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REVIEW ARTICLE

A critical overview of challenging roles of medicinal plants in improvement of wound healing technology

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Abstract

Purpose Chronic diseases often hinder the natural healing process, making wound infections a prevalent clinical concern. In severe cases, complications can arise, potentially leading to fatal outcomes. While allopathic treatments offer numerous options for wound repair and management, the enduring popularity of herbal medications may be attributed to their perceived minimal side effects. Hence, this review aims to investigate the potential of herbal remedies in efficiently treating wounds, presenting a promising alternative for consideration.

Methods A literature search was done including research, reviews, systematic literature review, meta-analysis, and clinical trials considered. Search engines such as Pubmed, Google Scholar, and Scopus were used while retrieving data. Keywords like Wound healing 'Wound healing and herbal combinations', 'Herbal wound dressing', Nanotechnology and Wound dressing were used.

Result This review provides valuable insights into the role of natural products and technology-based formulations in the treatment of wound infections. It evaluates the use of herbal remedies as an effective approach. Various active principles from herbs, categorized as flavonoids, glycosides, saponins, and phenolic compounds, have shown effectiveness in promoting wound closure. A multitude of herbal remedies have demonstrated significant efficacy in wound management, offering an additional avenue for care. The review encompasses a total of 72 studies, involving 127 distinct herbs (excluding any common herbs shared between studies), primarily belonging to the families Asteraceae, Fabaceae, and Apiaceae. In research, rat models were predominantly utilized to assess wound healing activities. Furthermore, advancements in herbal-based formulations using nanotechnology-based wound dressing materials, such as nanofibers, nanoemulsions, nanofiber mats, polymeric fibers, and hydrogel-based microneedles, are underway. These innovations aim to enhance targeted drug delivery and expedite recovery. Several clinical-based experimental studies have already been documented, evaluating the efficacy of various natural products for wound care and management. This signifies a promising direction in the field of wound treatment.

Conclusion In recent years, scientists have increasingly utilized evidence-based medicine and advanced scientific techniques to validate the efficacy of herbal medicines and delve into the underlying mechanisms of their actions. However, there remains a critical need for further research to thoroughly understand how isolated chemicals extracted from herbs contribute to the healing process of intricate wounds, which may have life-threatening consequences. This ongoing research endeavor holds great promise in not only advancing our understanding but also in the development of innovative formulations that expedite the recovery process.

Keywords Wound healing · Herbs · Wound dressing · Nanotechnology · Clinical trial

Introduction

Wounds encompass a spectrum, ranging from minor cuts to severe injuries like punctures, lacerations, or burns [1]. Factors like diabetes, atherosclerosis, and venous insufficiency in an aging population have led to a surge in chronic wounds [2]. Delayed wound healing escalates risks, potentially culminating in severe complications, including infection,

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sepsis, and, in extreme cases, necessitating amputation [3]. Pediatric orthopedic surgery for early-onset scoliosis, while often necessary, carries a substantial risk of wound-related complications, averaging an incidence of 15.5% [4]. The rise in chronic wounds has heightened awareness of their associated morbidity and financial burdens over recent decades [5]. Chronic wounds and burns significantly diminish patients' quality of life, underscoring the need for innovative, cost-effective technologies and treatments to sustain national health systems [6]. Opportunistic bacteria like *Staphylococcus aureus* and *Pseudomonas aeruginosa*, due to their inflammatory response-triggering ability, may play a role in sustaining chronic wounds. Research also indicates therapeutic potential in bacterial and host extracellular vesicles, with applications ranging from vaccine candidates to agents modifying bacterial species in chronic wound biofilms [7]. Patients with biofilms, responsible for 60% of burn-related fatalities and contributing to rapid antibiotic resistance spread, require isolation and specialized treatment before full admission to the hospital [8]. Infections in wounds lead to prolonged healing, chronicity, increased hospitalization, potential amputation, and elevated medical costs; biofilm presence exacerbates these issues, underscoring the critical importance of early detection and treatment for improved outcomes [9]. Implementing a structured assessment framework like the Tissue, Inflammation or Infection, Moisture, and Edge of the wound and Epithelial advancement model can enhance wound care, facilitating the detection of deviations from normal healing, including those arising from species-specific factors, and thereby averting potential delays in recovery or further tissue damage, beyond the influence of intrinsic and extrinsic factors [10]. Macrophages play a crucial role in regulating inflammation, fibrosis, and wound healing, owing to their phagocytic capabilities and secretion of cytokines and growth factors [11]. Growth factors serve as primary human regulators in wound healing, while fibroblasts, highly active cells, play a vital role in tissue fibrosis and the healing process [12]. Additionally, platelets, neurons, and glial cells not only aid in tissue repair but also establish the wound microenvironment, influencing the growth of immune cells, fibroblasts, and keratinocytes [13]. The dynamic expression of Programmed Death Ligand-1 on fibroblast-like cells within the granulation tissue during wound healing serves to establish an immunosuppressive microenvironment, facilitating the modulation of macrophage polarization from M1-type to M2-type and initiating the resolution of inflammation, ultimately expediting the wound healing process [14]. Tryptase, a mast cell mediator, triggers bronchial epithelial cells to enhance migration and proliferation, partially regulated by protease-activated receptor-2, ultimately enhancing epithelial wound healing [15]. Mesenchymal stem cells hold promise for cell-based therapy, primarily relying on their paracrine actions for wound healing and tissue repair [16]. Moreover, adipose-derived mesenchymal stem cell exosomes have recently demonstrated involvement in various wound-healing pathways, particularly aiding in the healing of diabetic wounds [17]. Thymosin-4, a naturally occurring protein abundant in various body fluids and cells, especially platelets, plays pivotal roles in wound healing, actively promoting angiogenesis while inhibiting fibrosis, apoptosis, and inflammation [18].

Herbal medicine is increasingly explored for its diverse therapeutic potential, with certain medicinal plants showing significant wound-healing effects in experimental studies [19]. These herbs, supported by evidence-based medicine, offer viable treatment options in various healthcare contexts [20]. For instance, the ancient text, Sushruta Samhita, highlights various medicinal plants with potential for wound cleansing and healing, although no current published data validate these properties [21]. Traditional Persian medicine also provides valuable insights into natural remedies for wound healing [22]. Additionally, research on wound healing agents is a burgeoning field in biomedical sciences, with Chinese medicinal herbs showing promise, particularly bioactive polysaccharides derived from natural resources [23]. Plants like *Acacia modesta, Aloe barbadensis, Azadirachta indica, Ficus benghalensis, Nerium oleander*, and *Olea ferruginea* are extensively utilized for wound healing and demonstrate high use values in traditional practices [24]. Certain herbs like *Vitis vinifera, Quercus spp., Punica granatum, Polygonum spp., Lilium spp., Gentiana lutea, Arnebia euchroma, Aloe spp.*, and *Caesalpinia spp*. possess verified biological and pharmacological mechanisms for wound healing [25]. Similarly, compounds from the convolvulaceae family such as *Evolvulus alsinoides, Evolvulus nummularius, Argyreia cuneata*, and *Ipomoea carnea* exhibit notable antidiabetic and wound healing activity, showing potential in diabetic wound care [26].

Antioxidants such as astaxanthin, beta-carotene, epigallocatechin gallate, delphinidin, and curcumin have shown efficacy in promoting cell proliferation, migration, angiogenesis, and inflammation control, presenting a promising approach for developing innovative treatments for cutaneous conditions [27]. Natural dietary antioxidants rich in flavonoids have been shown to influence keratinocyte physiology demonstrating notable skin repair benefits across different stages of the wound-healing process, including cell-cell and cell-matrix interactions, as well as collagen synthesis [28, 29]. In addition, numerous polyherbal formulations have demonstrated the ability to expedite wound healing in experimental models [30]. The effectiveness of combined herbal medications may be attributed to the synergy of diverse plant classes, each contributing different mechanisms that collectively lead to a more comprehensive therapeutic outcome [31]. These formulations show promise in enhancing wound healing by stimulating various physiological

functions, warranting clinical trials for further validation and upscaling production, potentially revolutionizing the development of polyherbal wound healing products [32]. For example, polyherbal formulations like Jathyadi Thailam and Jatyadi Ghritam from Indian traditional medicine demonstrate potent antibacterial and anti-inflammatory properties, suggesting their potential as an external adjunct therapy for chronic wound management, particularly in cases of multi-drug-resistant bacterial infections [33]. This review aims to investigate the potential of herbal extractions, their combinations (polyherbal formulations), and new developments in wound healing technology to enhance wound recovery abilities.

Methods

Literature search strategy

Database searches were conducted in PubMed and Google Scholar to identify articles published between 2014 and 2023, focusing on wound healing, herbal wound treatments, herbal wound dressings, nanotechnology, and wound dressings. Studies concerning the efficacy of herbal drugs in wound treatment were included, while non-English publications were excluded. Initially, 103,911 articles were identified. After removing duplicates, unrelated articles, and those with irrelevant titles, 476 articles remained for eligibility assessment. Ultimately, 282 articles were selected for inclusion in this review. Advanced filters in PubMed and Google Scholar were utilized during the screening process, followed by a manual assessment for eligibility. Data extraction was carried out using spreadsheet software like Microsoft Excel and Google Sheets. The flowchart detailing article inclusion is represented in Fig. 1. This review aimed to evaluate the significant effectiveness of medicinal plants in wound care and explore advancements in wound dressing technology to enhance wound healing capabilities.

Wound healing process

The epidermis, our body's outermost layer commonly known as the skin, plays a crucial role as a protective barrier, preventing harmful substances, pathogens, and environmental toxins from infiltrating our system [34]. It also plays a pivotal role in temperature regulation, managing heat loss through mechanisms like sweating and blood vessel constriction or dilation [35]. Being the most exposed organ, the skin is susceptible to various forms of injury and damage [36]. Any harm to this protective shield, be it cuts, burns, or wounds, can impair its safeguarding functions [37]. A wound, defined as any injury leading to a break in the skin or mucous membranes, can stem from a range of causes, from abrasions to surgical incisions [38, 39]. Following skin damage, a complex sequence of cellular and molecular events is set into motion, kickstarting the wound-healing process and fortifying the body against infections and further harm [40]. The skin, an intricate organ with diverse cell types, signaling pathways, and functions, makes wound healing a sophisticated undertaking [41]. Effectively enhancing cutaneous wound healing necessitates a diverse array of approaches that acknowledge the intricate nature of the skin and its healing mechanisms [42]. This process hinges on a dynamic interplay of cellular elements, growth factors, cytokines, antioxidants, and essential metal ions [43]. Wound healing, a meticulously organized procedure, seeks to reinstate the skin's barrier function and mechanical integrity. It unfolds through a well-coordinated series of stages, each playing a pivotal role in repairing tissue damage [44]. Restoring the skin's integrity and function post-injury is paramount for

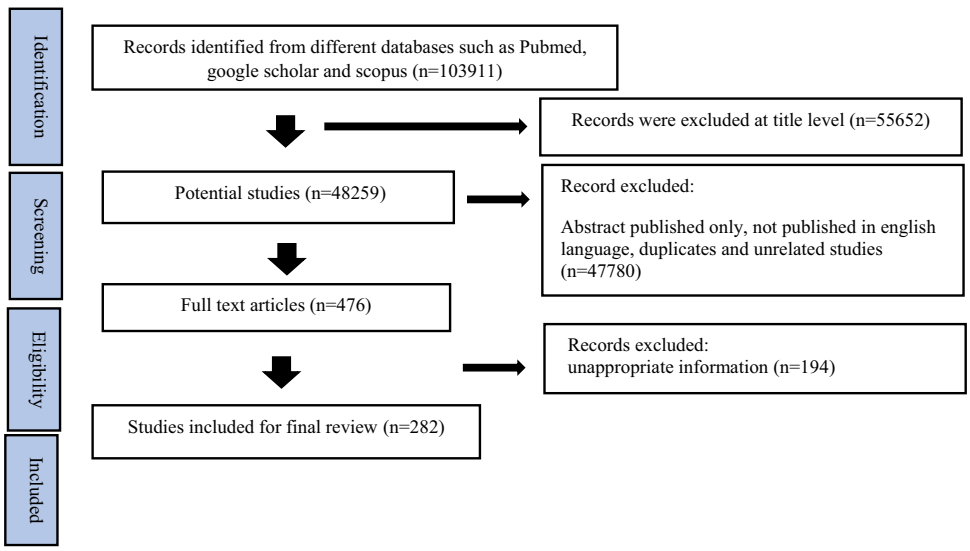

Fig. 1 PRISMA flowchart of included article

both wound healing and overall health. This intricate process involves the phased reconstitution of a functional epidermis and other skin layers [45], as depicted in Fig. 2.

