A Review of Healing Potential of Indian Flora: An Ethnopharmacological Evidence of Wound Healing Activity

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Abstract

Introduction: Healing a wound involves a complex series of coordinated chemical and cellular events to restore the integrity of skin and underlying tissues. Many people prefer using medicinal plants as an alternative therapy for this purpose globally. Objective: The focal point of the review is based on the ethnopharmacological profiling and validation of plants. The reviewed plants belong to the India region and have promising wound healing activity which has been scientifically proven by *in vivo* as well as *in vitro* studies. Numerous phyto extracts and their secondary metabolites are known as promising alternatives for wound healing agents due to the existence of miscellaneous dynamic constituents, ease of access, and their inadequate side effects. Methods: The plant profile was explored from various sources including scientific search engines such as Google Scholar, Niscare repository, Scopus, Pubmed, Sciencedirect, Sci-Finder, and Springer including reports and thesis from Proquest. Keywords such as wound healing property, plant extract, and animal models were employed in combination with the ethnopharmacological claim, pharmacological activity, etc. Conclusion: This review provides comprehensive data from published research work on medicinal plants over 10 years, focusing on wound healing activity and its ethnopharmacological profiling from different tribal belts. This review features the potential of medicinal plants to contribute to drug discovery as a compelling wound healer which may help in the discovery of a new drug molecule with a maximum margin of safety. However further studies are needed such as novel formulation, and target-based drug delivery systems by performing clinical studies for the scientific exploration and validation from laboratory to industry for societal value.

Keywords. Wound healing, Natural product, Phyto-medicine, Ethnopharmacology, Organic composites.

Significance | This review emphasizes the rich potential in traditional practices, offering valuable insights and solutions to current healing challenges.

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1. Introduction

Plants have been employed not only for essential human necessities but also for medicinal purposes since ancient era. Inherent awareness is gaining worldwide recognition for its innate importance and prospective active relevance in safeguarding phyto-diversity and advancing contemporary expansion of pharmaceutical(Ahmed, 2023).Perception of plant-derived products and therapeutics are steadily developing extensively across the globe, hence the acceptance and demand for herbal medicines have also escalated. However, few plants have been authenticated scientifically through rigorous *in vivo* animal

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experiments and scientific clinical trials. The majority of the accessible systematic information supporting the wound healing perspective of ethnobotanical flora requires precise experiments on their mode of action, effectiveness, steadiness, toxicity profile, and safety. Medicinal plants have the prospective to serve as preferred candidate for wound healing due to their assorted range of constituents, together with alkaloids, fatty acids, flavonoids, tannins, essential oil, terpenoids, saponins, and phenolics. These constituents have the potential to boost the wound healing process (Bahramsoltani et al., 2014).As outlined in various literature sources, 70% of wound healing drugs are derived from plants, 20% from minerals, and the enduring 10% from animal products (Siddique et al., 2019).Comprehensive scientific substantiation experiments are mandatory to validate conventional medications as substitutes and corresponding drugs on behalf of wound management. As per the approximate estimation, almost 200,000 natural products achieved from animals, higher plants, fungi, and marine organisms. These products have been explored in conventional and complementary medicines, in addition to contemporary drug innovation (Hiwa M.Ahmed, Seyed Nabavi, 2021).

Herbal therapy suggests added benefits such as affordability, extensive availability, and less allied side effects. In recent scenario, traditional herbal medicine has gained increased awareness, even with substantial advancements in modern medicine. Plants, traditionally valued for their pharmacological activities, are now acknowledged as potential alternatives for prevention and cure of disorders, contributing to the development of notable modern drugs. Nonetheless, there is still a thrust for enhanced perceptive of their medicinal and toxicological values (Jahandideh et al., 2017).

The fundamental role of the skin is to accommodate a defensive limitation of the body against the environment. In terms of protection, sensation, microbial infection, body temperature regulation, and metabolism the skin plays a pivotal role. A variety of prior studies have confirmed the antimicrobial protective function of divergent skin layers (Negm, 2023).

Wounds pose a substantial global health challenge, striking huge economic, financial, and social burdens on healthcare facilities, caretakers, patients along with families (Boakye et al., 2018). Phyto-medicines have been utilized for the treatment of wounds since antiquity. Wound, a clinical substance is as old as mankind; however, healing of unremitting cutaneous injuries is still a phenomenal issue. As per the Wound Healing Society (WHS) wound is defined as substantial damage that could escort to the opening or rupture of the skin structure and might facilitate interruption in the anatomy, physiology, and function of the Skin. Generally, a wound occurs due to accidental injury such as a cut of tissue or due to cell injury which leads to hampering the protective mechanisms of the cell. This process comprises different convergent phases: the inflammatory phase, proliferative phase, and maturation (Hajialyani et al., 2018). The wound is classified into two major types namely acute and chronic wound. Acute wounds are restored within a specific period such as surgical incision and chronic wound fails to improve through a normal phase of healing followed by a pathological inflammation phase (Alankar et al., 2018). Wound healing is categorized into primary and secondary healing. Primary healing occurs after 12-24 hours of wound formation and is also characterized as a balanced phase of healing. But in case an infected wound takes a few days for wound closure is categorized under the delayed type of primary healing. Secondary healing is characterized by pervasive damage of soft tissue. In this type of healing process, myofibroblast plays an important role by executing its property between the muscle cells and fibroblast(Stuart Enoch, 2010).

Several cells are implicated in the wound healing process for instance platelets, endothelial cells, macrophages, lymphocytes, neutrophils, fibroblasts, and keratinocytes. This healing process of the damaged tissue is influenced by many extrinsic as well as intrinsic factors. Most of them are divided into local and systemic categories respectively. Local factors have a prompt and direct influence on the wound surroundings such as oxygenation, foreign body, and blood supply. Systemic factors are considered as the individual's ability to heal such as age, gender, disease conditions, medications, etc(Gupta and Kumar, 2015).

Phyto composites can impact numerous phases of healing through diverse mechanisms. This takes account of uplifting various factors namely TGF-ß (transforming growth factor- beta), MCP-1 (monocytes chemo attractant protein-1), VEGF (vascular endothelial growth factor), IL-1 (interleukin-1), and the diminution of NO (nitric oxide), LDH (lactate dehydrogenase), and ROS (reactive oxygen species). Moreover, they contribute to enhance the antioxidant capacity of tissues and organs throughout the inflammatory phase. Likewise, it also assist to raise in EGF-receptor mediated metalloproteinase, matrix metalloproteinase, and endothelial cell proliferation during re-epithelialization, uphold the proliferation of scratched tissue cells in granulation, and advance angiogenesis by uplifting mediators like VEGF and TGF-ß. These combined property eventually escort to a fall in rate of wound contraction (Bahramsoltani et al., 2014).

In wound management, therapeutically advanced techniques like gene therapy, external supervision of growth factors, and nitric oxide should be adopted. This review confers the traditional wound healers from Indian origin over the last decade to recognize potent wound healer. The plants have various pharmacological activities like wound healing, antimicrobial, antioxidant, analgesic, and anti-inflammatory were also included in this study.

