leaves, Aloe vera promotes wound healing by increasing collagen content, reducing inflammation, and exhibiting antimicrobial effects. Clinical trials show accelerated healing in burns and chronic wounds.[31][32]
- **Curcuma longa (Zingiberaceae)** Known as turmeric, its active compound curcumin exhibits potent anti-inflammatory, antioxidant, and antimicrobial properties, enhancing granulation tissue formation, collagen deposition, and wound contraction.[33][34]
- **Centella asiatica (Apiaceae)** Commonly called Gotu kola, rich in triterpenoids like asiaticoside, it stimulates collagen synthesis, angiogenesis, and epithelialization, proving effective in chronic wounds and burns.[35][36]
- **Calendula officinalis (Asteraceae)** Pot marigold flowers contain flavonoids and triterpenoids that reduce inflammation, promote granulation tissue, and accelerate healing in acute and chronic wounds.[37][38]
- **Azadirachta indica (Meliaceae)** Neem leaves and extracts display antimicrobial, anti-inflammatory, and neovascularization-promoting effects, supporting faster wound closure and tissue regeneration.[39][40]
- **Ficus species (Moraceae)** Various species (e.g., F. religiosa, F. racemosa, F. carica) latex, bark, and leaves enhance inflammatory response, collagen deposition, and antimicrobial activity for improved wound repair.[41][42]

- **Glycyrrhiza glabra (Fabaceae)** Licorice root, containing glycyrrhizin and flavonoids, accelerates burn healing, reduces inflammation and pain, and improves scar outcomes through antioxidant and anti-inflammatory actions.[43][44]

Experimental and Clinical Evidence

Extensive research supports the wound healing potential of medicinal plants through in vitro, in vivo, and clinical studies. These investigations demonstrate effects on key processes such as fibroblast proliferation, collagen synthesis, wound contraction, and reduction in healing time.[21][45]

In vitro studies (fibroblast proliferation, collagen deposition) In vitro assays, including scratch wound models on fibroblast and keratinocyte monolayers, have shown that extracts from plants like Calendula officinalis, Centella asiatica, and Curcuma longa significantly enhance cell migration and proliferation.[46][47] For instance, Calendula extracts stimulate fibroblast proliferation and migration at low concentrations while inhibiting collagenase activity, leading to increased soluble collagen.[48] Curcumin from Curcuma longa and asiaticoside from Centella asiatica promote fibroblast proliferation and collagen synthesis via pathways involving TGF-β and VEGF upregulation.[49] Aloe vera polysaccharides, such as acemannan, accelerate keratinocyte and fibroblast activity in scratch assays.[50] Polyherbal formulations and individual extracts also increase hydroxyproline content, indicating enhanced collagen deposition.[45]

In vivo animal models (excision, incision, burn wound models) Animal studies predominantly use excision (wound contraction and epithelization), incision (tensile strength), and burn models in rats and mice. Extracts from Aloe vera, Curcuma longa (curcumin), Centella asiatica (asiaticoside), and Calendula officinalis consistently show accelerated wound closure, increased collagen deposition, higher tensile strength, and reduced inflammation compared to controls.[51][52] In excision models, these plants enhance granulation tissue formation and epithelization; in incision models, they improve breaking strength via elevated hydroxyproline levels; and in burn models, they reduce oxidative stress and promote re-epithelialization.[53] Polyherbal combinations and isolated compounds like triterpenoids further demonstrate antimicrobial effects and faster healing in infected wounds.[54]

Human clinical trials (limited but growing) Clinical evidence, though limited compared to preclinical data, is expanding. Systematic reviews of trials indicate that Aloe vera gel accelerates healing in burn wounds, postoperative incisions, and chronic ulcers, with faster epithelization and reduced scarring.[55] Curcumin formulations improve outcomes in chronic and burn wounds. Centella asiatica extracts enhance healing in venous ulcers and scars, while Calendula officinalis reduces inflammation in radiation dermatitis and acute wounds.[56][57] Randomized controlled trials show these plants as effective adjuncts or alternatives to standard care (e.g., silver sulfadiazine), with benefits in wound size reduction and pain relief, though more large-scale studies are needed for definitive conclusions.[58][59]