Comprehensive strategies for wound management

Comprehensive wound management encompasses the intricate multi-stage healing process, distinguishing between acute (pain, redness, warmth, and pus) and chronic infections (slow healing, discolored tissue, clear discharge, pockets, and an unpleasant odor) by their respective symptoms, with Fig. 3 illustrating diagnostic methods to identify wound infections [46]. Optimal wound management prioritizes creating a warm, moist environment to facilitate natural healing, with a strong emphasis on hygiene to reduce infection risks. This comprehensive approach involves crucial steps such as debridement [47–49] and the application of advanced treatments including wound bed preparation, antimicrobial dressings, and silver-based products [50–52]. In burn cases, topical antimicrobial agents like silver sulfadiazine cream play a pivotal role due to the heightened risk of bacterial infections, however, this approach has faced criticism for

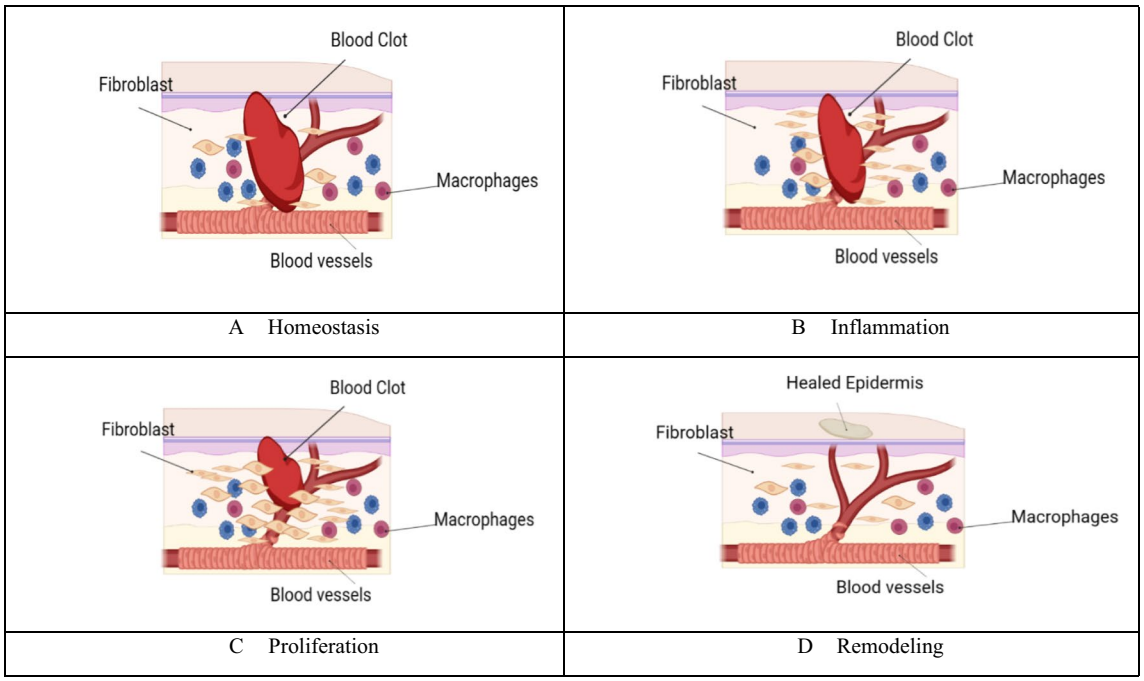

Fig. 2 Wound healing process (**A**) Homeostasis: After injury, the body initiates homeostasis to stop bleeding and form a blood clot at the wound site. **B** Inflammation: The inflammatory phase involves the recruitment of immune cells to the wound to combat potential infections and clear debris. **C** Proliferation: During this stage, new tissue is generated to fill the wound gap. Cells such as fibroblasts produce collagen to build a new extracellular matrix, and new blood vessels form through angiogenesis. **D** Remodeling: In the final phase, the wound undergoes remodeling as the newly formed tissue matures and gains strength. Collagen fibers realign, and the wound's overall tensile strength improves

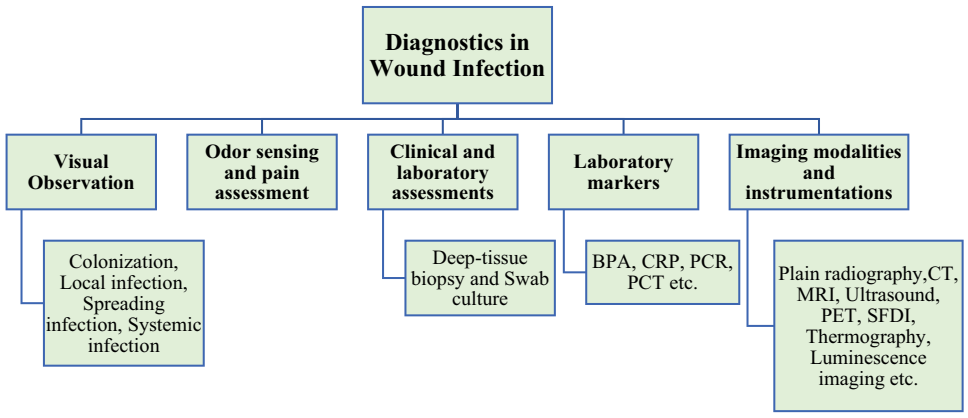

Fig. 3 Diagnostic methods for identification of wound infections. Note: BPA: Bacterial protease activity; CRP: C-reactive protein; PCR: Polymerase chain reaction; PCT; Procalcitonin, CT: Computed tomography; MRI: Magnetic resonance imaging; PET: Positron emission tomography; SFDI: Spatial frequency domain imaging

potential drawbacks including antimicrobial resistance, delayed healing, and cytotoxic effects on host cells [53]. While advanced therapies like negative pressure, growth factors, hyperbaric oxygen, and skin grafts present viable secondary options [54–63], their accessibility is limited by high costs and associated complications, including systemic issues, tissue availability, and donor-site morbidity, particularly in resource-poor settings. This underscores the urgent need for affordable wound treatments [64, 65]. Cost-effective clinical dressings like gauze sterilized absorbent cotton, and bandages offer valuable physical protection in wound healing and infection prevention. However, their adherence to the wound can sometimes lead to secondary damage upon separation [66]. Given the constraints of current wound healing agents, there is a critical imperative for the development of natural products to address non-healing wounds [67, 68].

Traditional Herbal Medicines, valued for their cultural significance and minimal side effects, have been esteemed for their proven efficacy, accessibility, growing scientific validation, and commercial viability [69–72]. These traditional therapies include herbal- and animal-derived compounds, living organisms, and traditional dressings [73]. Medicines with bioactive compounds from traditional sources hold promise in treating chronic wounds by reducing inflammation, promoting re-epithelization, and acting as potent antiseptics, even against antibiotic-resistant bacteria [74]. Herbal products and their active constituents like *Aloe barbadensis*, *Adiantum capillus, Commiphora molmol*, henna, *Nigella sativa, Teucrium polium, Nelumbo nucifera* and *Boswellia carteri* exhibit superior wound healing effects, surpassing the efficacy of standard antimicrobial agents (e.g., silver nitrate, povidone-iodine, silver sulfadiazine, mafenide, mupirocin, bacitracin) and commercially available wound dressings (Comfeel—hydrocolloid dressing, Kaltostat—alginate dressing) [75]. Ayurveda and folk medicine traditions incorporate potent healing agents like Honey, Ghee, and revered medicinal plants including *Glycyrrhiza glabra* and *Nerium indicum*, known for their well-established wound-healing properties with minimal adverse effects [76]. *Allium sativum, Aloe barbadensis*, *Centella asiatica*, and *Hippophae rhamnoides* exhibit potent burn wound healing due to their diverse phytochemical composition engaging in antimicrobial, anti-inflammatory, antioxidant, collagen synthesis stimulation, cell proliferation, and angiogenic mechanisms [77]. Incorporating bioactive natural compounds within wound dressings, in forms like nanofiber, hydrogel, film, scaffold, and sponge, coupled with bio- or synthetic polymers, shows remarkable promise in augmenting wound healing by addressing oxidative stress, inflammation, and microbial activity throughout distinct phases of the healing process [78]. Critical to tissue repair, maintaining proper nutrition with adequate protein, vitamin C, zinc, and hydration is essential [79, 80]. Active patient engagement, encompassing vigilant wound care, infection monitoring, timely dressing changes, and knowing when to seek medical help, plays a pivotal role in the recovery process [81, 82].

Herbs used for wound management

Plant-based medications are gaining prominence for their perceived effectiveness, cost-effectiveness, and safety in treating chronic wounds [83]. Research highlights flavonoids, glycosides, saponins, terpenes, and phenolic compounds as key contributors to herbal remedies' efficacy in wound management, exerting diverse beneficial effects at different stages of the healing process (Table 1).

Polyherbal a synergistic combination for wound management

Polyherbal compositions, also known as polyherbal therapy, have gained global recognition for their enhanced therapeutic potential compared to individual plant-based treatments, as they harness synergistic effects to amplify medicinal activity while reducing toxicity within specific proportions [144, 145]. This approach offers distinct advantages over single herbal formulations, demonstrating a more potent therapeutic outcome and necessitating lower quantities for desired pharmacological effects, thereby minimizing potential side effects [146, 147]. These collective benefits have substantially bolstered the market appeal of polyherbal remedies. In the context of wound infections, diverse herbal blends tailored for specific effects are available, as detailed in Table 2.

Recent advances in wound dressing technology for enhanced wound healing capacity

A wound dressing applied directly to a wound plays a crucial role in expediting healing and preventing complications associated with untreated wounds [172]. Wound healing involves four primary stages: hematoma creation, inflammation, neotissue formation, and tissue remodeling [173], with the involvement of macrophages being instrumental [174]. There's been significant development in wound dressings and technologies aimed at enhancing the body's natural healing and tissue regeneration processes [175]. Nanotechnologies have emerged, offering unique properties to address issues in wound repair mechanisms [176]. In fields like biomedicine, pharmaceuticals, and medicine, there's a growing emphasis on nano-formulations for wound care, particularly in cases of diabetes-induced wounds [177]. Herbal preparations have gained attention due to their diverse phytoconstituents and broad pharmacological activity compared to synthetic drugs. They are considered safe for extended use, leading to increased focus on designing herbal-loaded