Method

An extensive literature survey over a period ranging from 2012-2023was carried out on medicinal plants having potent wound-healing activity and the basic science behind wound healing. The reports were assessed and compiled from relevant sources including scientific search engines such as Google Scholar, Niscare repository, Scopus, Pubmed, Science Direct, Sci-Finder, and Springer including reports and thesis from Proquest. Keywords such as wound healing property, plant extract, and animal model were used in combination with ethnopharmacological claim, pharmacological activity, etc. Reports on wound healing activity were assembled along with plant species, family, part used, the model used/ mode of treatment, observation of the experiment, the active compound, activity reported, and traditional use of the reported plant were listed in Table 1.

Historical background

In ancient time (1400 BC) the physician of Egypt preferred the use of a mixture of honey, grease, and lint in an open wound for the removal of dead skin and pus for better healing. In the time of the Hippocratic in 400 BC, Greek society adopted the use of a piece of tin pine with an abscess cavity for the collection of pus as surgical drainage. In 280 BC the Greek barber invented the syringe for the easy collection of liquid wound exudates(Broughton et al., 2006). Since the earlier period of 40 years, the availability of sophisticated wound care dressings has developed at an extraordinary rate in different types as well as shapes and sizes. Thousands of years ago, the evolution of wound care dressings occurred to fulfill the need of humans as an alternative to prevent bleeding, accelerate the healing process, and manage difficult impaired wounds(Jones, 2015). In the year of 1908, Ilya Metchnikoff received the Nobel Prize for his contribution towards the sighting of phagocytosis along with the concept of inflammation was also to fetch phagocytes to the wounded region for bacteria engulfment (Tauber, 2003). In 1926 F. J. Lang of Chicago reported that the macrophage emerged from malformed tissue and converted to monocytes and also interpreted the damaged endothelial cells which further undergo differentiation and elongation to produce fibroblasts. Later this concept was considered as the mechanism of angiogenesis. Cytokines and growth factors, endogenous pyrogen or IL 1 nerve growth factor, and interferon concept were explained in the year 1950. Lymphokines are the mediators that evolved from lymphocyte cells and the TNF (tumor necrosis factor) were reported in the year 1960-1970. Towards the end of 1980 researchers focused on molecular technologies like monoclonal antibody technique, and grafting technique. Then subsequently researchers emphasize more to establishing the actual cellular mechanism of the healing process by characterizing of inflammatory mediators like chemokine, interleukin, growth factor, cytokine, etc (Broughton et al., 2006).

Wound healing process

The wound healing practice is accomplished over specific programmed stages: hemostasis, inflammation, and proliferation, followed by remodeling (Figure 1). All of the stages must be executed in a definite manner and time edge for a successful healing process.

Hemostasis: After a skin rupture or damage cell injury takes place followed by bleeding which can swill out the microbes, and antigens from the site of a wound. Subsequently, this bleeding leads to the activation of hemostasis by releasing the clotting factors. Coagulation takes place by forming a fibrin network to stop bleeding at the site of the wound which later turns into a scab to provide strength to the wounded tissue. Thus this stage takes part in defensive function in the healing process(Joshua S. Boateng et al., 2008).

The inflammation stage always coincides with the hemostasis stage, occasionally in between a short period of cell damage to 24 hours, and proceeds for at least three conjugative days. The proteinaceous wound exudates lead to the secretion of histamine and serotonin causing vasodilation. All the necrotic cells undergo phagocytosis. Ruptured blood vessels release platelets and subsequently, these are activated by mature collagen by forming aggregation. This stage focuses on setting up an immune barricade against invading microorganisms in two different way i.e. early and late inflammatory stages (Velnar et al., 2009).

The proliferation stage is otherwise known as granulation or contraction stage. This stage persists from 4 days to 3 weeks. This stage comprises fibroblast migration, synthesis of collagen, and angiogenesis followed by granulation tissue development. Accumulation of collagen fibers, and neovascularization takes place by reducing wounded areas and promoting epithelialization (Firdous and Sautya, 2018).The presence of collagen in the base of the wound leads to proliferation by replacing the dermal tissue followed by wound contraction.

The remodeling stage is the final of the healing progression otherwise known as maturation. In this stage, new epithelial tissue and scar tissue formation occurs and lasts up to 3 weeks to 2 years. Cross-linking between the collagen fibers takes place through vitamin C-dependent hydroxylation which helps to improve tissue tensile strength (Sayeed Mohammed, 2018; Velnar et al., 2009). Initially, fibroblast synthesizes collagen type III which will be replaced later by collagen type I. Previously formed thin scar tissue in epithelialization phage turns into deep pink thickened tissue. Fibroblast cells play a major role in the remodeling which may take up to two years for complete and successful healing (Orsted, 2018).

Assessment of wound

It is important to assess and diagnose the site of wound surroundings for its easy management. It should be started among

Table 1. Medicinal plants as a potent wound healer from Indian origin

Sl. No.	Species	Parts used	Models used/ Mode of treatment	Observation	Active compound	Activity reported	Traditional uses	References
	Datura stramonium Linn. Solanaceae	Leaves, aerial part	Incision, excision 2% and 5% of polyherbal carbopol-940 gel formulation containing methanol extract of *D. stramonium* L., *P. zeylanica* L., and *A. Mexicana* L. were applied over the wound i.e., 500mg in excised wound and 250mg in incised wound till healing of the rats.	Significant increases in wound area reduction, fast epithelialization, and high wound-breaking strength was observed. The possible mechanism may be due to the presence of different constituents of polyherbal gel which helps to enhance collagen synthesis resulting in potent wound-healing activity.	Flavonoids, phenolic content	Anti-inflammatory, antimicrobial, wound healing	Sores, fistula, neuralgia, abscesses	(Dev et al., 2019)
	Plumbago zeylanica Linn. Plumbaginaceae				Plumbagin , isoshinanolone, plumbagic acid, β-sitosterol, 4-hydroxybenzaldehyde, trans-cinnamic acid, vanillic acid, 2, 5-dimethyl-7-hydroxychromone, indole-3-carboxaldehyde	Antimicrobial, anti-malarial, anti-inflammatory, astringent, diuretic, anti-tumor, radio-modifying properties, wound healing	Abortifacient, anemia, diabetes, dyspepsia, diarrhea, leprosy, elephantitis	
	Argemone mexicana Linn. Papaveraceae				Alkaloids, 13-oxoprotopine, argenaxine, higenamine, 8-methoxy di-hydrosanguiranine	Anti-malaria, antiplasmodial, larvicidal, antiasthmatic, hepatoprotective, wound healing	Dermatological disease, warts, microbial infections, jaundice	
	Prosopis cineraria (L.) Druce Fabaceae	Fresh leaves	Incision, excision Butanol fraction of hydroethanolic extract was formulated into 5%, 10% w/w simple ointment and applied over the wounds of Wistar albino rats till complete healing.	Accelerated contraction of wound area and rapid epithelialization were observed in the case of 10% w/w ointment as compared to additional formulation in the excision model. Whereas in the incision model, significant tensile strength was observedagainstthe standard.	Rutin, luteolin, prosogerin A, B, C, D, gallic acid, β-sitosterol, hentriacontane, patulitrin, spicigerin	Antioxidant, antimicrobial, anti-inflammatory, anti-tumor, analgesic, wound healing	Leprosy, boils, blisters, mouth ulcers, leucoderma, rheumatism, asthma, eye disease	(Yadav et al., 2018)
	Pongamia pinnata (L.) Pierre Fabaceae	Leaves	Incision, excision Wounded Wistar rats were orally administered (100 mg/kg body weight)with methanol extract along with the vehicle. The drug was administered once a day for 19day (approximately 10mL/kg body weight)	Significant wound closure was observed along with epithelialization in open wound treatment. In the incised wound model, higher wound-breaking strength was observed against standard and other groups.	Alkaloids, β-sitosterol, kanugin, glabrin, saponin, glabrosaponin, pongamol, kaempferol, kanjone, pinnatin, karangin, neoglabrin, pongapin, quercitin, dimethoxy-kanugin, tannin	Antioxidant, antimicrobial, anti-inflammatory, ulcerogenic effect, wound healing	Swelling, piles, ulcers, skin infection	(Dwivedi et al., 2017)
	Boerhavia diffusa Linn. Nyctaginaceae	Leaves	In vitro, excision Cell viability assay and wound healing scratch assay of methanol and chloroform extract were performed by taking the HaCaT cell line in a cell culture plate. In vivo Similarly, 10%w/v ointment containing methanol and chloroform extract was applied over the excised wound of rats for 14 days (once per	In the cell viability assay method, enhancement of the viability of the keratinocyte was observed significantly. Keratinocytes migration was also observed towards the denuded area due to the treatment of both extracts resulting in significant wound closure. 91% wound closure was observed within 14 days in case of the methanol extract-treated group.	Quercetin, kaempferol	Anti-inflammatory, hepatoprotective, antimicrobial, anticonvulsant, antioxidant, anti-cancer, antidiabetic, antifibrinolytic, wound healing	Jaundice, kidney problems, skin troubles, eye diseases	(Kriti Juneja, Rutusmita Mishra, Samrat Chauhan, Sumeet Gupta, 2019)