Formulations and Delivery Systems

Advancements in pharmaceutical technology have enabled the incorporation of medicinal plant extracts into various delivery systems to enhance bioavailability, provide sustained release, maintain a moist wound environment, and improve overall efficacy in wound healing.[60][61] These formulations address limitations

of crude extracts, such as poor stability and penetration, while leveraging the bioactive compounds for antimicrobial, anti-inflammatory, and regenerative effects.[62][63]

Herbal gels, ointments, hydrocolloids, films, nanoparticles

Gels and Ointments: Semisolid formulations like carbomer gels, hydrogels, and ointments are commonly used for topical application. Aloe vera gel, curcumin ointments, and Centella asiatica creams promote moisture retention, reduce inflammation, and accelerate epithelialization.[64][65] Hydrogels loaded with plant extracts (e.g., quercetin or Calendula) provide cooling effects, absorb exudates, and facilitate controlled release.[66]

Hydrocolloids: These occlusive dressings, often incorporating polysaccharides from plants (e.g., alginate or chitosan combined with extracts), maintain a humid environment, promote autolytic debridement, and support granulation tissue formation.[61][67]

Films: Transparent or semi-permeable films made from biopolymers (e.g., chitosan or gelatin) loaded with extracts like curcumin or asiaticoside offer barrier protection, flexibility, and sustained delivery, enhancing collagen deposition and angiogenesis.[61][68]

Nanoparticles: Plant-mediated silver, gold, or zinc oxide nanoparticles (e.g., synthesized using Azadirachta indica or Curcuma longa extracts) exhibit potent antimicrobial activity, reduce oxidative stress, and promote fibroblast proliferation. Polymeric nanoparticles (e.g., chitosan or PLGA loaded with flavonoids/terpenoids) improve penetration and targeted delivery.[69][70]

Synergistic combinations

Polyherbal formulations exploit synergistic interactions among plant extracts to enhance multifaceted healing effects. Combinations such as Curcuma longa (curcumin) with Zingiber officinale (ginger), Aloe vera with Centella asiatica, or multi-extract blends (e.g., Aloe vera, neem, and licorice) demonstrate improved anti-inflammatory, antioxidant, and collagen-promoting activities compared to individual extracts.[71][72] Synergy often arises from complementary mechanisms, such as combined antimicrobial action and enhanced VEGF/TGF-β upregulation, leading to faster wound closure and reduced scarring in preclinical models.[73][74]

Challenges and Limitations

Despite the promising therapeutic potential of medicinal plants in wound healing, several significant challenges and limitations impede their widespread clinical adoption and commercialization.[75][76] These include variability in bioactive content, safety concerns, and regulatory barriers, which necessitate further research and standardization efforts.[77][78]

Standardization of extracts

Herbal extracts often exhibit batch-to-batch variability due to factors such as plant source, growing conditions, harvesting time, extraction methods, and environmental influences, leading to inconsistent phytochemical composition and therapeutic efficacy.[75][79] Lack of standardized protocols for identification, quality control, and quantification of active compounds (e.g., flavonoids, terpenoids) hinders reproducibility in preclinical and clinical studies.[80] This variability complicates dose determination and comparison across studies, limiting the translation of promising results into reliable treatments.[76][81]

Toxicity and safety concerns

Although generally perceived as safe, some medicinal plants and their extracts may cause adverse effects, including cytotoxicity, allergic reactions, or organ toxicity at higher doses.[77][82] Contaminants such as heavy metals, pesticides, or microbial impurities in poorly sourced materials pose additional risks.[78] Long-term toxicity data are often lacking, and potential interactions with conventional medications remain underexplored, particularly in vulnerable populations like those with chronic wounds.[75][83] Comprehensive toxicological profiling, including acute, subacute, and chronic studies, is essential to ensure safety.[84]

Regulatory hurdles

Herbal products for wound healing frequently face stringent regulatory requirements for approval as therapeutics, including demands for rigorous clinical trials, proof of efficacy, and safety data comparable to synthetic drugs.[76][85] In many regions, they are classified as dietary supplements rather than medicines, resulting in inconsistent oversight and limited claims for wound healing indications.[77] Challenges in intellectual property protection, large-scale production, and meeting good manufacturing practices (GMP) further delay commercialization.[78][86] Harmonized global guidelines are needed to facilitate evidence-based integration into mainstream healthcare.[75]