Table 1 Herbs used in wound management

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
1	*Dioscorea bulbifera*	Dioscoreaceae	Wound healing and anti-inflammatory, diuretic, anthelmintic cold, stomach and rectal cancer	Aqueous	Bulbil	In vitro: HDF cell line	Aloe vera gel	VLC	8-epidiosbulbin E acetate, 15,16-epoxy-6α-O-acetyl-8β-hydroxy-19-nor-clero-13, 14-diene-17,12;18,2-diolide, sitosterol-β-D-glucoside, 3,5-dimethoxyquercetin, catechin, quercetin, kaempferol, allantoin, 2,4,3',5'-tetrahydroxy-bibenzyl, 2,4,6,7-tetrahydroxy-9,10 dihydrophenanthrene, myricetin	15,16-Epoxy-6α-O-acetyl-8β-hydroxy-19-nor-clero-13(16),14-diene-17,12;18,2-diolide, catechin, quercetin and myricetin	Diterpenoid and flavonoid	Cell proliferation and migration	[84, 85]
2	*Boerhavia diffusa*	Nyctaginaceae	Anti-inflammatory, diuretic, cancer-preventive, hepatoprotective, antimicrobial, antioxidant and spasmolytic activity	Methanol	Leaf	In vivo: excision wound model in albino Wistar rat In vitro: HaCaT cell line	Povidone-iodine ointment	GC-MS	Ethylene glycol, valine, alanine, 2-Pyrrolidinone, proline, isoleucine, threonine, succinic acid, uracil, fumaric acid, serine, citramalic acid, malic acid, threonic acid, asparagine, glutamic acid, phenylalanine, 3,4-Dihydroxy-benzyl alcohol, 4-Methylcatechol, d-Fructofuranose, D-Pinitol, Tyrosine, Glucopyranose, d-Gluconic acid, Oxaloacetic acid, d-Glucuronic acid, Ferulic acid, Caffeic acid, Sucrose, mono palmitin	Caffeic acid, ferulic acid and D-pinitol	Hydrocinnamic acid, phenol, and inositol	Cell migration	[86, 87]
3	*Aegle marmelos*	Rutaceae	Anti-diarrheal, gastroprotective, antiviral, antidiabetic, anti-ulcerative colitis, cardioprotective, free-radical scavenging, and hepatoprotective	Hydroalcohol	Flower	In vivo: full thickness wound model in Sprague-Dawley rat In vitro: HaCaT, Hs68, RAW264.7 cell line	Betadine	HPLC	Cineol, eugenol, cuminaldehyde, aegelin, HDNC, luvangetin	1-Hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde (HDNC)	Flavonoid	Keratinocytes migration by Akt, beta-catenin, and ERK pathway	[88, 89]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
4	*Carthamus caeruleus*	Asteraceae	Hair growth and wound healing	Methanol	Root	In vivo: linear incision wound model in Wistar rat	Madecasol	GC-MS	Furfural, 2, 3-dihydro-3,5-dihydroxy-6-methyl-4 H-pyran-4-one, 7-Oct-enoic caid, 5-HMF, 1-pen-tadecene, Caryophyllene oxide, 13- tetradece-11-yn-1-ol, 1-octadecene, 8-methylene-3-oxatricy-clononane, tetradecanoic acid, 2-ethyl hexyl trans-4-methoxycinnamate, hexadecenoic acid, 1–2 benzene dicarboxylic acid, gamma sitosterol	Palmitic acid, 2-ethyl-hexyl phthalate, and 5-(hydroxymethyl)-2-furan carboxaldehyde	Fatty acid, Phthalate, and alcohol	Reduced inflamma-tion and oxidation	[90]
5	*Sasa veitchii*	Poaceae	Antimi-crobial, antidia-betic, and antihy-pertensive activity	Aqueous	Crude	In vivo: mice wound model In vitro: HaCaT cell line	No positive control	-	-	-	-	Promoted cutaneous aquaporin-3 expression	[91, 92]
6	*Gynura procumbens*	Asteraceae	Renal pro-tective, antirheu-matic, antiar-thritic, antidia-betic, and antihy-pertensive activity	Ethanol	Crude	In vivo: streptozo-tocin-induced diabetic model in mice	Solcoseryl jelly	TLC	Stigmasterol, kaempferol and quercetin	Stigmasterol, kaempferol and quercetin	Tetracyclic triterpenes and flavo-noids	Cell prolif-eration and migration	[93, 94]
7	*Reynoutria japonica*	Polygonaceae	Used in Inflam-mation, jaundice and hyper-lipemia	Ethanol	Rhizome	In vitro: HGF cell line	Betulinic acid	HPLC-MS	Malic acid, citric acid, procyanidin, catechin, epicatechin, piceatan-nol glucoside, Piceid, epicatechin-3-O-gallate, Resveratrol derivative, Aloesone hexoside, Emodin-glucoside, Lapa-thoside D, Torachrysone-hexoside, Torachrysone, Physcionin, Hydropipero-side, Phenylpropanoid-derived disaccharide esters, Vanicoside B, Questin, Physcion	Resveratrol, Procyanidins	Stillbene and flavonoid	Cell prolifera-tion, migra-tion, and increased collagen III synthesis	[95, 96]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
8	*Sorocea guilleminina Gaudich*	Moraceae	Wound healing, anti-inflammatory, and diuretic activity	Aqueous	Leaf	In vivo: excision and incision wound model in rat In vitro: fibroblastic N3T3 cell line	Fitoscar ointment	LC-MS	Salicylic acid, Cinnamic acid, Gallic acid, Siringic acid, Pinocembrin, Chlorogenic acid, Isoquercitrin, Epicatechin	Salicylic acid, gallic acid, pinocembrin and isoquercitrin	Carboxylic acid, Phenol and Flavonoid	Cell proliferation, increased collagen III synthesis, and collagen rearrangement	[97]
9	*Lafoensia pacari*	Lythraceae	Wound healing, antiulcer, antifungal, and gastroprotective activity	Hydroalcohol	Leaf	In vivo: excision model in albino mice In vitro: CHO-K1 and L929 cell line	Madecassol	ESI-MS	ellagic acid, punicalagin, punicalin, kaempferol, Quercetin-3-O-xylopyranoside, Quercetin-3-O-rhamnopyranoside	ellagic acid, punicalagin, punicalin, kaempferol, Quercetin-3-O-xylopyranoside, Quercetin-3-O-rhamnopyranoside	Ellagic acid derivatives and Flavonoids	Cell proliferation and migration rate of fibroblasts and higher expression of p-ERK 1/2 protein	[98]
10	*Panax ginseng*	Araliaceae	Anti-allergic activity	Aqueous (Hot)	Root	In vivo: full-thickness skin wound in Sprague–Dawley rat	Placebo	HPLC	Ginsenoside Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, Rg2s, Rg3s, Rg3r	Ginsenoside	Steroid glycoside	Increased expression of TGF-β, VEGF, MMP-1 and MMP-9	[99]
11	*Coccinia grandis*	Cucurbitaceae	Relieving insect bite itching and swelling	Methanol	Leaf	In vitro: HFb and HaCaT cell line	Allantoin	LC-ESI-MS/MS	Rutin, quercetin-hexoside deoxyhexoside, kaempferol-3-O-glucoside, oleuropein and ligstroside	Rutin, quercetin-hexoside deoxyhexoside, kaempferol-3-O-glucoside, oleuropein and ligstroside	Flavonoids and secoiridoids	Reduced hydrogen peroxide-induced oxidative stress by increasing cell survival rate	[100, 101]
12	*Peucedanum ostruthium*	Apiaceae	stimulant, stomachic, and diuretic, treats rheumatic, chronic inflammatory, skin problems, and musculoskeletal diseases	Hydroalcohol	Rhizome and Leaf	In vitro: HaCaT, L929 fibroblast cell line	Allantoin	LC-ESI-MS	Caffeoylquinic acid, p-Coumaroylquinic acid, Feruloylquinic acid, p-Coumaroyl glucose, Quercetin-3-O-rutinoside, Hesperidin, Quercetin-3-O-(6″acetyl-glucoside), 3,7-Dimethylquercetin, Oxypeucedanin-hexoside, Kaempferol 3-O-acetyl-glucoside, Osthenol-7-O-glucoside, Oxypeucedanin, Ostruthol, Isoimperatorin, Imperatorin, Ostruthin	Caffeoyl and feruloylquinic derivatives, ostruthin, and isoimperatorin, Quercetin	Phenols, coumarins, flavonoids	Inhibit cyclooxygenase and lipoxygenase activity	[102]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
13	*Artemisia absinthium*	Asteraceae	Used to treat gastrointestinal ailments, helminthiasis, anemia, insomnia, bladder diseases, wounds, and fever	Methanol (Hot)	Leaf	In vivo: wound model in Wistar rat	Povidone Iodine cream	GC-MS	Epiyangambin, flavone, octadecanoic acid, 2,3-dihydroxypropyl ester, palmitic acid β - monoglyceride, á-D-manno-furanoside, camphor, and terpineol	Stearic acid and palmitic acid	Fatty acid	Modulated cytokine networks and apoptosis markers levels	[103, 104]
14	*Portulaca oleracea*	Portulacaceae	Relieving fever, dysentery, diarrhea, carbuncle, eczema, and hematochezia	Hydroalcohol	Leaf	In vivo: deep tissue pressure injury model in mice In vitro: HaCaT and HUVEC cell line	No positive control	-	Hyperoside, kaempferol and quercetin-3-O-α-L-arabino pyranoside	-	-	Increased new blood vessels, collagen deposition, and re-epithelization and decreased inflammatory infiltration	[105, 106]
15	*Premna integrifolia*	Lamiaceae	Used in the treatment of bronchitis, diabetes, edema, chyluria, dyspepsia, inflammation, liver problems, constipation, piles, and fever	Standardized extract procured	Crude	In vivo: wound model In vitro trypsinized cells	Povidone-iodine ointment	-	-	-	-	Cell proliferation, migration, and keratinization	[107]
16	*Urtica dioica*	Urticaceae	Anti-epileptic and treat boils and blisters	Methanol	Crude	In vivo: full-thickness wound model in rat In vitro: HEK-293 and HaCaT cell line	Madecassol	1 H NMR	Saponins, flavonoids, carbohydrates, ketoses, resins, and coumarins		Saponins, flavonoids, carbohydrates, ketoses, resins, and coumarins	Cell proliferation	[108, 109]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
17	*Clinacanthus nutans*	Acanthaceae	Anti-venom for snake, scorpion, and insect bites, treat skin rashes, Pruritic rash, burn, inflammation	Sequential extraction with hexane, chloroform, and ethanol	Leaf	In vitro: RAW 264.7 and HGF cell line	TLC, FTIR, HRES-MS	Genistein	Purpurin-18 phytyl ester	Purpurin-18 phytyl ester	Dihydroporphyrin	Inhibit lipopolysaccharide (LPS)-induced NO production	[110, 111]
18	*Cinnamomum verum*	Lauraceae	Anti-diabetic, antimicrobial skin infections and anticancer activity	Hydroalcohol	Bark	In vivo: Two circular full-thickness excisional wound mouse model	No positive control	HPLC	Caffeic acid, epicatechin, quercetin, coumarin, 2-hydroxyl cinnamaldehyde, cinnamyl alcohol, cinnamic acid, cinnamaldehyde, 2-methoxy cinnamaldehyde, eugenol	Cinnamaldehyde and 2-hydroxyl cinnamaldehyde	Flavonoid	Fibroblast proliferation, collagen deposition, re-epithelialization, and increased expression of cyclin D1, IGF1, GLUT 1	[112]
19	*Zataria multiflora*	Lamiaceae	Antibacterial and antioxidant properties	Essential oil	-	In vivo: full-thickness excisional skin mouse model	Mupirocin ointment	GC-MS	α-Thujene, α-Pinene, Camphene, β-Pinene, 3-Octanone, Myrcene, 3-Octanol, α-Phellandrene, α-Terpinene, p-Cymene, Limonene, 1,8-Cineole, γ-Terpinene, cis-Sabinene hydrate, Terpinolene, Linalool, Borneol, Terpinen-4-ol, α-Terpineol, Thymol, Carvacrol, Caryophyllene, Aromadendrene, α-Humulene, Viridiflorene, Spathulenol	Thymol, p-cymene, γ-terpinene, carvacrol	Monoterpene and monoterpene phenol	Increased expression of TGF-β, IL-10 IGF-1, FGF-2, and VEGF	[113]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
20	*Glycyrrhiza glabra*	Fabaceae	Hepatoprotective, anti-inflammatory, and flavoring agent	Ethanol	Root	In vivo: cutaneous wound model in Wistar rat	No positive group	UPLC-PDA-MS/MS	Licoagroside B, Kaempferol-3-O-rutinoside, HBMA, Isoshaftoside, Isoshaftoside, Liquiritin derivative, Glycyroside, Butein-4-O—glucopyranosyl-apiofuranoside, Licorice glycoside, Isoliquiritin, Licochalcone B, Isoliquiritigenin, Pinocembri, Echinatin, Glycyrrhizin, Formononetin, Prenylated flavonoid, Esculin, Glabrone	Glycyrrhetinic acid, Glycyrrhizic acid, glabridin and licochalcone A	Pentacyclic triterpenoid, Triterpenoid saponin, Hydroxyisoflavan and Chalconoid	Re-epithelialization and collagen synthesis	[114]
21	*Derris scandens*	Fabaceae	Analgesic, anti-inflammatory, antimicrobial, antioxidant, and anticancer	Hydroalcohol	Stem	In vitro: HSF cell line	Ascorbic acid	HPLC	Genistein, lupeol	Genistein, lupeol	Flavonoid and Pentacyclic lupane-type triterpenes	Cell migration lowered oxidative stress and proinflammatory markers	[115]
22	*Astragalus floccosus*	Leguminosae	Immunomodulatory, antiviral, hepatoprotective, antiperspirant, and anti-diabetic activity	Methanol	Root	In vitro: HDF cell line In vivo: full thickness wound model in rats	Silver sulfadiazine	LCMS	Calycosin-7-O-beta-D-glucoside, 7,4′-Dihydroxy-3′-methoxyflavone 7-glucoside, 3′-O-Methylorobol-7-O-glucoside, Quercetin derivative, Kaempferol derivative and Formononetin	Calycosin-7-O-beta-D-glucoside and Formononetin	Isoflavonoid	Fibroblast proliferation and epithelization	[116]
23	*Launaea procumbens*	Asteraceae	Used in skin problems, tumors, and dysentery, for wound healing activity, painful urination, and reproductive diseases	Methanol	Aerial parts	In vivo: excision wound model in rabbit	MEBO ointment	LC-HRMS	Orientin, Loganic acid, Touruosamine, Esculin, Vulgaxanthin-I, Chlorogeniacidid, Cimigenol, Isobetanidin, Glycerol 1-alkanoates, Bullatacinone, Phytol, Fumaflorine, Catechin-5-o- glucoside	Orientin	Flavonone	Increased expression of TGF-β and decreased levels of TNF-α and IL-1β	[117]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
24	*Verbascum sinaiticum*	Scrophulariaceae	Curing wounds, abdominal dropsy, anthrax, diarrhea, and fungal infections	Methanol	Leaf	In vivo: excision and Incision wound model in Wistar rats	Nitrofurazone ointment	LC-MS	Quercetin, rutina harpagoside, protocatechuic acid, gentisic acid, *p*-coumaric acid, ferulic acid, salicylic acid, and rosmarinic acid	-	Saponins, flavonoids, terpenoids	Wound contraction and epithelialization	[118, 119]
25	*Astragalus membranaceus*	Fabaceae	Reduce swelling, drain pus, and eradicate toxins	Ethanol	Root	In vitro: HSF cell line In vivo: full-thickness excision wound in mouse	Jingwanhong ointment	Ion-exchange chromatography	APS2-1	APS2-1	Novel polysaccharide	Increased expression of TGF-β1, bFGF ,and EGF	[120]
26	*Marantodes pumilum*	Primulaceae	Used in female reproductive-related problem	Distilled water	Leaf and Root	In vivo: excision wound model in Sprague-Dawley rats	Acriflavine	LC-MS/MS	Cinnamic acid, quinic acid, gallic acid, caffeic acid, ellagic acid, p-hydroxybenzoic acid, catechin, myricetin derivative, protocatechuic acid hexoside	Gallic acid, ellagic acid, and caffeic acid,	Phenolic compound	Fibroblast proliferation, and collagen formation	[121]
27	*Artocarpus communis*	Moraceae	Antiinflammatory, antitumor, antimicrobial, and antioxidant activity	Dichloromethane	Heartwood	In vitro: HaCaT, GM05386, HSF cell line **In-vivo** excisional wound model in mice	No positive control	Successive extraction and HPLC	Artocarpin	Artocarpin	Prenylated flavonoid	Fibroblast proliferation and collagen synthesis by activating JNK, Akt, and P38 pathway	[122]
28	*Gliricidia sepium*	Fabaceae	Anti-inflammatory, analgesic, and antimicrobial activity	Powder leaves to form an ointment	Leaf	In vivo: wound model Wistar rats	Commercial wound healing agent	-	-	-	-	Lowered the expression of IL-1β and IL-6	[123]
29	*Olea europaea*	Oleaceae	Relieving Skin diseases and wounds	Ethyl alcohol	Leaf	In vivo: full thickness incision wound model in Balb/c mice	No positive group	Solvent extraction and HPLC	Oleuropein	Oleuropein	Glycosylated seco- iridoid	Increased VEGF, collagen deposition and re-epithelisation	[124]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
30	*Apium graveolens*	Apiaceae	Used in Skin infections, chronic ulcers, antioxidant, and antimicrobial activity	Methanol	Dried celery	In vivo: wound model in Sprague Dawley rat	Positive control	-	-	-	-	Decreased inflammatory cells and increased expression of CK-17 to promote proliferation and epithelization	[125]
31	*Euphorbia hirta*	Euphorbiaceae	Analgesic, antiinflammatory, antidiabetic and antimicrobial activity	Methanol	Leaf	In vivo: excision wound model in Wistar rat In vitro: HDF cell line	Gentamicin sulfate	-	Euphorbin, A, euphorbin-B, euphorbin-C, euphorbin-E, Quercitrin, myricitrin, rutin, kaempferol, quercetin, gallic acid and protocatechuic acid, β-amyrin, 24-methylene-cycloartenol, β-sitosterol, heptacosane, nonacosane, shikimic acid, camphol and quercitol	-	-	Collagen production and fibroblast proliferation	[126]
32	*Blumea balsamifera*	Blumea	Antirheumatic and used to treat dermatitis, beriberi, lumbago, snake bites, and bruises	Methanol	Leaf	In vivo: excisional wound in Sprague-Dawley rats	Jing Wan Hong ointment	UPLC Q-TOF-MS/DAD	DiCQA, Rutin, 2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4 H-chromen-3-yl6-O-(6-deoxy-α-L-mannopyranosyl)-D-glucopyranoside, Hyperoside, Isoquercitrin, Myricitrin, Flavonone derivative, Luteolin and its derivative, Chrysoeriol, Kaempferide, Hydranngetin, Diosmetin, Blumeatin, Ayanin	Rutin, Hyperoside, Isoquercitrin, Myricitrin, Luteolin Chrysoeriol	Flavonoid	Capillary regeneration and re-epitheliali-zation	[127]
33	*Libidibia ferrea*	Fabaceae	Antirheumatic, anticancer, antidiabetic, and gastroprotective activity	Ethanol	Leaf, fruit, and flower	In vivo: excision model in dogs	Commercial veterinary ointment (allantoin and zinc oxide)	TLC	Rutin	Rutin	Hydrolysable tannins and flavonoids	Wound retraction by fibroplasia	[128]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
34	*Astragalus membranaceus*	Leguminosae	Antioxidant, anti-inflammatory, antidiabetic and hepatoprotective activity	Ethanol	Root	In vitro: HDF and HaCaT cell line In vivo: wound model in mice	No positive control	Solvent extraction and silica gel chromatography	AS-I, AS-II, AS-III, AS-IV, AS-VI, Iso AS-I, Iso As-II, cycloastragenol-6-O-beta-D-glucoside	Astragaloside VI and cycloastragenol-6-O-beta-D-glucoside	Triterpenoid saponin	Proliferation and migration of skin cells by EGFR/ERK signaling pathway.	[129]
35	*Urtica simensis*	Urticaceae	Antirheumatic and antiarthritic activity, treat wounds such as burns and skin rash	Methanol	Leaf	In vivo: excision, incision, and burn wound model in mice	Nitrofurazone ointment	-	-	-	-	Fibroblasts proliferation	[130]
36	*Dipsacus asper*	Dipsacaceae	Analgesic and anti-inflammatory activity and treat spermatorrhoea	-	Root	In vivo: Full-thickness wound model rat In vitro: HUVEC cell line	bFGF	-	Asperosaponin VI (procured)	Asperosaponin VI	Triterpene saponin	Enhanced angiogenesis by up-regulating the HIF-1α/VEGF pathway	[131]
37	*Haplophyllum tuberculatum*	Rutaceae	Antiseptic, antiarthritic, antidiabetic, antihypertensive, antiulcer, and analgesic activity	Hydroalcohol	Aerial part	In vivo: Burn wound model in rat	Madecassol ointment	LC-MS	p-Coumaric acid, Quercetin-3-O-glucoside, Kaempferol-3-O-glucose, Isorhamnetin-7-O-pentose, Luteolin 7-O-glucoside, Kaempferol-3-O-glucuronic acid, Protocatechuic acid, Salicylic acid, Gentisic acid, Synaptic acid, Ferulic acid, Epigallocatechin, Procyanidins, Rutin, Naringin	p-Coumaric acid, derivative of Quercetin, Kaempferol, Isorhamnetin, Luteolin, Rutin, Procyanidins, Epigallocatechin	Phenolic compound	Regulated growth factors and cytokines	[132]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
38	*Oroxylum indicum*	Bignoniaceae	Antidiabetic and anticancer activity	Ethanol	Leaf	In vitro: HaCaT cell line In vivo: excisional wound model in rat	Sudocrem cream	LC-TOF-MS/MS	Ginkgetin, Orientin, Chrysin, Pinoquercetin, Cupressuflavone, Puerarin xyloside, Forsythiaside, Phlorizin chalcone, Azelaic acid, Luteolin 7-O-glucuronide, Naringenin chalcone, Paederoside,	Orientin, Chrysin, Pinoquercetin, Cupressuflavone, Puerarin xyloside, Forsythiaside and Paederoside	Flavonoid and glycoside	Wound contraction	[133]
39	*Hydnophytum formicarum*	Rubiaceae	Antioxidant, anti-inflammatory, and antimicrobial activity	Ethanol	Whole	In vivo: Excision wound model Sprague–Dawley rats	No positive control	-	-	-	-	Promoted angiogenesis and re-epithelialization	[134]
40	*Siegesbeckia orientalis*	Asteraceae	Antiarthritic, antimalarial, analgesic and cardioprotective activity	-	-	In vivo: excision wound model in Wistar rats In vitro: L929 cell line	No positive control	-	Kirenol (procured)	-	Diterpenoid	Reduced the levels of NF-κB, COX-2, iNOS, MMP-2 and MMP-9	[135]
41	*Dittrichia viscosa*	Asteraceae	Anti-inflammatory, antispasmodic, antiseptic, antirheumatic, treat wound and hemorrhoids	Ethanol	Leaf	In vivo: circular full-thickness wound model Swiss Webster mice	Vehicle is used as a positive control	HPLC-DAD-ESI/MS	Dicaffeoylquinic isomers, quercetin derivatives, isoorientin, apigenin-glucoside, myricetin, and isorhamnetin-O-glucuronopyranoside	Phenolic compounds and Caffeoylquinic Acid	Phenol	Re-epithelialization	[136]
42	*Panax ginseng*	Araliaceae	Hepatoprotective and vasoprotective activity	Procured	Root	In vivo: full-thickness wound model Wistar rats	No positive control	-	Ginsenosides	Ginsenosides	Steroid glycosides	Increased expression of VEGF	[137]
43	*Actinidia deliciosa*	Actinidiaceae	Anti-inflammatory, anticancer, and cardioprotective activity	Ethanol	Fruit	In vitro: HGF cell line	No positive control	-	-	-	Vitamin C, carotenoids, tannins, and saponin	Fibroblast migration and angiogenesis	[138]