			day).					
	Vitex negundo Linn. Lamiaceae	Leaves	Excision, Scratch assay A polyherbal mixture was formulated by combining the aqueous extract of *V. negundo* L., *E. officinalis* Gaertn, and *T. procumbens* L. in equal proportion. In vitro scratch assay was performed by using fibroblast and keratinocytes cell lines in a cell culture plate and treated with 5µg/mL of polyherbal mixture. Wistar rats were excised to make a wound (300-400mm^2) and the polyherbal ointment was applied over the wound locally till healing.	5µg/mL treated group showed significant closure of the gap of the scratch of keratinocytes cell lines and the 3µg/mL treated group showed remarkable migration of keratinocytes followed by gap closure as compared to other treated concentrations. The polyherbal formulation exhibited the highest percentage of wound contraction i.e., 99.2% as compared to the standard.	Tri foliate, Penta foliate	Laxative, anti-inflammatory, antihistaminic, antioxidant, analgesic, hepatoprotective, wound healing, anticonvulsant	Toothache, skin ulcer, leucoderma, rheumatoid arthritis	(Yogesh P. Talekar, Kishori G. Apte, Shubhangi V. Paygude, Prasad R. Tondare, 2017)
	Emblica officinalis Gaertn. Phyllanthaceae	Bark			Ascorbic acid, chebulinic acid, chebulagic acid, 3-ethylgallic acid, gallic acid, ellagic acid, isostrictinin, terchebin, quercetin, corilagin, Punigluconin, Pedunculagin, trigalloyl glucose, Emblicanin –A, Emblicanin -B	Antimicrobial, anti-inflammatory, antioxidant, antipyretic, hepatoprotective, anti-tumor, anti-ulcerogenic, wound healing	Gonorrhoea, astringent, diarrhoea	
	Tridax procumbens Linn. Asteraceae	Whole plants			Flavonoids, alkyl ester, sterols, triterpenes, fatty acids, polysaccharides, procumbenetin	Antimicrobial, anticoagulant, antifungal, wound healing, hepatoprotective	Immunomodulation, blood pressure, acne, boils, blisters treatment, insect repellent, heart burning	
	Ziziphus mauritiana Lam. Rhamnaceae	Leaves	Excision 5%w/w ethanolic and aqueous extract containing simple ointment was formulated separately. Both of the ointment was applied to the excised wound of the respective groups once daily for 16days.	Both of the extract formulations possessed significant healing whereas ethanolic extract showed 99% of wound closure.	Protein, fiber, saponin, tannin, alkaloid, flavonoids, glycosides, terpenoids, phenolic compounds	Anti-nausea, anti-rheumatic, anti-diarrhoeal, hepatoprotective, wound healing, antioxidant	Abscesses, ulcers, swelling, fever, gonorrhea, liver diseases, asthma, laxative, sedative, pulmonary ailments, skin diseases	(D. Senthil Rajan, M. Rajkumar, 2013)
	Aegialitis rotundifolia Roxb. Plumbaginaceae	Leaves	Excision, incision, burn wound Ethanol extract containing 2.5%, 5% w/w ointment was applied over the wound daily of Wistar rats.	A better result was found in 5% w/w ointment against other treated groups. The wound closure percentage was increased significantly followed by quicker epithelialization. The highest weight of both wet and dry granulation tissue was found. Maximum wound breaking strength was found in the highest concentration in terms of percentage of tensile strength.	Alkaloids, tannins, steroids, saponins, flavonoids	Antioxidant, anti-cancer, anti-bacterial, anti-thrombolytic, analgesic, antipyretic, wound healing	Pain, inflammation, an antidote for the insect bite	(Ghosh et al., 2019)
	Lepidium meyenii Walp. Brassicaceae	Roots	Diabetic wound Streptozotocin-induced diabetic Wistar rats were subjected to excision by forming an open wound of 500mm^2. Wounded rats were treated with 5%, 10% w/w hydroalcoholic extract containing ointment topically. Another group is treated with 200mg/kg body weight of hydroalcoholic extract orally.	A higher significant healing effect i.e., reduced wound contraction was observed in 200mg/kg body weight of the hydroalcoholic extract-treated group and 10% w/w ointment-treated group.	Essential oils, glucosinolates, alkalmides, macamides	Antimicrobial, antioxidant, wound healing, anti-inflammatory, hypoglycemic	Fertility enhancing property	(B.V.B. et al., 2017)