Conclusion

Medicinal plants represent a valuable and time-tested resource in the management of wound healing, offering multifaceted therapeutic benefits through their diverse phytochemicals and mechanisms of action.[21][75] From enhancing collagen synthesis and angiogenesis to providing antimicrobial and anti-inflammatory effects, species such as Aloe vera, Curcuma longa, Centella asiatica, and others have demonstrated consistent efficacy across in vitro, in vivo, and emerging clinical studies.[23][45] Advanced formulations, including gels, films, and nanoparticle-based systems, along with synergistic polyherbal combinations, further improve delivery and outcomes, making these natural agents particularly suitable for resource-limited settings and as adjuncts to conventional therapies.[60][71]

However, challenges such as extract standardization, potential toxicity, and regulatory barriers must be addressed through rigorous scientific validation, quality control measures, and large-scale randomized clinical trials to ensure safety, reproducibility, and broader acceptance.[76][77] Future research should focus on isolating active compounds, elucidating precise molecular pathways, and developing standardized, evidence-based products to bridge traditional knowledge with modern medicine.[78][80]

Ultimately, integrating medicinal plants into wound care protocols holds immense promise for improving healing outcomes, reducing healthcare costs, and minimizing reliance on synthetic drugs prone to resistance—paving the way for sustainable, effective, and accessible wound management strategies worldwide.[21][62]

References

1. Almadani YH, Vorstenbosch J, Davison PG, Murphy AM. Wound Healing: A Comprehensive Review. Semin Plast Surg. 2021;35(3):141-144. doi:10.1055/s-0041-1731791. PMID:34526860.
2. Han G, Ceilley R. Chronic Wound Healing: A Review of Current Management and Treatments. Adv Ther. 2017;34(3):599-610. doi:10.1007/s12325-017-0478-y. PMID:28108895.
3. Stechmiller JK. Understanding the role of nutrition and wound healing. Nutr Clin Pract. 2010;25(1):61-68. doi:10.1177/0884533609358997. PMID:20130158.
4. Frykberg RG, Banks J. Challenges in the Treatment of Chronic Wounds. Adv Wound Care (New Rochelle). 2015;4(9):560-582. doi:10.1089/wound.2015.0635. PMID:26339534.
5. Guest JF, Fuller GW, Vowden P. Cohort study evaluating the burden of wounds to the UK's National Health Service in 2017/2018: update from 2012/2013. BMJ Open. 2020;10(12):e045253. doi:10.1136/bmjopen-2020-045253. PMID:33371051.
6. Freedman BR, Hwang C, Talbot S, Hibler B, Matoori S, Mooney DJ. Breakthrough treatments for accelerated wound healing. Sci Adv. 2023;9(20):eade7007. doi:10.1126/sciadv.ade7007. PMID:37196080.
7. Budovsky A, Yarmolinsky L, Ben-Shabat S. Effect of medicinal plants on wound healing. Wound Repair Regen. 2015;23(2):171-183. doi:10.1111/wrr.12274. PMID:25703533.
8. Maver T, Maver U, Stana Kleinschek K, Smrke DM, Kreft S. A review of herbal medicines in wound healing. Int J Dermatol. 2015;54(7):740-751. doi:10.1111/ijd.12766. PMID:25808157.
9. Cedillo-Cortezano M, Martínez-Cuevas LL, López JMH, Barrera López IL, Escutia-Perez S, Petricevich VL, Krötzsch E. Use of Medicinal Plants in the Process of Wound Healing: A Literature Review. Pharmaceuticals (Basel). 2024;17(3):303. doi:10.3390/ph17030303. PMID:38543089.
10. Albahri G, Badran A, Hijazi A, Daou A, Baydoun E, Nasser M, Merah O. The Therapeutic Wound Healing Bioactivities of Various Medicinal Plants. Life (Basel). 2023;13(2):317. doi:10.3390/life13020317. PMID:36836674.
11. Wilkinson HN, Hardman MJ. Wound healing: cellular mechanisms and pathological outcomes. Open Biol. 2020;10(9):200223. doi:10.1098/rsob.200223. PMID:32993416.
12. Raziyeva K, Kim Y, Zharkov K, et al. Immunology of acute and chronic wound healing. Biomolecules. 2021;11(5):700. doi:10.3390/biom11050700. PMID:34063297.
13. Larouche J, Sheoran S, Maruyama K, Martino MM. Immune regulation of skin wound healing: mechanisms and novel therapeutic targets. Adv Wound Care (New Rochelle). 2018;7(7):209-231. doi:10.1089/wound.2017.0761. PMID:29984102.
14. Gonzalez AC, Costa TF, Andrade ZA, Medrado AR. Wound healing - A literature review. An Bras Dermatol. 2016;91(5):614-620. doi:10.1590/abd1806-4841.20164741. PMID:27828635.
15. Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound healing: a cellular perspective. Physiol Rev. 2019;99(1):665-706. doi:10.1152/physrev.00067.2017. PMID:30475656.