Table 1 (continued)

S. No.	Herbs	Family	Traditional uses	Extract	Plant part used	Study model type	Positive control	Analytical method for isolation	Isolated compound	Most active compound for activity	Category of most active compounds for activity	Mechanism	Reference
44	*Althaea officinalis*	Malvaceae	Analgesic, Antiinflammatory, treat respiratory diseases, skin ailments and digestive diseases	Hydroalcohol	Leaf	In vivo: Excision wound model in rat	Zinc oxide ointment	-	-	-	-	Accelerated wound healing processes	[139]
45	*Aster koraiensis*	Asteraceae	Used to treat chronic bronchitis, pneumonia, and pertussis	Ethanol	Aerial parts	In vivo: Wound model in male Sprague Dawley rat In vitro: HaCaT cell line	No positive control	HPLC	chlorogenic acid and 3,5-di-O-caffeoylquinic acid	chlorogenic acid and 3,5-di-O-caffeoylquinic acid	Phenol	Inhibited expression of MMP-2/9	[140]
46	*Amphimas pterocarpoides*	Leguminosae	Antimalarial, antiarthritic, anti-inflammatory, analgesic, and used to treat respiratory tract infections	Methanol	leaf and stem bark	In vivo: excision model in Sprague-Dawley rats	Silver sulphadiazine	HPLC	-	-	Tannin, triterpenoid, phytosterol, flavonoid, saponin and coumarin	Wound contraction	[141]
47	*Curcuma longa*	Zingiberaceae	Anti-inflammatory, antioxidant, and antibacterial activity	-	Rhizome	In vitro: HGF cell line	-	-	Curcumin	Curcumin	Diarylheptanoid	Upregulated expression of KGF-1 and EGFR	[142]
48	*Poincianella pluviosa*	Fabaceae	Antimalarial and wound healing activity	Ethanol	Bark	In vivo: wound model in Wistar rat	No positive control		-	-	-	Collagen formation and re-epithelialization	[143]

Table 2 Polyherbal formulation for wound management

S.No.	Herbal extract	Composition	Family	Part of the plant	Experimental model	Control	Chemical constituents	Application	Reference
1	Chinese herb microneedle patch	*Premna microphylla*	Lamiaceae	Leaf	In vivo: excision wound model in rat In vitro: NIH-3T3 cell line	Microneedle patch without asiatic acid	Pectin and amino acid	Relieved heat, detoxicated, caused detumescence, and treated hemostatis.	[148]
		Centella asiatica	Apiaceae	Leaf			Asiatic acid	Encouraged the expression of important growth factor genes in fibroblasts	
2	Polyherbal combination	*Punica granatum*	Punicaceae	Flower	In vivo: excision wound model in rat	No Control group (different concentrations of single and combinational herbs were used to compare with each other)	Tannins, punicalagin, and ellagic acid, gallic acid, maslinic, ursolic acid, and asiatic acid	Strong antioxidant activity and anti-inflammatory activity of the combination	[149]
		Matricaria chamomilla	Asteraceae	Flower			Quercetin, apigenin, coumarins, and terpenoids, α-bisabolol and chamazulene		
3	San Huang Powder	*Rheum officinale*	Polygonaceae	Stem and root	In vivo: burn wound model in female Lee-Sung pigs In vitro: LPS-induced HMEC-1 and RAW264.7 cell line	Different combination of herbs was used as comparator for each other	Chrysophanol	Reduced the production of inflammatory mediators such as cytokines and interleukins.	[150]
		Scutellaria pekinensis	Lamiaceae	Root			Chrysin		
		Phellodendron amurense	Rutaceae	Bark			Berberine hydrochloride		
		Coptis chinensis	Ranunculaceae	Rhizome			Berberine hydrochloride		
4	Chinese medicine ANBP	*Agrimonia eupatoria*	Rosaceae	Formulation was procured from the market	In vivo: full-layer skin defect model in rat	Control group without treatment	-	Facilitated the wound healing process and reduced the wound healing time.	[151]
		Nelumbon nucifera	Nelumbonaceae						
		Boswellia carteri	Burseraceae						
		Typha orientalis	Typhaceae						