	Caulerpa scalpelliformis Caulerpaceae	Leaves	Excision Silver nanoparticles synthesized extract (40µg/mL) and only the leafy extract (150mg/mL) was formulated into a hydrogel. The excised wound of Wistar rats was treated with different hydrogel locally till healing.	Silver nanoparticles synthesized extract containing hydrogel possessed accelerated healing effect in comparison with other treated groups.		Anti-neoplastic, antibacterial, wound healing, Anti-proliferative	Repellent	(Manikandan et al., 2019)
	Albizia amara (Roxb.) B. Boivin Fabaceae	Leaves	Excision Topical gel (5%, 10%, and 15%) was prepared by using methanol extract and applied over the excised wound of rats for 15 days.	Maximum wound contraction was found in the highest concentration of dose treated group resulting in significant wound closure.	Alkaloids, cardiac glycosides, phenols, flavonoids, tannins, saponins	Anti-microbial, anti-inflammatory, antioxidant, wound healing	Diarrhea, piles, gonorrhea, leprosy, wounds, boils, abscesses, dandruff	(Ramya Devi et al., 2018)
	Jasminum sambac (L.) Sol. Oleaceae	Leaves	Excision, incision The ethanol extract was treated to the albino rats having open excised and closed incised wounds locally every day till healing.	Wound contraction was found 100% on the 18th day in the ethanolic extract-treated group and a significantly higher wound-breaking strength was observed.	Alkaloids, steroids, carbohydrates, tannins, flavonoids, terpenoids, saponins, phenolic compounds	Antioxidant, antimicrobial, wound healing	Dermatitis, eczema, cancer	(Anima et al., 2019)
	Annona reticulata Linn. Annonaceae	Seeds	Excision, incision Wistar albino rats were subjected to both excision and incision to create a wound and an ointment formulation (both 5% and 10% w/w) was applied topically on the wound site daily for 27 days.	A remarkably increased tensile strength was observed in the case of 10% w/w ointment as compared to standard and other formulations. Also increase in wound closure was observed.	Palmitic acid, stearic acid, sitosterol, limonene, solamin, annoreticuin, pinene, myrcene, annomonicin, murisolin, squamosine, daucosterol, rolliniastatin	Anti-proliferative, astringent, Anti-hyperglycemic, analgesic, anti-inflammatory, anthelmintic, wound healing	The cardiac problem, epilepsy, parasite and worm infestations, constipation, hemorrhage, dysuria, fever, ulcer, insecticide	(Jamkhande, Prasad G., 2015)
	Aegle marmelos L. (Haw.) Rutaceae	Flower	In vitro Cutaneous wound healing activity was performed using HaCaT keratinocytes, Hs68 dermal fibroblasts and RAW264.7 macrophages to determine cell viability, nitric oxide production, collagen expression, cell migration, and beta-catenin activation. Results	A significant increasein mRNA expression, inhibited nitric oxide, PGE2 release, mRNA expression of mediators in RAW 264.7 macrophages, and enhanced motility of HaCaT keratinocytes was observed.	Cineol, Eugenol, Cumi- naldehyde, Aegelin, 1-hydroxy-5, 7-dimethoxy-2 naphthalene-carboxaldehyde (HDNC), Luvangetin	Antibacterial, antidiabetic, anti-ulcer, anti-viral, gastro-protective, cardio protective, anti diarrheal, anti-cancer, wound healing	Microbial infection, ulcer and viral infection, diarrhea, peptic ulcer, dysentery, laxative	(L. Azmi, I. Shukla, A. Goutam, Allauddin, Ch. V. Rao, T. Jawaid, M. Kalmal, a. S. Awaad, S I. Alqasoumi, 2019)
	*Annona reticulata*L. Annonaceae	Leaves	In vitro Using Human primary dermal fibroblast (HDF) cells the wound healing potency was evaluated by performing cell proliferation and migration assay. In vivo In diabetic Swiss albino mice, a topical solution of ethanol extract was evaluated (150 mg/kg) using an excision wound model.	The extract exhibited potent activity by stimulatingthe proliferation and migration of HDF, skin fibroblast, and keratinocyte significantly in a dose-dependent manner. Significantly earlier wound closure was foundinthe alcoholic extract-treated group with the early emergence of granulation tissue, and faster re-epithelialization with a sound-healed dermis.	Quercetin, ß-sitosterol	Anti-epileptic, antihelmintic, antibacterial, anti-spasmodic agent, wound healing	Lice infestation, dysentery, cardiac problems, constipation, hemorrhage, dysuria, fever, wounds, cuts, ulcer	(Mazumdar et al., 2021)
	Celastrus paniculatus Willd. Celastraceae	Bark	In vivo The isolated stigmastatone from petroleum ether extract was screened for healing activity using Swiss albino	The treated animal group exhibited a significant reduction in the wound area (97.1 %) along with anincrease in skin	Stigmastatone, methide, lupeol, pristimerin, celastrol, zeylaseral, n-triacontanol, zeylasterone,	Cardiovascular, anti-infertility, antioxidant, anti-arthritic, anxiolytic, wound healing, anti-	Abdominal disorder, beri beri, snake bite antidote, memory enhancer, emollient,	(Gowdru et al., 2012)

			rats in excision, incision, and dead space models. The stigmastatone was administered in both topical and oralroutes at 100 mg and suspension of 10mg/ml respectively. In silico Stigmastatone molecule was screened by docking with GSK3-β protein to check the inhibition of the target protein through β-catenin dependent Wnt cell signaling pathway.	breaking-strength (537.4±3.01g) and an increase in the dry weight of the granuloma tissue (21.4±0.31mg). Stigmastatone was found to be excellent binding activity towards GSK3-β as the finest promoter of cutaneous wound healing via the induction of ß catenin dependent Wnt pathway through GSK3-β inhibition.		inflammatory,neuroprotective,	sedative, wound,	
	Ixora coccinea L. Rubiaceae	Leaves	In vivo Using a circular excision model in Wistar rat, 2.5% w/w methanolic extractwas screened for wound healing activity to find out the rate ofwound contraction and hydroxyproline Content. In vitro Fibroblast proliferation assay was carried out using a Human dermal fibroblast (HDF) cellline against extract having a 1.56 to 100 µg/mL dose range to study the cell viability.	The treated animal group exhibited a significantcontraction rate i.e., 96.78% which showed a high density of mononuclear cells with distinct commencement of re-epithelialization. The test extract stimulated the fibroblast growth factor and showed a significant result and Smad-mediated collagen production in wound tissue.	Rutin, lupeol, anthocyanins, ursolic acid, kaempferol, oleanolic acid, quercetin, linoleic acid	Anti-neoplastic, antioxidant, gastro protective, anti-diarrhoeal, anti-inflammatory, anti-nociceptive, antimicrobial, wound healing	Infection, sores, hypertension, dysmenorrhoea, sprain, hemoptysis, chronic ulcer, skin diseases, scabies,wounds	(Upadhyay et al., 2014)
	Symplocos racemosa Roxb. Symplocaceae	Stem bark	In vivo The formulated extract (Jatyadi taila) was evaluated in an excision wound using a rat model.	The topical formulated showed a significant result in a dose-dependent manner by reducing the wound area with high proteins, hydroxyproline, and hexosamine content.	Symplocoside, betulinic acid, quercetin, oleanolic acid, acetyl oleanolic acid, β-sitosterol, lupeol, karanjin	Antioxidant, antidiabetic, anti-cancer, anti-androgenic, hepato-protective, wound healing, anti-inflammatory	Skin disease, eye, ear infection, tumour, uterine disorders, snake bite, asthma, arthritis, gonorrhea, dental carries, gum infection	(Acharya et al., 2016)
	Cestrum nocturnum (L.) Solanaceae	Leaves	In vivo Using Wistar albino rat, 2% & 5% (w/w) ointment of ethanolic extract was evaluated to figure out the percentage of wound contraction, epithelialization period, breaking strength, and hydroxyproline content was evaluated in the excision and incision model.	In the excision model, the test drug was found to confirm its accelerating epithelialization rate inless time to complete the epithelialization process. Similarly in the incision model, the test drug significantly increased the tensile strength in a dose-dependent manner.	Nocturnoside A, propyl gallate, cinnamic acid,gallic acid, vanillin, rutin, caffeic acid, quercetin, chlorogenic acid, hispertin, luteolin, kaempferol	Wound healing, antimicrobial, antioxidant, anti inflammatory, astringent, analgesic, anti tumor, anti diabetic	Insecticidal, moisturizer, pain killer, spasmolytic, digestive	(Nagar et al., 2016)
	Selaginella bryopteris Linn. Bak Selaginellaceae	Whole plant	In vivo 5% and 10% of ethanolic extract ointment wereevaluated for its healing potency using Wistar ratin an excision wound model.	10%ethanolic extract treated group possessed significant escalation in healingwith earlier wound contraction which could be for theshortening of the inflammatory phase followed bythe	Oleic acid, palmitic acid, flavone, gluco pyranosiddes, lanaroflavone, sciadopitysin, sequoiaflavone, hinokiflavone	Antimicrobial,Anti carcinogenic, antidiabetic, anti-depressant, wound healing	Tonic, spermatorrhoea, colitis, indigestion, constipation, urinary disorder,	(Paswan et al., 2020)