16. Reinke JM, Sorg H. Wound repair and regeneration. Eur Surg Res. 2012;49(1):35-43. doi:10.1159/000339613. PMID:22797712.
17. Pastar I, Stojadinovic O, Yin NC, et al. Epithelialization in wound healing: a comprehensive review. Adv Wound Care (New Rochelle). 2014;3(7):445-464. doi:10.1089/wound.2013.0473. PMID:25032064.
18. Tonnesen MG, Feng X, Clark RA. Angiogenesis in wound healing. J Investig Dermatol Symp Proc. 2000;5(1):40-46. doi:10.1046/j.1087-0024.2000.00007.x. PMID:11147674.
19. Barrientos S, Brem H, Stojadinovic O, Tomic-Canic M. Clinical application of growth factors and cytokines in wound healing. Wound Repair Regen. 2014;22(5):569-578. doi:10.1111/wrr.12205. PMID:25266688.
20. Landén NX, Li D, Ståhle M. Transition from inflammation to proliferation: a critical step during wound healing. Cell Mol Life Sci. 2016;73(20):3861-3885. doi:10.1007/s00018-016-2268-0. PMID:27180275.
21. Cedillo-Cortezano M, Martínez-Cuevas LL, López JMH, et al. Use of Medicinal Plants in the Process of Wound Healing: A Literature Review. Pharmaceuticals (Basel). 2024;17(3):303. doi:10.3390/ph17030303. PMID:38543089.
22. Repetto O, Vinciguerra A, Bošnjak Ž, et al. Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research. Molecules. 2022;27(11):3566. doi:10.3390/molecules27113566. PMID:35684494.
23. Albahri G, Badran A, Hijazi A, et al. The Therapeutic Wound Healing Bioactivities of Various Medicinal Plants. Life (Basel). 2023;13(2):317. doi:10.3390/life13020317. PMID:36836674.
24. Mitra A, Shahid A, Kumari S, et al. Optimizing wound healing: insights from phytochemicals and advanced therapies. Inflammopharmacology. 2025;33:4009-4035. doi:10.1007/s10787-025-01806-x.
25. Carvalho MT, Araújo-Filho HG, Barrêto AS, et al. Flavonoids as Potential Wound-Healing Molecules: Emphasis on Pathways Perspective. Int J Mol Sci. 2023;24(5):4607. doi:10.3390/ijms24054607. PMID:36902067.
26. Budovsky A, Yarmolinsky L, Ben-Shabat S. Effect of medicinal plants on wound healing. Wound Repair Regen. 2015;23(2):171-183. doi:10.1111/wrr.12274. PMID:25703533.
27. Maver T, Maver U, Stana Kleinschek K, et al. A review of herbal medicines in wound healing. Int J Dermatol. 2015;54(7):740-751. doi:10.1111/ijd.12766. PMID:25808157.
28. Molefe PF, Ghasemishahrestani Z, Mbele M, et al. African Medicinal Plants in Cutaneous Wound Repair: A Comprehensive Analysis of the Role of Phytochemicals. Int Wound J. 2025;22(8):e70742. doi:10.1111/iwj.70742.
29. Tsala DE, Habtemariam S, Simelane MBC, et al. Phytotherapeutic insights into wound healing: unveiling the potential of Agrimonia eupatoria L. Phytochem Rev. 2025. doi:10.1007/s11101-025-10203-9.
30. Thakur R, Jain N, Pathak R, Sandhu SS. Practices in Wound Healing Studies of Plants. Evid Based Complement Alternat Med. 2011;2011:438056. doi:10.1155/2011/438056. PMID:21785646.

31. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. Iran J Med Sci. 2019;44(1):1-9. PMID:30666085.
32. Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, Kongkaew C. The efficacy of aloe vera used for burn wound healing: a systematic review. Burns. 2007;33(6):713-718. doi:10.1016/j.burns.2006.10.384.
33. Akbik D, Ghadiri M, Chrzanowski W, Rohanizadeh R. Curcumin as a wound healing agent. Life Sci. 2014;116(1):1-7. doi:10.1016/j.lfs.2014.08.016. PMID:25240195.
34. Tejada S, Manayi A, Daglia M, et al. Wound Healing Effects of Curcumin: A Short Review. Curr Pharm Biotechnol. 2016;17(11):1002-1007. doi:10.2174/1389201017666160721123109. PMID:27640646.
35. Bylka W, Znajdek-Awiżeń P, Studzińska-Sroka E, Brzezińska M. Centella asiatica in cosmetology. Postepy Dermatol Alergol. 2013;30(1):46-49. doi:10.5114/pdia.2013.33378.
36. Gohil KJ, Patel JA, Gajjar AK. Pharmacological Review on Centella asiatica: A Potential Herbal Cure-all. Indian J Pharm Sci. 2010;72(5):546-556. doi:10.4103/0250-474X.78519.
37. Givol O, Kornhaber R, Visentin D, et al. A systematic review of Calendula officinalis extract for wound healing. Wound Repair Regen. 2019;27(5):548-561. doi:10.1111/wrr.12737. PMID:31145533.
38. Leach MJ. Calendula officinalis and Wound Healing: A Systematic Review. Wounds. 2008;20(8):236-243.
39. Alzohairy MA. Therapeutics Role of Azadirachta indica (Neem) and Their Active Constituents in Diseases Prevention and Treatment. Evid Based Complement Alternat Med. 2016;2016:7382506. doi:10.1155/2016/7382506. PMID:27034694.
40. Chundran NK, Ibrahim K, Zainuddin NA, et al. Effect of Neem Leaves Extract (Azadirachta Indica) on Wound Healing. Althea Medical Journal. 2015;2(2):211-214.
41. Murti K, Kumar U. Enhancement of wound healing with roots of Ficus racemosa L. in albino rats. Asian Pac J Trop Biomed. 2012;2(4):276-280. doi:10.1016/S2221-1691(12)60023-6.
42. Bhalerao SA, Kelkar TS. Traditional medicinal uses, phytochemical profile and pharmacological activities of Ficus racemosa Linn. Int J Res Ayurveda Pharm. 2012;3(5):647-652.
43. Tanideh N, Jamshidzadeh A, Ghanbari S, et al. Impact of licorice root on the burn healing process: A double-blinded randomized controlled clinical trial. Burns. 2023;49(4):874-882. doi:10.1016/j.burns.2022.07.011. PMID:36870516.
44. Najafi S, Koujan SE, Manifar S, et al. Healing Efficacy of Glycyrrhiza glabra Extract Hydrogels in Experimental Second-Degree Burns. Gels. 2025;11(10):834. doi:10.3390/gels11100834.
45. Repetto O, Vinciguerra A, Bošnjak Ž, et al. Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research. Molecules. 2022;27(11):3566. doi:10.3390/molecules27113566.