Table 2 (continued)

S.No.	Herbal extract	Composition	Family	Part of the plant	Experimental model	Control	Chemical constituents	Application	Reference
5	Abnormal Savda Munziq	*Lavandula angustifolia*	Lamiaceae	Formulation was procured from market	In vivo: comb burn model in Sprague-Dawley rat	Control group without treatment	-	Reduced oxidative stress and apoptosis	[152]
		Foeniculum vulgare	Apiaceae						
		Anchusa italica	Boraginaceae						
		Euphorbia humifusae	Euphorbiaceae						
		Melissa officinalis	Lamiaceae						
		Adiantum capillusveneris	Pteridaceae						
		Glycyrrhiza uralensis	Fabaceae						
		Cordia dichotoma	Boraginaceae						
		Ziziphus jujuba	Rhamnaceae						
		Alhagi pseudoalhagi	Fabaceae						
6	AnoacH/PiloTab	*Mimosa pudica*	Fabaceae	Formulation was procured from market	In vivo: human hemorrhoid and fistula specimen	Vehicle control	-	Decreased the migration of immunological cells and mesenchymal cells	[153]
		Euphorbia hirta	Euphorbiaceae						
		Messua ferrea	Calophyllaceae						
		Berberis aristata	Berberidaceae						
7	Japanese herbal medicine hange-shashinto	*Pinellia ternata*	Araceae	Tuber	In vitro: HOK Cell line	Vehicle control	-	Improved the migration of human oral keratinocytes.	[154]
		Scutellaria pekinensis	Lamiaceae	Root			Baicalin, baicalein, wogonin		
		Zingiber officinale	Zingiberaceae	Rhizome			Shogaol, gingerol		
		Glycyrrhiza glabra	Fabaceae	Root			Glycyrrhizin, glycyrrhetinic acid, liquiritin, isoliquiritin, liquiritin apioside, liquiritigenin, isoliquiritigenin		
		Ziziphus jujuba	Rhamnaceae	Fruit			-		
		Panax ginseng	Araliaceae	Root			-		
		Coptis occidentalis	Ranunculaceae	Rhizome			-		

Table 2 (continued)

S.No.	Herbal extract	Composition	Family	Part of the plant	Experimental model	Control	Chemical constituents	Application	Reference
8	Novel Distillate from Fermented Mixture	*Angelica gigas*	Apiaceae	Root	In vivo: ultraviolet B-induced skin damage in mice	Vehicle control	2, 6, 10-trimethyldodecane, 2, 6, 11, 15-tetramethylhexadecane, n-heptadecane, n-docosane, Siloxane derivatives	Reduced expressions of TNF-alpha and IL-1	[155]
		Lonicera japonica	Caprifoliaceae	Bloom					
		Dictamnus dasycarpus	Rutaceae	Root					
		Dioscorea oppositifolia	Dioscoreaceae	Root					
		Ulmus davidiana	Ulmaceae	Bark					
		Hordeum vulgare	Gramineae	Seed					
		Xanthium strumarium	Asteraceae	Seed					
		Cnidium officinale	Apiaceae	Root					
		Houttuynia cordata	Saururaceae	Leaf					
9	Traditional Chinese medicine ARCC	*Angelica Sinensis*	Apiaceae	Root	In vivo: full-thickness wound model in mice and also assessed in diabetic patients with gangrene	Control without treatment	-	Re-epithelization, vascularization and Increased levels of TGF-β1 and CD31 cells	[156]
		Radix Rehmanniae	Scrophulariaceae	Root					
10	Herbal ointment blend	*Punica granatum*	Punicaceae	*Fruit*	In vivo: excision wound model in Wistar rat	Gentamycin	Ellagic tannins, ellagic acid and gallic acid	Increased rate of wound contraction and decreased rate of epithelisation period	[157]
		Commiphora myrrha	Burseraceae	Stem resinous exudate			Furanosesquiterpenoid, water-soluble and alcohol-soluble resins		
		Laurus nobilis	Lauraceae	Leaf			Linalool, p-cymene, α-pinene, limonene and β-pinene		
11	Herbal cream	*Pelargonium graveolens*	Geraniaceae	Flower	In vivo: diabetic foot ulcers rat animal model	Placebo without treatment	β-citronellol, geraniol, and phenyl ethyl alcohol	Anti-ulcerogenic effect and tissue regeneration	[158]
		Oliveria decombens	Apiaceae	Flower			Thymol, γ-terpinene, croweacin, and sabinene		

Table 2 (continued)

S.No.	Herbal extract	Composition	Family	Part of the plant	Experimental model	Control	Chemical constituents	Application	Reference
12	Polyherbal formulation	*Elephantopus scaber*	Asteraceae	Leaf	In vivo: excision, incision and burn wound model in Swiss albino mice	Povidone iodine	Deoxyelephantopin	Increased antioxidant activity that surges the rate of wound contraction	[159]
		Clinacanthus nutans	Acanthaceae	Leaf			lupeol, *β*-sitosterol, stigmasterol, botulin, and myricyl alcohol, vitexin, isovitexin, shaftoside, isomollupentin 7-O-*β*-glucopyranoside, orientin, and isoorientin		
13	Jinchuang Ointment	*Calamus draco*	Arecaceae	Resin	In vitro: HaCaT and HUVEC cell line, also assessed on nonhealing diabetic wounds in patients	VEGF	Dracorhodin perchlorate, Catechin, Epicatechin, Acetyl-11-keto-β-boswellic acid, (E)-Guggulsterone	Stimulated angiogenesis, cell proliferation, and cell migration	[160]
		Cinnamomum camphora	Lauraceae	Wood					
		Uncaria gamber	Rubiaceae	Aqueous extract from leaf and shoot					
		Boswellia serrata	Burseraceae	Resin					
		Commiphora myrrha	Burseraceae	Resin					
14	Polyherbal formulation	*Vitex negundo*	Verbenaceae	Leaf	In vitro: L929 and HaCaT cell line	Cipladine	Flavonoids, phenols, and tannin	Skin regeneration and collagen synthesis and increased levels of antioxidants (catalase and GSH)	[161]
		Emblica officinalis	Euphorbiaceae	Fruit					
		Tridax procumbens	Asteraceae	Leaf					
15	Herbal Mixture	*Adiantum capillus-veneris*	Adiantaceae	Leaf	In vivo: streptozotocin-induced diabetic rats wound model in Wistar rat	Vaseline control	Tannin, gallic acid, resin, flavonoid, coumarin and anthraquinone	Modulated the expression of TGF-b1, MMP-3/6, IL-6 and TNF-*α*	[162]
		Commiphora molmol	Burseraceae	Resin					
		Aloe barbadensis	Liliaceae	Leaf					
		Lawsonia inermis	Lythraceae	Leaf					
16	Aloe vera-based extract of *Nerium oleander*	*Nerium oleander*	Apocynaceae	Flower	In vivo: Partial-thickness second-degree burn injury in Wistar albino rat	Silverdin	-	Modulated the levels of MDA, GSH, MPO, TNF-α, IL-1β and DNAT	[163]
		Aloe barbadensis	Liliaceae	Leaf					

Table 2 (continued)

S.No.	Herbal extract	Composition	Family	Part of the plant	Experimental model	Control	Chemical constituents	Application	Reference
17	Thai herbal formulation	*Centella asiatica*	Apiaceae	Leaf	In vitro: HaCaT cell line	Untreated cells	-	Upregulate the expression of TIMP-1, VEGF, and TGF-β and downregulated the expression of TNF-α, IL-6, and MMP-9	[164]
		Curcuma longa	Zingiberaceae	Rhizome					
		Zingiber cassumunar	Zingiberaceae	Rhizome					
		Garcinia mangostana	Guttiferae	Peel					
		Zingiber officinale	Zingiberaceae	Rhizome					
		Eleutherine americana	Iridaceae	Rhizome					
		Piper nigrum	Piperaceae	Seed					
		Senna alata	Leguminosae	Leaf					
		Areca catechu	Arecaceae	Fruit					
18	Iranian traditional medicine	*Malva sylvestris*	Malvaceae	Leaf	In vivo: Second-degree burn wound in rat	Silver sulfadiazine	Phenol and tannins	Re-epithelialization with remarkable neovascularization	[165]
		Solanum nigrum	Solanaceae	Leaf					
		Rosa damascena	Rosaceae	Petal					
19	Herbal formulation	*Adiantum capillus-veneris*	Adiantaceae	Leaf	In vitro: mouse skin fibroblasts cell line	Untreated cell	Tannin, gallic acid, resin, flavonoid, coumarin and anthraquinone	Improved the gene expression of TGF-β1 and VEGF-A	[166]
		Commiphora molmol	Burseraceae	Resin					
		Aloe barbadensis	Liliaceae	Leaf					
		Lawsonia inermis	Lythraceae	Leaf					
20	Tuo-Li-Xiao-Du-San	*Radix Angelica sinensis*	Apiaceae	Root	In vivo: full-thickness excision wound in Sprague-Dawley rat	Untreated group	-	Reduced infiltration of neutrophils and macrophages and enhanced angiogenesis, and collagen formation	[167]
		Radix Astragali	Fabaceae	Root					
		Angelica dahurica	Apiaceae	Root					
		Gleditsia sinensis	Fabaceae	Thorn					
21	Traditional Chinese Medicine Herbal Mixture Sophora flavescens	*Sophora flavescens*	Fabaceae	Root	In vivo: rat model of perianal ulceration	Potassium permanganate solution	-	Inhibited pro-inflammatory cytokines PGE2 and IL-8	[168]
		Phellodendron amurense	Rutaceae	Bark					
		Radix sanguisorbae	Rosaceae	Leaf					
		Scutellaria baicalensis	Lamiaceae	Root					
		Paeonia suffruticosa	Paeoniaceae	Root					
		Gardenia florida	Rubiaceae	Flower					
		Areca catechu	Arecaceae	Seed					
		Rheum officinale	Polygonaceae	Rhizome					
		Glycyrrhiza glabra	Fabaceae	Root					

Table 2 (continued)

S.No.	Herbal extract	Composition	Family	Part of the plant	Experimental model	Control	Chemical constituents	Application	Reference
22	Iranian Traditional Medicine	*Aloe barbadensis*	Liliaceae	Leaf	In vivo: excision wound model in rat	Tetracycline ointment	Boswellic acid, sesqui- and triterpenoids, glucomannan, arabinorhamnogalactan, pectic substances, e, and glucuronic acid-containing polysaccharide	Reduced inflammatory cells	[169]
		Commiphora myrrha	Burseraceae	Resin					
		Boswellia carteri	Burseraceae	Resin					
23	Kampo Medicine Rokumigan	*Rehmannia glutinosa*	Orobanchaceae	Root	In vitro: human gingival epithelial cell line	Aloe vera extract	-	Inhibited IL-6 secretion, fibroblast proliferation and migration	[170]
		Dioscorea batatas	Dioscoreaceae	Rhizome					
		Cornus officinalis	Cornaceae	Fruit					
		Poria cocos	Polyporaceae	Sclerotium					
		Paeonia suffruticosa	Paeoniaceae	Root cortex					
		Alisma orientale	Alismataceae	Root					
24	Topical herbal patch (Perio Patch)	*Centella asiatica*	Apiaceae	Formulation was procured from the market	In vivo: Full-thickness flaps in rat wound model	Placebo	-	Increased number of proliferating cells, collagen, and blood vessel formation	[171]
		Echinacea purpurea	Asteraceae						
		Sambucus nigra	Adoxaceae						

HDF Human dermal fibroblast, HaCaT: Human keratinocyte cell line, Hs68: human foreskin fibroblast cell line, RAW: macrophage cell line of mouse, *VLC* Vaccum Liquid Chromatography, *GC-MS* Gas chromatography- Mass spectroscopy, High-performance liquid chromatography, *HGF* human gingival fibroblast cell line, CHO-K1: Chinese hamster ovary epithelial cells, *ESI-MS* Electrospray ionization and mass spectrometry, *TGF- β1* transforming growth factor-β1, *VEGF* vascular endothelial growth factor, *MMP* matrix metalloproteinase, HFb: Human fibroblast cell line, Human embryonic kidney 293 (HEK-293) cells, *HSFs* Human skin fibroblast cell, *HUVECs* Human umbilical vein endothelial cells, bFGF: Human basic fibroblast growth factor, *HGF* Human gingival fibroblasts cell, HMC-1: Human mast cell, *HOKs* Human oral keratinocytes, OBA-9: Human gingival epithelial cell line

wound dressings [178]. Accelerated wound healing has also been associated with various substances including probiotics, food supplements, metal nanoparticles, polymers, and others [179].