				antimicrobial effectiveness of the phytoconstituents.				
	Turbinaria ornata (Turner) J. Phaeophyceae	Green algae	In vivo Formulation containing 500µg of ethanolic extract was evaluated using Wild-type zebrafish of the TL/Ek strain to establish the wound healing activity.	A significant regeneration of the caudal fin was observed and maximum growth measurement was found on the 14th day against the test extract.	Sulfated polysaccharides, fucoids	Wound healing, antioxidant, anti-coagulant, anti-inflammatory, antibacterial	Infection, wound, cut	(Shaibi et al., 2022)
	Anacardium occidentale Anacardiaceae	Leaves	In vivo 0.5% and 2% ethanolic extract ointment was tested against the excised open wounds in the experimental rat model.	The observation confirmed that rats treated with 2% ointment showed a significantincrease rate in the percentage of wound contraction followed by a shortening epithelialization period.	Anacardic acid, cardanol, cardol, ethyl gallate, caffeic acid, quercetin, lycopene, palmitic acid	Anti-inflammatory, anti-tumor, antibacterial, anti-fungal, antidiabetic, wound healing	Malaria, tooth-ache, cough, psoriasis, skin disease	(K et al., 2020)
	Senna auriculata L. Fabaceae	Leaves	In vitro Wound scratch assay was carried out using a L929 cell line against methanolic extract having a 25 to 50 µg/mL dose range to study the cell viability.	The result showed that methanolic extract Exhibited maximum wound healing characteristic in L929 mouse fibroblast cell lines.	Alkaloids, phenolics, tannins, flavonoids	Wound healing, antioxidant, antimicrobial, anti-inflammatory, anti-diabetic	Diabetes, rheumatism, ophthalmia, skin disease, urinary infection, constipation, leprosy	(Prasathkumar et al., 2021)
	Glycyrrhiza glabra Fabaceae	Stem, roots	In vitro The vero cell line was used to evaluate the cytotoxicity and cell migration in MTT assay and scratch assay of ethanolic extract respectively	The result showed that at highest concentration the extract has no toxicity effect and significant cell migration in scratch assay in comparison with control group.	Glycyrrhizin, isoliquiritin, triterpinoids, isoflavones, glycyrrhetic acid	Wound healing, anti cancer, anti-inflammatory, antimicrobial, antioxidant, antiulcer, antidiabetic, antispasmodic, antiviral	Infections, burn wound, mucosal ulcer, fever, psoriasis, malaria, leucorrhea, jaundice	(Roy et al., 2023)
	Dodonaea viscosa Jacq. Sapindaceae	Whole plant	In vivo 2.5% w/w and 5.5% w/w of ethyl acetate fraction containing ointment was tested against the excision and incision wounds using Sprague-Dawley rat model.	It was observed that (2.5% and 5.0% w/w) ointment significantly accelerated wound healing in both models, as confirmed by faster wound contraction, epithelialization, elevated hydroxyproline levels and improved tensile strength.	Flavonoid, quercetin, penduletin, kaempferol, pinocembrin	Anti-aging, anti-inflammatory, anti-cancer, antimicrobial, anti viral, antiparasitic, immunomodulatory, wound healing, cardio-protective	Wound, burns, gout, snake bite, swelling,	(Subramanian et al., 2023)

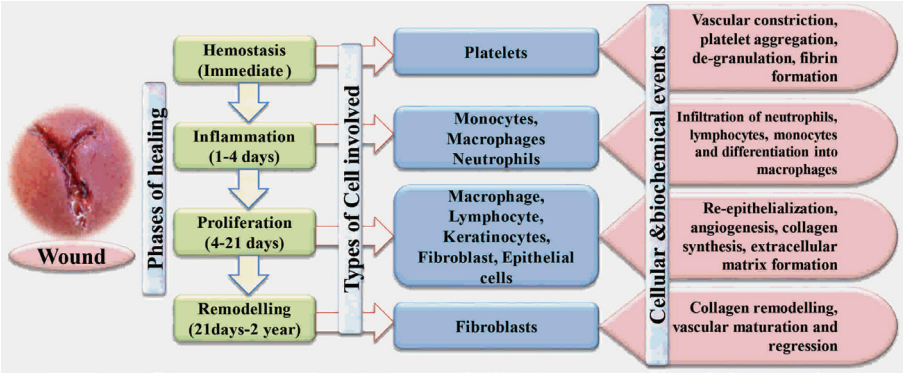

Figure 1. Schematic chart showing different phases of wound healing process.