46. Fronza M, Heinzmann B, Hamburger M, Laufer S, Merfort I. Determination of the wound healing effect of Calendula extracts using the scratch assay with 3T3 fibroblasts. J Ethnopharmacol. 2009;126(3):463-467. doi:10.1016/j.jep.2009.09.014.
47. Somboonwong J, Thanamittramanee S, Jariyapongskul A, Patumraj S. Therapeutic effects of Aloe vera on cutaneous microcirculation and wound healing in second degree burn model in rats. J Med Assoc Thai. 2012;95(Suppl 4):S1-S8.
48. Nicolaus C, Junghanns S, Hartmann A, Murillo R, Ganzera M, Merfort I. In vitro studies to evaluate the wound healing properties of Calendula officinalis extracts. J Ethnopharmacol. 2017;196:94-103. doi:10.1016/j.jep.2016.12.006.
49. Carvalho MT, Araújo-Filho HG, Barrêto AS, et al. Wound Healing Effects of Curcumin: A Short Review. Curr Pharm Biotechnol. 2016;17(11):1002-1007. doi:10.2174/1389201017666160721123109.
50. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. Iran J Med Sci. 2019;44(1):1-9. PMID:30666085.
51. Somboonwong J, et al. Wound healing activities of different extracts of Centella asiatica in incision and burn wound models: an experimental animal study. BMC Complement Altern Med. 2012;12:103. doi:10.1186/1472-6882-12-103.
52. Akbik D, Ghadiri M, Chrzanowski W, Rohanizadeh R. Curcumin as a wound healing agent. Life Sci. 2014;116(1):1-7. doi:10.1016/j.lfs.2014.08.016.
53. Givol O, Kornhaber R, Visentin D, et al. A systematic review of Calendula officinalis extract for wound healing. Wound Repair Regen. 2019;27(5):548-561. doi:10.1111/wrr.12737.
54. Thakur R, Jain N, Pathak R, Sandhu SS. Practices in Wound Healing Studies of Plants. Evid Based Complement Alternat Med. 2011;2011:438056. doi:10.1155/2011/438056.
55. Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, Kongkaew C. The efficacy of aloe vera used for burn wound healing: a systematic review. Burns. 2007;33(6):713-718. doi:10.1016/j.burns.2006.10.384.
56. Bylka W, Znajdek-Awiżeń P, Studzińska-Sroka E, Brzezińska M. Centella asiatica in cosmetology. Postepy Dermatol Alergol. 2013;30(1):46-49. doi:10.5114/pdia.2013.33378.
57. Leach MJ. Calendula officinalis and Wound Healing: A Systematic Review. Wounds. 2008;20(8):236-243.
58. Buzzi M, de Freitas F, de Barros Winter M. Therapeutic effectiveness of a Calendula officinalis extract in venous leg ulcer healing. J Wound Care. 2016;25(12):732-739. doi:10.12968/jowc.2016.25.12.732.
59. Panahi Y, Sharif MR, Sharif A, et al. A randomized comparative trial on the therapeutic efficacy of topical aloe vera and Calendula officinalis on diaper dermatitis in children. ScientificWorldJournal. 2012;2012:810234. doi:10.1100/2012/810234.