Nanoparticle-based materials excel in wound healing due to their antibacterial properties, compatibility with the body, and ability to provide mechanical strength [180]. Soft nanoparticles, derived from organic sources, encompass liposomes, micelles, nanoemulsions, and polymeric nanoparticles [181]. When incorporated into hydrogels, they show potential for enhancing wound healing, offering improved texture, adherence, skin penetration, controlled drug release, and enhanced user comfort compared to traditional forms [182]. While epidermal growth factor (EGF) is highly effective in wound healing, challenges such as vulnerability to enzymatic degradation and maintaining therapeutic levels at the wound site have been significant hurdles. Encapsulating EGF within chitosan nanoparticles has shown promise, significantly increased wound closure rates, and promoted re-epithelialization and collagen deposition, ultimately contributing to a more efficient wound healing process [183]. The use of silver-modified chitosan and alginate-integrated nanoparticles in wound care provides supplementary benefits, including inhibiting bacterial growth, accelerating re-epithelialization, reducing inflammation, and enhancing collagen fiber deposition [184].

Hydrogels, known for their high-water content and excellent flexibility, stand out as highly promising materials for wound dressings. They regulate inflammation by scavenging free radicals, sequestering chemokines, and promoting macrophage transition, thereby promoting effective wound healing [185, 186]. Bioactive polypeptide hydrogel, composed of silk fibroin and angiogenic peptide, demonstrates impressive wound healing capabilities. It effectively reduces inflammation, stimulates angiogenesis, and leads to notable improvements in vessel formation and wound area reduction in a mouse skin wound model [187]. Peptide-based hydrogels, known for their biocompatibility and biodegradability, offer unique benefits in ligand-receptor recognition and stimulus-responsive self-assembly. This makes them highly promising for wound treatment [188]. Stimuli-responsive hydrogels, known as "smart hydrogels," have gained traction for diabetic wound healing as they possess the unique ability to alter mechanical properties, swelling behavior, hydrophilicity, and permeability to bioactive molecules in response to stimuli like temperature, pH levels, protease activity, and other biological factors [189].

Growth factors hold promise for tissue regeneration, but their instability and rapid clearance from tissues pose significant challenges [190]. Utilizing **liposomal** drug delivery systems to encapsulate and deliver growth factors has emerged as a potential solution to address these limitations [191]. Liposomes, composed of bilayered lipids, are versatile carriers capable of encapsulating both lipophilic and hydrophilic drugs. This makes them an excellent choice for delivering substances like curcumin effectively [192]. Citicoline-loaded chitosan-coated liposomes have demonstrated remarkable efficacy in enhancing skin wound healing in diabetic rats through a multi-faceted approach, including inflammation reduction, accelerated re-epithelization, enhanced angiogenesis, increased fibroblast proliferation, and improved connective tissue remodeling [193].

Polysaccharide **nanofibers**, created through electrospinning for wound dressings, hold significant promise for wound healing. They facilitate cell adhesion and proliferation in the wound bed and provide a permeable network structure that mimics the natural extracellular matrix [194]. Polymeric nanofibers are highly prospective as scaffolds for wound healing due to their ability to replicate the extracellular matrix [195]. Another promising avenue lies in hierarchical structure dressings. The top layer, made of hydrophobic polycaprolactone, prevents foreign microbe adherence. The middle layer comprises hydrophilic Janus nanofibers, produced through electrospinning. The bottom layer, consisting of hydrophilic gelatin, creates a moist nurturing environment for the wound [196]. A new class of nanomaterial, electrospun nanofibers, shows great promise in various biological processes. This includes tissue redesigning, using bandages and scaffolds for wound repair, and enabling multimodal drug delivery [197]. Utilizing hyaluronic acid-based nanofibers, which release nitric oxide due to their biodegradable nature, can help control inflammation and eliminate bacterial infections, making it valuable for wound healing [198].

Nanocomposite hydrogels incorporating **polymeric micelles** offer a dual advantage. They enhance the mechanical, self-healing, and chemical properties of hydrogels while also improving the in vivo stability of the micelles themselves [199]. Polymeric micelles have emerged as a highly auspicious drug delivery platform, particularly for poorly soluble, potent, and potentially toxic compounds. They efficiently encapsulate such molecules [200]. Their strong core-shell structure, exceptional kinetic stability, and innate ability to solubilize hydrophobic drugs make them stand out in this field [201]. Polymeric micelles form through the self-assembly of amphiphilic polymers with both hydrophilic and hydrophobic segments, occurring when polymer concentrations exceed critical micelle concentrations [202]. An innovative approach involves a novel hybrid hydrogel sheet, composed of polyethylene glycol-grafted chitosan and a reactive polymeric micelle. This combination enhances the material's functionality and improves therapeutic outcomes [203].

A newly developed composite biological dressing, composed of polyvinyl alcohol, carbon **nanotubes**, and epidermal growth factor, demonstrates a uniformly distributed structure. It effectively releases the epidermal growth factor

at a steady rate, creating an environment conducive to expedited wound healing [204]. Even at low concentrations, nanocomposites like carbon nanotube-loaded hydrogels can substantially enhance cell migration within the hydrogel, leading to accelerated tissue regeneration and wound healing [205]. Both single-wall and multi-wall carbon nanotubes, when complexed with chitosan, enhance the re-epithelization of wounds and contribute to increased fibrosis, indicating a positive effect on wound healing and tissue regeneration [206]. The incorporation of zinc oxide nanoparticles and multiwall carbon nanotubes as nanofillers in gellan gum alters the film microstructure, creating a sponge-like texture. This transformation enhances fluid uptake capacity, making it particularly beneficial for wound healing applications [207]. A gold-halloysite nanotubes-chitin composite hydrogel demonstrates dual benefits, exhibiting strong hemostatic activity while also promoting wound healing. This combination maintains low cytotoxicity, making it highly promising for biomedical applications [208]. Advancing the field of biomaterial scaffolds for effective wound healing involves microfabricating biomaterials into various forms, such as 3D-bioprinted structures, microneedles, and electrospun scaffolds [209].

Silicon-based wound dressings, developed into different kinds of scaffolds, are of interest due to their high biocompatibility and mechanical strength [210]. Non-crosslinked collagen-based bi-layered composite dressings have shown promise in promoting wound healing and expediting re-epithelialization [211]. Hydrogels, meticulously designed and prepared to possess specialized qualities, have demonstrated significant promise for skin wound healing [212]. Researchers are increasingly exploring the use of biopolymers in fiber production and their potential applications in wound treatment [213]. Biopolymers like alginate, chitosan, collagen, and hyaluronic acid are frequently employed in wound therapy due to their biocompatibility, biodegradability, and similarity to biomolecules recognized by the human system [214]. The rapidly evolving field of adjustable bioelectronics, with benefits including daily wear, affordability, and easy application, also presents a significant possibility for customized wound therapy [215]. Figure 4 and Table 3 provide examples of advancements in wound dressing technology that have contributed to enhanced wound healing capacity.

Discussion

Wounds, encompassing damage to skin integrity from incisions, burns, scalds, or specific lesions (e.g., diabetic foot ulcers, venous ulcers, pressure sores) [229], require proper treatment to prevent complications like bleeding, infection, inflammation, and scarring. These complications can impede angiogenesis and tissue regeneration [230]. Effective wound management plays a crucial role in healthcare, as prolonged healing periods can lead to increased burdens on institutions, healthcare professionals, patients, and their families, both economically and socially [231, 232]. Maintaining proper hygiene is foundational in wound care to minimize infection risks. Wound healing therapies, categorized into traditional and modern (skin grafts, modern dressings, bioengineered skin substitutes, and cell or growth factor therapies), vary in efficacy, clinical acceptance, and side effects notably. The wound management process begins with debridement, involving the removal of necrotic tissue, followed by the application of topical treatments like antimicrobial dressings and products containing silver sulfadiazine, which actively promote optimal wound healing [233]. In cases where wound healing stalls, advanced techniques become crucial. These include negative pressure therapy, growth factors, hyperbaric oxygen, and skin grafts [234]. However, it's important to note that these treatments may come

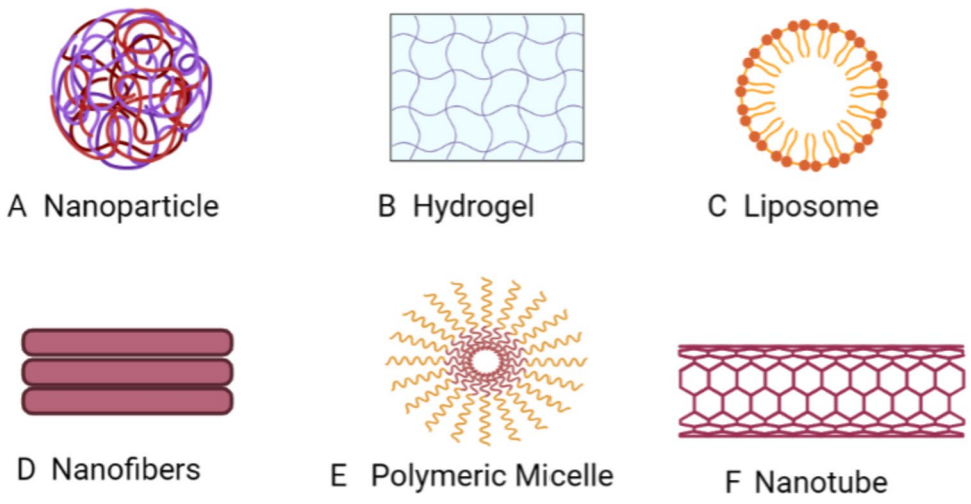

Fig. 4 Nanotechnology used as drug delivery systems (Created by Biorender.com)

Table 3 Wound dressing technology for enhanced healing capacity

S.No.	Herbs	Family	Plant part	Wound dressing technology	Model	Positive control used	Mechanism	Reference
1	*Scutellaria barbata*	Lamiaceae	Whole	**Nanoparticle**: Plant aqueous extract silver nanoparticles coated with cotton fabrics	In vitro: L929 fibroblast cell	Untreated cells	Increased cell proliferation and migration	[216]
2	*Pluchea indica*	Asteraceae	Leaf	**Nanoparticle**: Plant leaf extract nanoparticles oral spray formulation	In vitro: HO-1-N-1 cells	Untreated cells	Increased cell proliferation and migration	[217]
3	*Bletilla striata*	Orchidaceae	-	**Hydrogel**: Plant polysaccharide mixed with methylcellulose and methylparaben	In vitro: L929 fibroblast cell **In vivo: Full-thickness** wound model in rat	wound area treated with only sterile cotton as a control	High efficacy in wound healing	[218]
4	*Aloe barbadensis*	Asphodelaceae	Leaf	**Electrospun polymer fiber**: keratin, chitosan, and polycaprolactone-based- based matrix	In vitro: L929 fibroblast cell	Untreated cells	Increased cellular growth and adhesion	[219]
5	*Centella asiatica (Asiatic acid)*	Apiaceae	Active compound purchased from the market	**Hydrogel**: chitosan-polyvinyl alcohol-based microneedles of asiatic acid (herb-isolated compound)	In vivo: excision wound model in rat	Tegaderm	Increased wound closure rate	[220]
6	*Rosmarinus officinalis*	Lamiaceae	-	**Nanostructured lipid carrier**: Plant extract dissolved in Miglyol, Poloxamer	In vivo: full-thickness wound model in rat	Mupirocin ointment	Increasing the vascularization, fibroblast infiltration, re-epithelialization, collagen production	[221]
7	*Mentha piperita*	Lamiaceae	Leaf	**Nanocomposites**: γ-AlOOH (bohemite)-based nanocomposite of Au/γ-AlOOH-NC using Chitosan	In vivo: full-thickness wound model in a mouse	Mupirocin ointment	Decreased the expression of TNF-α, and increased the expression of Caspase 3, Bcl-2, Cyclin-D1, and FGF-2	[222]
8	*Moringa oleifera*	Moringaceae	Seed	**n-hexane Hydrogel**	In vivo: Excision and incision wound model in mouse	Povidone-iodine	Decreased the no. in inflammatory cells and accelerated tissue regeneration	[223]
9	*Cissus quadrangularis*	Vitaceae	-	**Electrospun Nanofiber**: CQ extract-loaded chitosan nanofibers were coated on chitosan/POSS nanocomposite sponge	In vitro: NIH/3T3 fibroblast cell line	Untreated cell	Induced cell proliferation and collagen deposition	[224]

Table 3 (continued)