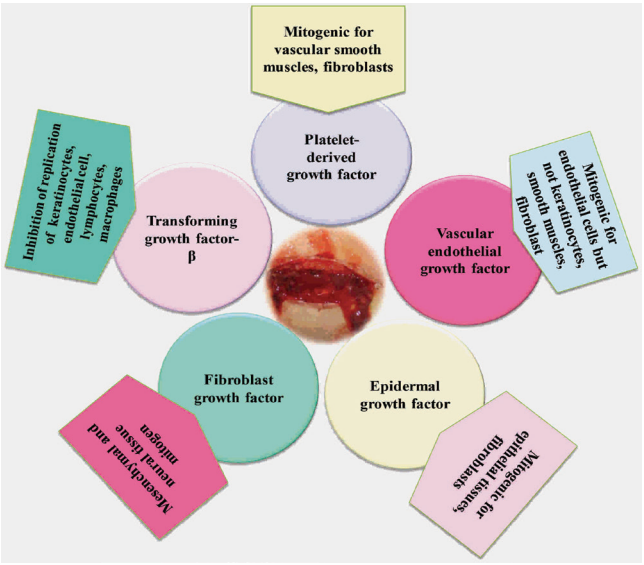

Figure 2. Growth factor involving wound healing process (Dinh et al., 2015)

the extent of the injured region. The degree of the wound can be determined through invasive as well as non-invasive technologies. Parameters like length, width, surface area, volume; tissue viability, etc come under noninvasive whereas invasive methods are used to quantify the wound extent. A variety of attributes like blood flow, oxygen, duration, oedema, inflammation, trauma, wound metabolism, nutrition, and systemic factor helps to describe a wound and its status clearly. Complete history and physical tests help to determine the attributes. The wounds ought to be evaluated by their consequence on the host in terms of wound burdens along with wound rigorousness. Wound burdens can be explained as a purpose of wound extent and its aspects whereas wound rigorousness indicates the wound burdens, host factor, and the surroundings which can change during the healing period. The simplest method of wound gradation is performed by evaluating the issues of healing and expressing them in terms of minimally, acceptably, or ideally healed. As this healing process is influential and progressive, the evaluation process is comparably challenging. The approach of this evaluation process encompasses the estimation of the following process: inflammation, angiogenesis, fibroplasia, wound contraction, remodeling, epithelization, differentiation, restoration of the connective tissue matrix, etc(Lazarus et al., 1994).

One more significant aspect is the assessment of a histological profile of healing wounds, especially in post-operative cases. The helialization by keratinocytes for acquiring the locomotive phenotype. In regeneration fibroblasts and the endothelial cells help in angiogenesis and deposition of matrix. Various clinical experiments have supported the crucial function performed by the growth factor (Figure 2) during the healing process due to their exclusive capacity to trigger repeated mitosis of quiescent cells. Angiogenesis also exhibits the principal role in the healing process through which fresh blood vessels are constituted from the subsisting vessels. The recently produced vessels afford the injured tissue with vital nutrients with oxygen by removing waste products (Imran et al., 2023) (de Mendona 2012, Sorg et al., 2017) consequently pro-angiogenic agents would abridge the healing duration.

Discussion

Commencing from ancient era, medicinal plants have served as the principal figure in the management of several disease, infection, trauma, and wounds (Shedoeva et al., 2019).As per the global conventional medicinal system, wounds have been treated with a topical regimen exclusively based on herbal extracts individually or in a combined formulation. In different tribal belts, they also arrange medicines by formulating combinations of numerous plant parts that help quick recovery from diseases. As the demand for the therapy of wound healing is increasing gradually, researchers are focusing on the exploration and validation of promising resources as a potential remedy in medical management (Ayyanar and Ignacimuthu, 2009). The employment of phyto-medicine plays an essential function in global community healthcare. Enhancing the treatment of a variety of infirmity involves either the establishment of innovative medicine or the upgrading of accessible ones to make certain added efficient and safer treatment (Hiwa M.Ahmed, Seyed Nabavi, 2021).The manuscript is arranged scientifically and covers almost all plants having proven wound-healing potential, including animal models in a very mechanistic way.

These plants are helpful in the management of numerous ailments as well as a disorder like chest pain, fever, ulcers, insect bite, skin disorders, sores, fistula, neuralgia, abscesses, scabies, dysentery, gonorrhea, eczema, stomach-ache, boils, cough, diabetes, dyspepsia, ear-ache, gastric troubles, jaundice, mouth ulcers, rheumatism, scorpion sting, tooth-ache, and wounds. Generally, these remedies were used in juice, paste, and decoction form which is administered orally as well as topically in a combination of some additives to accelerate the recovery process and tolerability. Phyto-composites established optimistic effects at different phases of wound healing, employing a variety of mechanisms. These encompass antimicrobial, antioxidant, anti-inflammatory, collagen production, initiation of cell proliferation,

healing parameters include the evaluation of epidermal closure, its differentiation, migration, hyperplasia, formation of granulation tissue, and matrix remodeling. By evaluating these above-mentioned parameters, we can able to assess the newly formed epidermis, early as well as late epidermal differentiation, migration and proliferation of cells, and deposition of collagen and elastin fiber. This provides a brief idea regarding the cascade of processes in wound healing. Various parameters may be evaluated for histological assessment of wounds using both quantitative and semi-quantitative methods. It provides insight into point-to-point changes that take place at the tissue and cell level in various stages of healing like re-epithelialization, keratinocyte migration, angiogenesis, incidence or deficiency of various inflammatory cells, fibroblasts, and collagen fibers. An in-depth assessment of a wound can be able to extrapolate the accurate pathophysiology, which may give a hand to develop a better approach towards its management. Another advantage of this histological assessment is to figure out the adverse effects and effectiveness of novel combined drug therapy(Gupta and Kumar, 2015).

Mechanism of action of wound healing

Moreover, different types of cell-cell interactions are influenced by cytokines, growth factors, and nitric oxide during the progression of wound healing. In the inflammation stage, a few inflammatory mediators and leukocytes are added to the wound sight followed by re-epit

and angiogenic property (Bahramsoltani et al., 2014).Among the reviewed data, most of the remedies are prepared from leaves, barks, and roots of single plants or different plant parts in polyherbal formulations. This review is an attempt to explore the plants having medicinal properties irrespective of wound healing activity. These data were verified with accessible reported literature. Pharmacological explorations of the herbal formulations should be an integrative analysis comprising of investigation and revelation of synthetic elements having a biological property which can be of huge implication in curative regimens.

Future perspectives

This review will be helpful to support the relationship between conventional medications; and pharmacological profiling followed by drug discovery from which evidence may be found to explore advanced wound-healing formulations. Therefore more chemical exploration, as well as clinical trials, is required to identify desirable leads that can be convenient for society.

Conclusion

In conclusion, our review provides a wealth of information available in traditional practices, offering potential solutions to current therapeutic challenges. Despite the promise of conventional methods, a significant portion of the global population still struggles with access to modern medication due to affordability issues. Consequently, conventional medicine remains the primary and often sole treatment option for many individuals. Wound healing approaches should incorporate patient-centered, holistic, evidence-based, and interprofessional themes, considering the diverse types of wounds and their intricate healing processes. While various medicinal plants have demonstrated potent wound-healing properties, further research is needed to understand their mechanisms and develop effective drugs. Clinical assessments are recommended to confirm the efficacy of herbal formulations, including dose selection criteria. Standardization in authentication, validation, and result interpretation is crucial for comparing activities across different plant species.

Author contribution

R.J., D.M.K. developed the hypothesis and wrote the initial draft, D.M.K., S.P. contributed to data curation and analysis, D.M.K. contributed to conceptualization and supervision. B.N.R. edited the article. All authors reviewed and approved the paper.

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Competing financial interests

The authors have no conflict of interest.