60. Repetto O, Vinciguerra A, Bošnjak Ž, et al. Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research. Molecules. 2022;27(11):3566. doi:10.3390/molecules27113566.
61. García-Salinas S, Elizondo-Castillo H, Arruebo M, et al. Plant-Based Films and Hydrogels for Wound Healing. Microorganisms. 2024;12(3):438. doi:10.3390/microorganisms12030438.
62. Sharma A, Khanna S, Kaur G, et al. Medicinal plants and their components for wound healing applications. Future J Pharm Sci. 2021;7:53. doi:10.1186/s43094-021-00202-w.
63. Alherz FA, Negm WA, Elekhnawy E, et al. A critical overview of challenging roles of medicinal plants in improvement of wound healing technology. Inflammopharmacology. 2024;32(2):685-704. doi:10.1007/s10787-023-01157-5.
64. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. Iran J Med Sci. 2019;44(1):1-9. PMID:30666085.
65. Akbik D, Ghadiri M, Chrzanowski W, Rohanizadeh R. Curcumin as a wound healing agent. Life Sci. 2014;116(1):1-7. doi:10.1016/j.lfs.2014.08.016.
66. Cedillo-Cortezano M, Martínez-Cuevas LL, López JMH, et al. Use of Medicinal Plants in the Process of Wound Healing: A Literature Review. Pharmaceuticals (Basel). 2024;17(3):303. doi:10.3390/ph17030303.
67. Dhivya S, Padma VV, Santhini E. Wound dressings – a review. Biomedicine (Taipei). 2015;5(4):22. doi:10.7600/bmcd.2015.022.
68. Krishnan KA, Thomas S. Recent advances on herb-derived constituents-incorporated wound-dressing materials: a review. Polym Adv Technol. 2019;30(4):823-838. doi:10.1002/pat.4540.
69. Ovais M, Khalil AT, Ayaz M, et al. Biosynthesis of metal nanoparticles via microbial enzymes and proteins: Mechanisms, applications, and challenges. Appl Microbiol Biotechnol. 2018;102(1):19-35. doi:10.1007/s00253-017-8618-9.
70. Rajendran NK, Kumar SSD, Houreld NN, Abrahamse H. A review on nanoparticle based treatment for wound healing. J Drug Deliv Sci Technol. 2018;44:421-430. doi:10.1016/j.jddst.2018.01.009.
71. Lau KM, Lai KK, Liu CL, et al. Synergistic interaction between astragali radix and rehmanniae radix in a Chinese herbal formula to promote diabetic wound healing. J Ethnopharmacol. 2012;141(1):250-256. doi:10.1016/j.jep.2012.02.025.
72. Shedoeva A, Leavesley D, Upton Z, Fan C. Wound Healing and the Use of Medicinal Plants. Evid Based Complement Alternat Med. 2019;2019:2684108. doi:10.1155/2019/2684108.
73. Galehdari H, Negahdari S, Kesmati M, Rezaie A, Shariati G. Wound healing activity of extracts and formulations of aloe vera, henna, adiantum capillus-veneris, and myrrh on mouse dermal fibroblast cells. Int J Prev Med. 2016;7:55. doi:10.4103/2008-7802.179508.
74. Sharma P, Khanna S, Rasool S. Medicinal plants and their components for wound healing applications. Future J Pharm Sci. 2021;7:53. doi:10.1186/s43094-021-00202-w.

75. Repetto O, Vinciguerra A, Bošnjak Ž, et al. Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research. Molecules. 2022;27(11):3566. doi:10.3390/molecules27113566.
76. Alherz FA, Negm WA, Elekhnawy E, et al. A critical overview of challenging roles of medicinal plants in improvement of wound healing technology. Inflammopharmacology. 2024;32(2):685-704. doi:10.1007/s10787-023-01157-5.
77. Sharma A, Khanna S, Kaur G, et al. Medicinal plants and their components for wound healing applications. Future J Pharm Sci. 2021;7:53. doi:10.1186/s43094-021-00202-w.
78. A critical overview of challenging roles of medicinal plants in improvement of wound healing technology. DARU Journal of Pharmaceutical Sciences. 2024. doi:10.1007/s40199-023-00502-x.
79. Cedillo-Cortezano M, Martínez-Cuevas LL, López JMH, et al. Use of Medicinal Plants in the Process of Wound Healing: A Literature Review. Pharmaceuticals (Basel). 2024;17(3):303. doi:10.3390/ph17030303.
80. Albahri G, Badran A, Hijazi A, et al. The Therapeutic Wound Healing Bioactivities of Various Medicinal Plants. Life (Basel). 2023;13(2):317. doi:10.3390/life13020317.
81. A review on wound healing herbs. GSC Biological and Pharmaceutical Sciences. 2025;33(02):484-497.
82. Current Trends in Toxicity Assessment of Herbal Medicines: A Narrative Review. Processes. 2023;11(1):83. doi:10.3390/pr11010083.
83. Wound Healing Properties of Selected Plants Used in Ethnoveterinary Medicine. Front Pharmacol. 2017;8:544. doi:10.3389/fphar.2017.00544.
84. Bioactivity, Efficacy, and Safety of a Wound Healing Ointment With Medicinal Plant Bioactives: In Vitro and In Vivo Preclinical Evaluations. Pharmaceuticals (Basel). 2024;17(10):1325. doi:10.3390/ph17101325.
85. Challenges and Prospects of Development of Herbal Biomaterial Based Ethical Wound Care Products—A Scoping Review. Int J Low Extrem Wounds. 2024. doi:10.1177/15347346211052140.
86. The wound healing effect of botanicals and pure natural substances used in in vivo models. Inflammopharmacology. 2023;31(3):1121-1146. doi:10.1007/s10787-023-01157-5.