S.No.	Herbs	Family	Plant part	Wound dressing technology	Model	Positive control used	Mechanism	Reference
10	*Satureja khuzistanica*	Lamiaceae	Leaf and Stem	**Hydrogel alginate**	In vivo: Excision wound model in rat	No positive control	Accelerated wound healing without scar formation	[225]
11	*Narcissus tazetta*	Amaryllidaceae	bulb	**Non-ionic surfactant vesicles / niosomes** by film hydration method	In vitro: HDF cell line	Fetal bovine serum	Decreased the gap width on human dermal fibroblasts	[226]
12	*Centella asiatica*	Apiaceae	-	**Nanoparticle**: Polyurethane foam dressing consists of natural polyols, silver nanoparticles, and asiaticoside	In vivo: Excision wound model in farm pigs	No positive control	Increased the absorption property and compressive strength and enhanced the wound closure rate	[227]
13	*Opuntia ficus-indica*	Cactaceae	Seed	**Self**-nano emulsifying **formulation**: OFI seed oil poured in 2% HPMC solution	In vivo: Full-thickness excision wound model in rat	Mebo ointment	Enhanced expression of transforming factor-beta and VEGF,	[228]

with a higher cost and limited accessibility, particularly in low-resource settings. Additionally, they carry potential risks such as bleeding, infection, barotrauma, and even the potential development of cancer [235, 236]. Silver dressings are highly effective due to their antimicrobial properties, ease of use, and cost-effectiveness in wound healing, however, their application requires careful consideration, as improper usage may lead to potential cytotoxic effects [237]. Biomaterial-based dressings, including grafts and engineered skin substitutes, play a crucial role in restoring tissue function, especially in cases of severe burns or chronic wounds with significant skin loss but these solutions face challenges such as limited vascularity, weaker mechanical strength, and potential risk of immune rejection [238]. Also, cell and growth factor therapy hold promise for regenerating chronic wounds, but the presence of chronic wound fluid can lead to the rapid degradation of growth factors, hindering stem cell proliferation [239, 240]. Similarly, artificial dressings made from polymers can mimic tissue properties, but they may also lack bioactive components critical for optimal wound healing [241]. Considering the limitations of current wound healing treatments, there is a crucial need for the development of natural products to effectively address wound healing [242–244]. Traditional therapies hold significant value due to their safety, accessibility, established effectiveness, and natural origins, effectively addressing the drawbacks associated with modern approaches, which often entail high costs, lengthy production processes, and the rising challenge of bacterial resistance [245–249]. Recognizing this potential, the World Health Organization advocates for the integration of traditional methods into formal health systems and underscores the power of phytochemicals in not only combating infections but also in supporting the intricate process of wound healing [250]. Ayurveda attributes unique medicinal properties to individual herbs, yet it believes that combining these herbs, termed polyherbal formulations, in specific ratios and proportions can amplify their therapeutic benefits while reducing potential toxicity [251, 252].

This review offers valuable insights into a diverse range of natural remedies explored for wound healing. When focusing on studies of individual herbs (Fig. 5), a significant number of them were found to belong to the Asteraceae family, followed by the Fabaceae and Leguminosae families in terms of frequency. In the dataset (Fig. 6), the Apiaceae family emerges as predominant, with 24 studies utilizing polyherbal formulations for wound care. It is followed by the Burseraceae and Fabaceae families in terms of representation. When considering both single herbs and those utilized in polyherbal formulations, a total of 72 studies encompassing 127 different herbs (excluding any overlapping herbs) were examined. These herbs were predominantly from the Asteraceae family, followed by the Fabaceae and Apiaceae families (Fig. 7). Noteworthy, herbs with wound healing

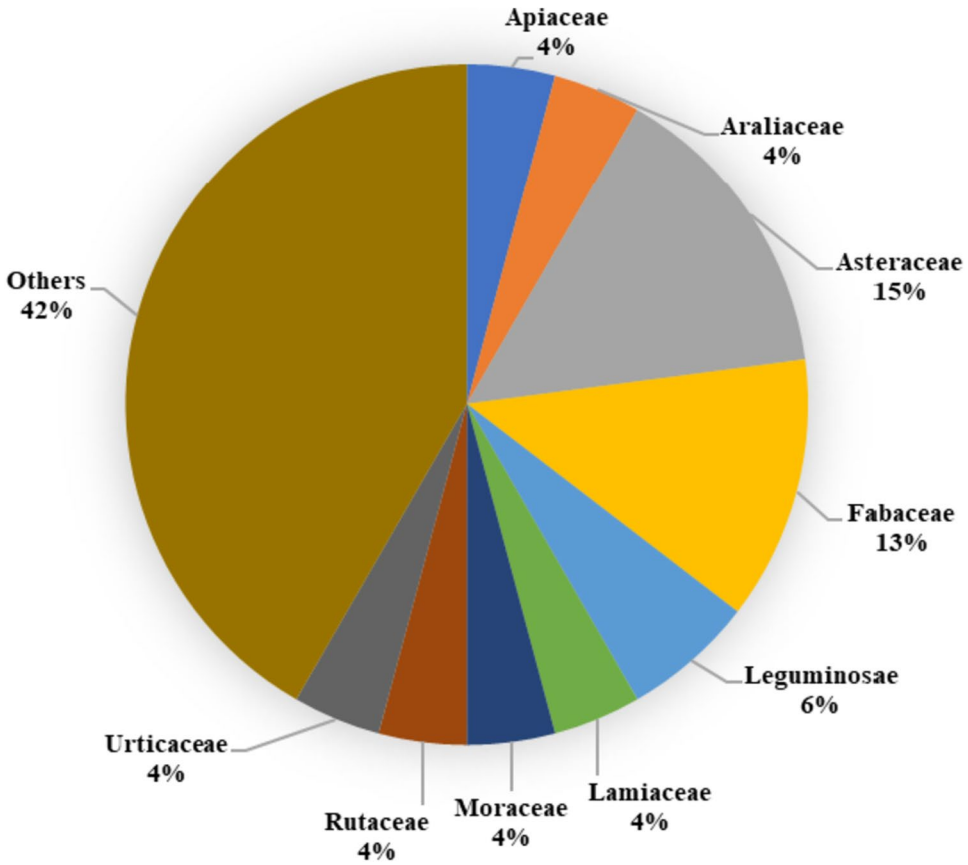

Fig. 5 %age of individual herbs from the same botanical family exhibit wound healing properties

efficacy belonging to the Asteraceae family include *Areca catechu, Calamus draco, Artemisia absinthium, Carthamus caeruleus, Dittrichia viscosa, Echinacea purpurea, Elephantopus scaber, Gynura procumbens, Launaea procumbens, Matricaria chamomilla, Siegesbeckia orientalis, Tridax procumbens, Xanthium strumarium*, and *Aster koraiensis*. Likewise, in another study, the effectiveness of *Ageratina pichinchensis* and *Calendula officinalis* in wound healing underscores the potential of Asteraceae plants for the development of impactful wound-healing drugs [253]. Also, *Achillea asiatica*, commonly known as Asian yarrow, from the Asteraceae family, demonstrates the potential to stimulate wound healing and support the growth of keratinocytes, the predominant cells in the epidermis [254]. Additionally, a study conducted in 2020 focused on the plant's wound-healing potential reported that the Fabaceae or Leguminosae family exhibited an abundance of herbs beneficial for wound healing [255]. Traditional remedies from the Fabaceae and Rosaceae families have a significant presence among plants used in traditional medicine for various health conditions, including wound care [256].

Figure 8 illustrates the sequential steps involved in evaluating the wound healing efficacy of bioactive compounds extracted from herbs. Among the various plant parts studied for wound healing efficacy, leaves were the most utilized, followed by roots, rhizomes, and fruits. These plant parts were initially extracted using solvents such as ethanol, methanol, and hydroalcoholic solvents. This choice of solvents can be attributed to their wide compatibility, high solubility, moderate toxicity, scalability, cost-effectiveness, and stability. Once bioactive compounds were extracted from different plant parts, they were further assessed using in-vivo rat wound models, including incisions, excisions, deep tissue pressure injuries, burns, and medically induced wounds. Additionally, in-vitro models were employed to measure enzyme levels and conduct various cell assays, representing the diverse mechanisms involved in promoting wound healing efficacy. The review highlighted the significant wound-healing efficacy of phenolic acids, flavonoids, glycosides, and other phytochemicals, contributing to wound-healing activity. They operate through diverse mechanisms, enhancing various stages of wound healing, including upregulating vital factors like VEGF and TGF-β, crucial for re-epithelialization, angiogenesis, granulation tissue formation, and collagen deposition. Other studies reported the presence of diverse polyphenols, alkaloids, saponins, terpenes, essential oils, and polyphenols in various plants positively impacts different stages of the wound healing process [257]. These compounds modulate steps in wound healing, including cell proliferation, fibroblast migration, reduction of oxidative

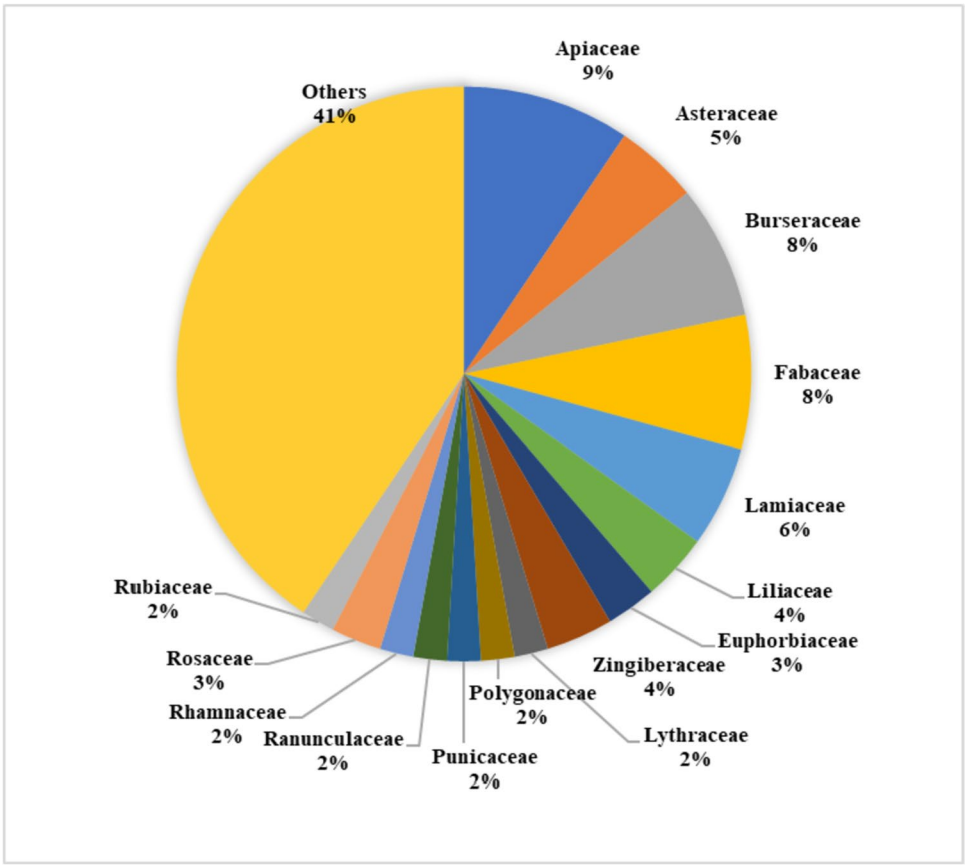

Fig. 6 %age of herbs included in polyherbal formulations, which belong to the same botanical family, possess wound healing properties

stress, improvement of collagen synthesis, and modulation of the expression of various factors. Flavonoids also positively regulate pathways involved in wound healing [258]. Phytochemicals also act as inhibitors of inflammatory factors, conferring antioxidant and anti-inflammatory effects throughout the healing process [259]. Specific compounds like saponins, flavonoids, and quercetin signify the potential wound-healing properties of certain herbs [260]. Molecular approaches are now gaining importance in understanding the underlying mechanisms of action and assessing potential herbal or synthetic compounds for wound management [261]. Phytochemicals, with their potent antimicrobial, antioxidant, and wound-healing properties, play a vital role in encouraging blood clotting, combating infections, and expediting wound recovery. Medicinal plants rich in polyphenols demonstrate notable efficacy in this regard [262–264].