References

Acharya, N., Acharya, S., Shah, U., Shah, R., Hingorani, L., 2016. A comprehensive analysis on Symplocos racemosa Roxb .: Traditional uses , botany , phytochemistry and pharmacological activities. J. Ethnopharmacol. 181, 236–251. https://doi.org/10.1016/j.jep.2016.01.043

Ahmed, H.M., 2023. Ethnopharmacology of medicinal plants used in choman community , Hewler (Erbil), Kurdistan Region , Iraq. Genet. Resour. Crop Evol. https://doi.org/10.1007/s10722-023-01800-8

Alankar shrivastav, Arun Kumar Mishra, Syed Salman Ali, Aftab Ahmad, mohammed F. Abuzinadah, N.A.K. e tal., 2018. In vivo models for assesment of wound healing potential: Asystematic review. wound Med. 20, 43–53. https://doi.org/.1037//0033-2909.I26.1.78

Anima, P., Arun, M., Satish, S., 2019. Scientific validation of wound healing potential of Jasminum sambac Ait. South African J. Bot. 121, 584–589. https://doi.org/10.1016/j.sajb.2018.11.018

Ayyanar, M., Ignacimuthu, S., 2009. Herbal medicines for wound healing among tribal people in Southern India: Ethnobotanical and scientific evidences. Int. J. Appl. Res. Nat. Prod. 2, 29–42.

B.V.B., B., H.S., V., H.V., S., Shyam Prasad, K., 2017. Hydroalcoholic extract from Lepidium meyenii (Black Maca) root exerts wound healing activity in Streptozotocin-induced diabetic rats. Wound Med. 19, 75–81. https://doi.org/10.1016/j.wndm.2017.10.003

Bahramsoltani, R., Farzaei, M.H., Rahimi, R., 2014. Medicinal plants and their natural components as future drugs for the treatment of burn wounds: an integrative review. Arch. Dermacology Res. 36, 601–617. https://doi.org/10.1007/s00403-014-1474-6

Boakye, Y.D., Agyare, C., Ayande, G.P., Titiloye, N., Asiamah, E.A., Danquah, K.O., 2018. Assessment of wound-healing properties of medicinal plants: The case of Phyllanthus muellerianus. Front. Pharmacol. 9, 1–12. https://doi.org/10.3389/fphar.2018.00945

Broughton, G., Janis, J.E., Attinger, C.E., 2006. A brief history of wound care. Plast. Reconstr. Surg. 117, 6–11. https://doi.org/10.1097/01.prs.0000225429.76355.dd

D. Senthil Rajan, M. Rajkumar, C.T.K. and K.L.S.K., 2013. Wound healing activity of an herbal ointment containing the leaf extract of Ziziphus Mauritiana Lam. African J. Pharm. Pharmacol. 7, 98–103. https://doi.org/10.5897/ajpp12.795

Dev, S.K., Choudhury, P.K., Srivastava, R., Sharma, M., 2019. Antimicrobial, anti-inflammatory and wound healing activity of polyherbal formulation. Biomed. Pharmacother. 111, 555–567. https://doi.org/10.1016/j.biopha.2018.12.075

Dinh, T., Braunagel, S., Rosenblum, B.I., 2015. G ro w t h F a c t o r s in Wo u n d Healing The Present and the Future ? Growth Factors Wound Heal. 32, 109–119.

Dwivedi, D., Dwivedi, M., Malviya, S., Singh, V., 2017. Evaluation of wound healing, anti-microbial and antioxidant potential of Pongamia pinnata in wistar rats. J. Tradit. Complement. Med. 7, 79–85. https://doi.org/10.1016/j.jtcme.2015.12.002

Firdous, S.M., Sautya, D., 2018. Medicinal plants with wound healing potential. Bangladesh J. Pharmacol. 13, 41–52. https://doi.org/10.3329/bjp.v13i1.32646

Ghosh, D., Mondal, S., Ramakrishna, K., 2019. A topical ointment formulation containing leaves extract of Aegialitis rotundifolia Roxb., accelerates excision, incision and burn wound healing in rats. Wound Med. https://doi.org/10.1016/j.wndm.2019.100168

Gowdru, H.B., Rajashekarappa, S., Manjunatha, H., 2012. Molecular docking and evaluation of wound healing activity of stigmastatone isolated from bark of Celastrus paniculatus Willd . J. Biochem. Technol. Technol. 3, 134–137.

Gupta, A., Kumar, P., 2015. Assessment of the histological state of the healing wound. Plast. Aesthetic Res. 2, 239. https://doi.org/10.4103/2347-9264.158862

Hajialyani, M., Tewari, D., Sobarzo-Sánchez, E., Nabavi, S.M., Farzaei, M.H., Abdollahi, M., 2018. Natural product-based nanomedicines for wound healing purposes: Therapeutic targets and drug delivery systems. Int. J. Nanomedicine 13, 5023–5043. https://doi.org/10.2147/IJN.S174072

Hiwa M.Ahmed, Seyed Nabavi, S.B., 2021. Herbal Drugs and Natural Products in the light of Nanotechnology and Nanomedicine for Developing Drug Formulations. Mini-Reviews Med. Chem. 21, 302–313. https://doi.org/10.2174/1389557520666200916143240

Imran, H., Saleem, U., Anwar, F., Khan, Z., Saleem, F., Ahmad, B., Waqar, A.B., 2023. Evaluation of angiogenic and wound healing activity of bergenia ciliata rhizome : in ovo and in vivo study using histological and analytical tools. J. Anim. Plant Sci. 33, 805–816. https://doi.org/https://doi.org/10.36899/JAPS.2023.4.0674

Jahandideh, M., Hajimehdipoor, H., Mortazavi, S.A., Dehpour, A., Hassanzadeh, G., 2017. Evaluation of the wound healing activity of a traditional compound herbal product using rat excision wound model. Iran. J. Pharm. Res. 16, 153–163.

Jamkhande, Prasad G., A.S.W., 2015. Annona reticulata Linn. (Bullock's heart)_ Plant profile, phytochemistry and pharmacological properties _ Elsevier Enhanced Reader.pdf. J. Tradit. Complement. Med. 5, 144–152.

Jones, M.L., 2015. A short history of the development of wound care dressings. Br. J. Healthc. Assist. 9, 482–485. https://doi.org/10.12968/bjha.2015.9.10.482

Joshua S. Boateng et al., 2008. Wound Healing Dressings and Drug Delivery Systems : A Review. J. Pharm. Sci. 97, 2892–2923. https://doi.org/DOI 10.1002/jps.21210

K, M.K., Vittalrao, A.M., Se, P.K., Prabhath, S., 2020. Evaluation of Wound Healing Activity of an Ethanolic Extract of Anacardium occidentale Leaves in Wistar Rats. Biomed. Pharmacol. J. 13, 2061–2068. https://doi.org/https://dx.doi.org/10.13005/bpj/2086

Kriti Juneja, Rutusmita Mishra, Samrat Chauhan, Sumeet Gupta, P.R., 2019. metabolite profiling and wound healing activity of Boerhavia diffusa leaf extrats using in vitro and in vivo models. J. Tradit. Complement. Med. article in, 1–9. https://doi.org/.1037//0033-2909.I26.1.78