Conventional treatments for chronic wounds, like skin grafting or negative pressure wound therapy, may lead to tissue damage or functional restrictions, prompting the exploration of nanobiotechnology, an interdisciplinary field integrating engineering, chemistry, and biology, for innovative biomedical applications [265]. By incorporating nanoparticles, both biopolymers and synthetic polymers have been tailored for use as wound dressings, addressing contemporary wound care challenges including tissue repair, scarless healing, and tissue integrity [266]. This review emphasizes advancements in utilizing nanotechnology-based wound dressings in herbal-based formulations to enhance targeted drug delivery and accelerate recovery. These innovative drug delivery systems, benefiting from high stability, extensive surface area, and customizable compositions, have shown promise in both in vitro and in vivo models. Materials for wound dressing include electrospun nanofiber guar gum and polyvinyl alcohol-based matrices, sodium alginate nanofiber mats, cellulosic textile nanoemulsions, polycaprolactone nanofibers with silver nanoparticles, and chitosan-polyvinyl alcohol hydrogel microneedles. In other studies, advanced techniques utilizing nanoparticles and hydrogels loaded with bioactive molecules and non-bioactive substances, particularly smart hydrogels, hold promise for enhancing diabetic wound healing. These approaches can be further enhanced with technologies like photothermal therapy, layer-by-layer self-assembly, and 3D printing [267]. Nanotechnology provides molecularly designed nanostructures for both therapeutic and diagnostic use in burns, categorized as organic and non-organic (e.g., polymeric and silver nanoparticles), with many exhibiting multifunctional properties [268]. Self-assembled nanomaterials, serving as wound dressings and growth factor carriers, characterized by superb biocompatibility and versatile functionalities like mimicking

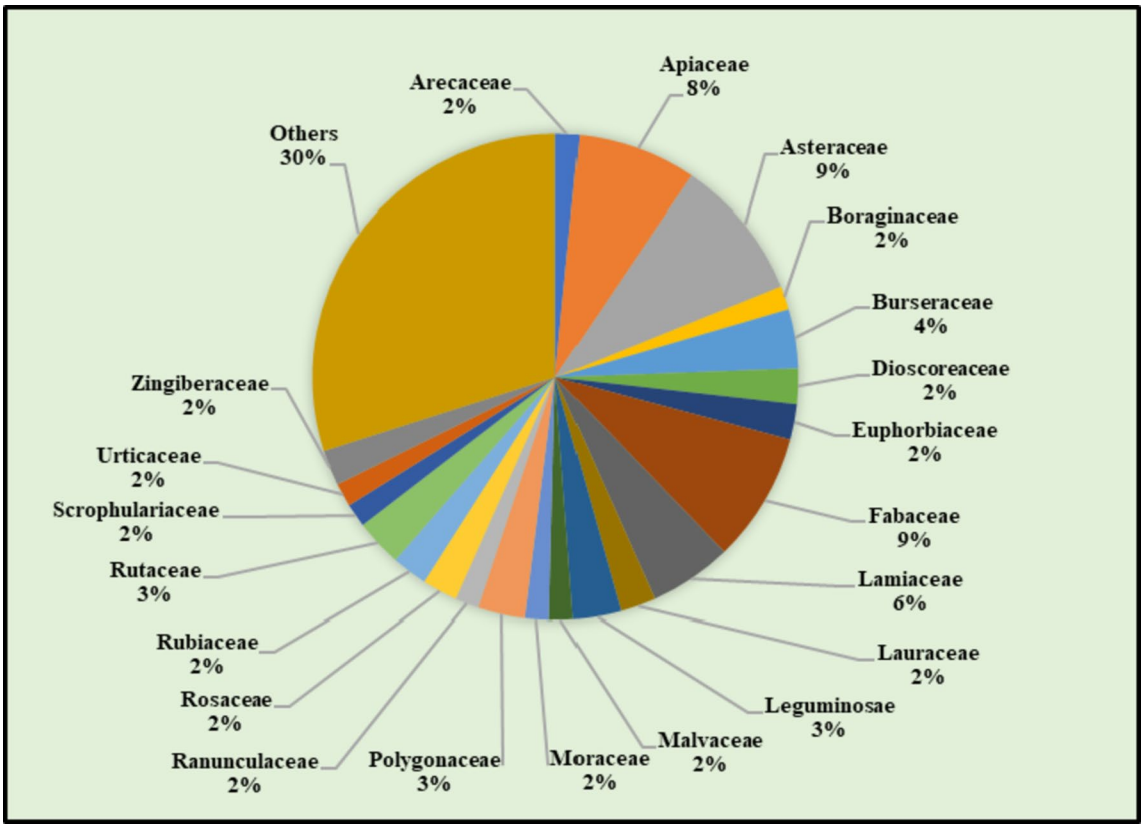

Fig. 7 %age of herbs, found in both individual herb and polyherbal formulation studies, and belonging to the same botanical family, demonstrate wound healing properties across a total of 72 studies, which encompass 127 unique herbs (excluding duplicates)

extracellular matrix, drug delivery, and adjustable mechanics, offer promising therapeutic prospects for chronic wound healing [269]. With rising clinical demands, botanical applications are increasingly integrating with nanotechnologies. This fusion, particularly through electrospinning, creates nanofibrous membranes ideal for skin wound healing [270]. Noteworthy breakthroughs in tissue regeneration and skin wound therapy, including 3D-printing, cell-imprinted substrates, nano-architectured surfaces, and gene-editing tools, hold substantial promise for advancing burn wound therapies [271].

Perspectives and future direction

Numerous preclinical research on herbs with shown wound healing properties have been undertaken. Several clinical studies employing single herbs or effective herb combinations have demonstrated efficacy in the therapy of wounds. Here, in "Table 4," are some of the clinical experiments that were done to create safe medications (herbal or polyherbal formulations) and ensure the quickest recovery period. To achieve this and lessen the significant challenges associated with conducting clinical studies, an appropriate research design that mimics the wound conditions is needed. Future research is required to understand how these herbs' isolated compound helps wound linked with disease heal and to develop new formulations containing herbal extracts and phytochemicals that will lessen the risk of medication resistance and drug allergies or many other associated factors that interfere with wound healing.

Conclusion

This critical overview highlights the multifaceted roles of medicinal plants in advancing wound healing technology. The rich repository of bioactive compounds found in these plants offers a promising avenue for promoting tissue regeneration, combating infections, and reducing inflammation. By leveraging the therapeutic potential of medicinal plants, we can address the complex challenges associated with wound care. There is a need for in-depth studies to unravel the specific mechanisms of action underlying the wound-healing properties of individual bioactive compounds in medicinal plants. This understanding will pave the way for the development of targeted interventions tailored to different types of wounds. Collaborative efforts between traditional healers and scientific researchers can lead to the

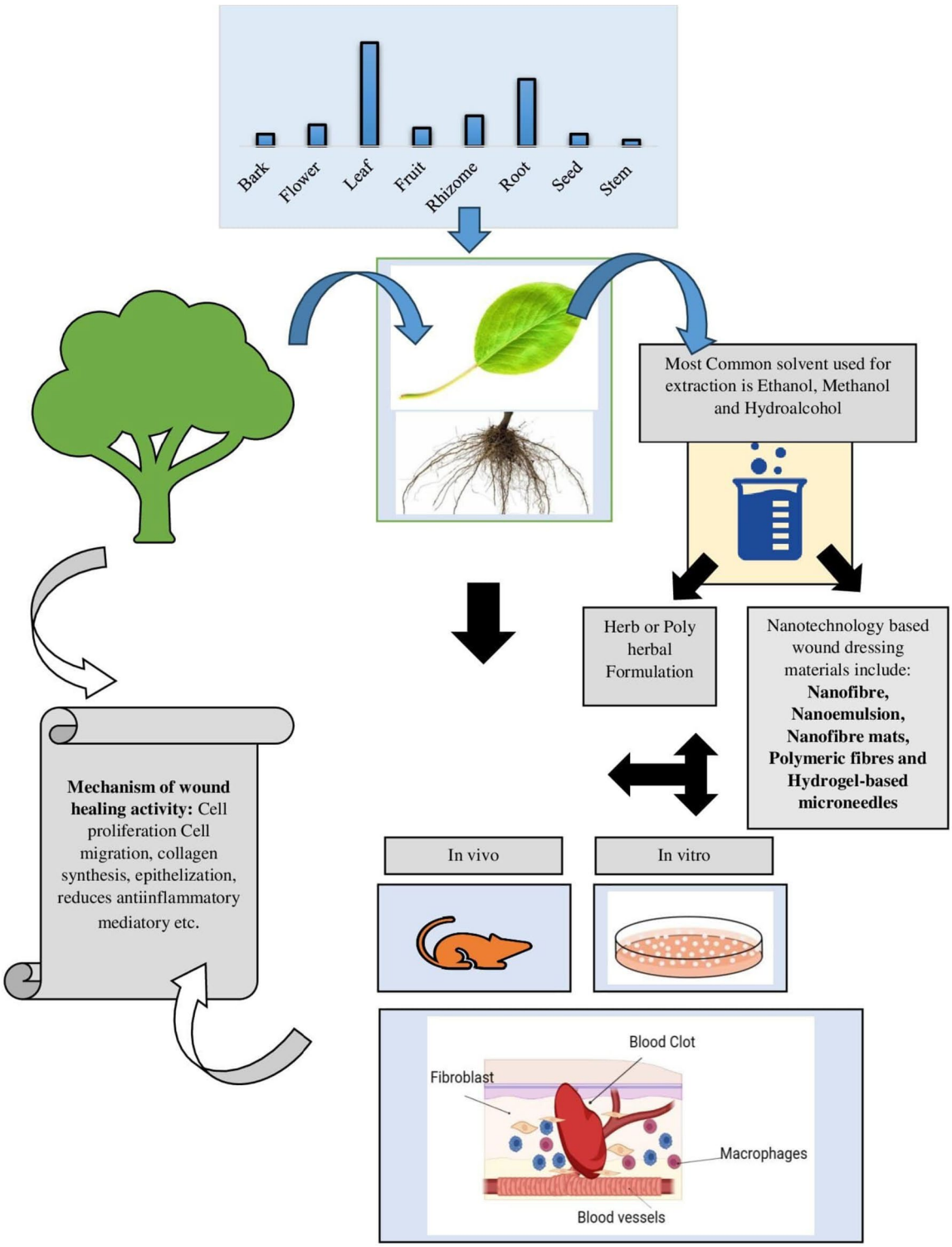

Fig. 8 Herb-derived bioactive compounds for wound healing activity (from extraction to evaluation). The diagram illustrates the comprehensive process of harnessing bioactive compounds from selected herbs for wound healing. Primarily utilizing leaves, followed by roots, rhizomes, and flowers, the herbs undergo extraction with specific solvents. The extracted compounds are then utilized to prepare either individual herb formulations or polyherbal blends. These formulations are subsequently evaluated for wound healing efficacy through both in vivo and/or in vitro models, showcasing their diverse mechanisms in promoting wound recovery

Table 4 Clinical trials conducted to determine herbs wound healing efficacy

S.No.	Sample	Treatment	Control	Indication	Efficiency	Reference
1	90 (primiparous women)	*Commiphora myrrha* and *Boswellia carteri*	Betadine sitz bath	Episiotomy (wound)	Myrrh demonstrated significantly superior wound healing in episiotomy patients compared to frankincense or betadine	[272]
2	210 women diagnosed with vaginitis	St. John's wort, yarrow, shepherd's purse chamomile, calendula, and tea tree oil	Probiotic	Vaginitis (wound)	Tea tree oil-based vaginal suppositories exhibited superior effectiveness compared to alternatives	[273]
3	12 patients with 24 donor sites	Aloe vera	Placebo	Burns and split-thickness skin graft donor sites	Aloe vera gel topically showed marked improvement in the healing of split-thickness skin graft donor sites	[274]
4	60	Nanocurcumin	Placebo	Diabetic foot ulcer	Incorporating nano curcumin into the treatment of diabetic foot ulcers led to notable enhancement in glycemic control	[275]
5	30	*Centella asiatica*	Placebo	Facial acne scars	*Centella asiatica* demonstrated a significantly greater reduction in skin erythema	[276]
6	87 (primiparous women)	*Silybum marianum*	Placebo	Episiotomy (wound)	*Silybum marianum* showed a reduction in episiotomy pain severity and expedited wound healing	[277]
7	17	30% garlic ointment	Vaseline	Surgical wound	Surgical wounds treated with 30% garlic ointment resulted in more cosmetically appealing scars compared to those treated with Vaseline	[278]
8	90 (primiparous women)	*Verbascum Thapsus*	Placebo	Episiotomy (wound)	*Verbascum Thapsus* is effective in repairing episiotomy wounds	[279]
9	50	*Vasconcellea cundinamarcensis* (0.1% proteolytic fraction)	Hydrogel	Chronic foot ulcers (neuropathic patients of diabetes type-2)	*Vasconcellea cundinamarcensis* notably accelerates foot ulcer healing compared to hydrogel treatment	[280]
10	129 (women)	2.5% and 5% grape seed extract	Petrolatum	Cesarean wound	Utilizing 5% grape seed extract may offer therapeutic benefits in enhancing cesarean section wound healing	[281]
11	20 patients	Grape seed extract 2% herbal cream	Placebo	Surgical patients	Wounds treated with 2% grape seed extract achieved full repair in fewer days compared to the placebo group	[282]

identification of novel wound-healing agents and innovative treatment approaches.

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Declarations

Consent for publication Not applicable.

Conflict of interest The authors declare no conflict of interest.

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