L. Azmi, I. Shukla, A. Goutam, Allauddin, Ch. V. Rao, T. Jawaid, M. Kalmal, a. S. Awaad, S I. Alqasoumi, O.A.A., 2019. In vitro wound healing activity of 1-hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde (HDNC) and other isolates of Aegle marmelos L._ Enhances keratinocytes motility via Wnt_Î2-catenin and RAS-ERK pathways. Saudi Pharm. J. 27, 532–539. https://doi.org/https://doi.org/10.1016/J.jsps.2019.01.017

Lazarus, G.S., Cooper, D.M., Knighton, D.R., Margolis, D.J., Percoraro, R.E., Rodeheaver, G., Robson, M.C., 1994. Definitions and guidelines for assessment of wounds and evaluation of healing. Wound Repair Regen. 2, 165–170. https://doi.org/10.1046/j.1524-475X.1994.20305.x

Manikandan, R., Anjali, R., Beulaja, M., Prabhu, N.M., Koodalingam, A., Saiprasad, G., Chitra, P., Arumugam, M., 2019. Synthesis, characterization, anti-proliferative and wound healing activities of silver nanoparticles synthesized from Caulerpa scalpelliformis. Process Biochem. 79, 135–141. https://doi.org/10.1016/j.procbio.2019.01.013

Mazumdar, S., Ghosh, A.K., Dinda, M., Das, A.K., Das, S., Jana, K., Karmakar, P., 2021. Journal of Traditional and Complementary Medicine Evaluation of wound healing activity of ethanol extract of Annona reticulata L . leaf both in vitro and in diabetic mice model. J. Tradit. Complement. Med. 11, 27–37. https://doi.org/https://doi.org/10.1016/j.jtcme.2019.12.001

Nagar, H.K., Srivastava, A.K., Srivastava, R., Kurmi, Madan Lal, Harinarayan Singh Chandel, M.S.R., 2016. Pharmacological Investigation of the Wound Healing Activity of Cestrum nocturnum (L .) Ointment in Wistar Albino Rats. J. Pharm. 1–8. https://doi.org/http://dx.doi.org/10.1155/2016/9249040

Negm, S.A.E.S.W.A., 2023. The wound healing effect of botanicals and pure natural substances used in in vivo models. Inflammopharmacology 31, 755–772.

Orsted, H.L., 2018. Skin: Anatomy, Physiology and Wound Healing. Can. Assoc. Wound Care.

Paswan, S.K., Srivastava, S., Rao, C., 2020. Wound Healing Activity of Ethanolic Extract of Selaginella Bryopteris on Rats. Pharmacogn. J. 12, 335–341. https://doi.org/DOI : 10.5530/pj.2020.12.53 Article

Prasathkumar, M., Raja, K., Vasanth, K., Khusro, A., Sadhasivam, S., Sahibzada, M.U.K., Gawwad, M.R.A., Al Farraj, D.A., Elshikh, M.S., 2021. Phytochemical screening and in vitro antibacterial, antioxidant, anti-inflammatory, anti-diabetic, and wound healing attributes of Senna auriculata (L.) Roxb. leaves. Arab. J. Chem. 14, 1–13. https://doi.org/10.1016/j.arabjc.2021.103345

Ramya Devi, D., Sowmiya Lakshna, S., Veena Parvathi, S., Vedha Hari, B.N., 2018. Investigation of wound healing effect of topical gel of Albizia amara leaves extract. South African J. Bot. 119, 400–409. https://doi.org/10.1016/j.sajb.2018.10.005

Roy, I., , Karuppur Thiagarajan Magesh , Mayilvakanam Sathyakumar , Annamalai Sivachandran, n Deenadayalan Purushothaman, R.A., 2023. Evaluation of Wound Healing Property of the Ethanolic Extract of Glycyrrhiza Glabra on Vero Cell Lines Using In Vitro Scratch assay Test. J. Pharm. Bioallied Sci. 15, 630–635. https://doi.org/10.4103/jpbs.jpbs

Sayeed Mohammed, D.S., 2018. Medicinal plants with wound healing potential. A J. Bangladesh Pharmacol. Soc. 13, 41–52. https://doi.org/10.3329/bjp.v13i1.32646

Shaibi, K.M.M., Leeba, B., Jamuna, S., Babu, R., 2022. Phytochemical Analysis , In Vitro Antioxidant , and Wound Healing Activities of Turbinaria ornata (Turner) J . Agardh from Gulf of Mannar, India. Appl. Biochem. Biotechnol. 194, 395–406. https://doi.org/10.1007/s12010-021-03752-0

Shedoeva, A., Leavesley, D., Upton, Z., Fan, C., 2019. Wound Healing and the Use of Medicinal Plants. Evidence-based Complement. Altern. Med. 2019, 1–30. https://doi.org/https://doi.org/10.1155/2019/2684108

Siddique, Z., Shah, G.M., Ahmed, H.M., Nisa, S., Khan, A., Idrees, M., Naz, S., Hassan, S.W., Mohiuddin, M., 2019. Ethnophytotherapy Practices for Wound Healing among Populations of District Haripur , KPK , Pakistan. Evidence-based Complement. Altern. Med. 2019, 1–11. https://doi.org/https://doi.org/10.1155/2019/4591675

Stuart Enoch, D.J.L., 2010. Basic science of wound healing. Surgery 23, 37–42. https://doi.org/10.1016/j.mpsur.2010.05.007

Subramanian, S., Duraipandian, C., Alsayari, A., Ramachawolran, G., Wong, L.S., Sekar, M., Gan, S.H., Subramaniyan, V., Seethalakshmi, S., Jeyabalan, S., Dhanasekaran, S., Chinni, S. V., Mat Rani, N.N.I., Wahab, S., 2023. Wound healing properties of a new formulated flavonoid-rich fraction from Dodonaea viscosa Jacq. leaves extract. Front. Pharmacol. 14, 1–16. https://doi.org/10.3389/fphar.2023.1096905

Tauber, A.I., 2003. Metchnikoff and the phagocytosis theory. Nat. Rev. Mol. Cell Biol. 4, 897–901. https://doi.org/10.1038/nrm1244

Upadhyay, A., Chattopadhyay, P., Goyary, D., Mazumder, P.M., Veer, V., 2014. Ixora coccinea Enhances Cutaneous Wound Healing by Upregulating the Expression of Collagen and Basic Fibroblast Growth Factor. ISRN Pharmacol. 2014, 1–9. https://doi.org/10.1155/2014/751824

Velnar, T., Bailey, T., Smrkolj, V., 2009. The Wound Healing Process : an Overview of the Cellular and Molecular Mechanisms. J. Int. Med. Res. 37, 1528–1542. https://doi.org/10.1177/147323000903700531

Yadav, E., Singh, D., Yadav, P., Verma, A., 2018. Antioxidant and anti-inflammatory properties of Prosopis cineraria based phenolic rich ointment in wound healing. Biomed. Pharmacother. https://doi.org/10.1016/j.biopha.2018.09.180

Yogesh P. Talekar, Kishori G. Apte, Shubhangi V. Paygude, Prasad R. Tondare, P.B.P., 2017. Studies on wound healing potential of polyherbal formulation using invitro and invivo assay. J. Ayurveda Integr. Med. 8, 73–81. https://doi.org/dx.doi.org/10.1016/j.jaim.2016.11.007