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REVIEW ARTICLE

Some Versatile Medicinal Plants for Healing Wounds: A Review

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Abstract:

The cellular and biochemical stages of the wound-healing process are interrelated and work to repair the wound. The body heals wounds in stages, and each stage that is postponed raises the risk of microbial infection. The time needed for healing can be sped up, and unwanted events can be reduced to improve wound healing. To aid in the healing of the wounds, the medications are administered locally or systemically. In order to promote wound healing, antibiotics, antiseptics, desloughing agents, extracts, *etc*. have been employed. Due to their adverse effects, several synthetic medications are subject to restrictions. Investigation, identification, and formulation of plants or plant-derived combinations are required for the management and therapy of wound healing. Because they have fewer adverse effects and have been used to treat wounds for a longer period, medicinal plants are becoming more popular for use in wound healing. According to studies, medicinal herbs help diabetic, infected, and opened wounds heal more quickly. It has been claimed that medicinal herbs can speed up wound healing through a variety of processes. Many medicinal plants, including *Allium sativum, Commiphora myrrha, Curcuma longa (L.), Rauwolfia serpentia, and Vateria indica,* have demonstrated the ability to treat wounds.

Keywords: Wound-healing, Medicinal herbs, *Allium sativum*, *Commiphora myrrha*, *Curcuma longa*, *Rauwolfia serpentia*.

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1. INTRODUCTION

A wound can be defined as a disruption of cellular and anatomic continuity of tissue with or without microbial infection. Physical, chemical, thermal, immunological, and microbiological exploitation of the skin's epithelial cells results in the disruption of the functional continuity of live tissue in wounds [1]. Inconvenience, inflammation, infection, and possibly organ failure can ensue from untreated wounds [2]. Promoting wound healing involves a complex series of events, such as the proliferative phase, the inflammatory phase, and remodelling phase [3].

Skin is critical to our existence because it senses the environment, regulates our body's physicochemical and thermal balance, stores vital nutrients, offers passive and active defence and reacts to shock and injury. It takes strong and efficient systems to protect it from injury and repair vital skin functions that are lost or injured to maintain these vital functions [4, 5]. Human health care has included herbal medicine for thousands of years. Herbal extracts contain a diverse array of chemical components that are effective against certain diseases. According to data from WHO, more than 80% of people worldwide rely on herbal remedies [6, 7]. The biological mechanisms of plant extracts' ability to speed up wound healing have been intensively investigated in recent years [8].

Several plant extracts have been cited to enhance wound healing by the activation of NF-B [9], favouring pro-inflammatory cytokines, an increase of iNOS, and alpha-1 type-1 collagen [10 - 12].

1.1. Effect of Medicinal Herbs on Wounds to Speed up Healing

Wounds recover *via* three stages: inflammatory, proliferative, and remodelling. Immediately following the damage, an inflammatory phase sets in, lasting up to 48 hours and occasionally even more than two weeks. This phase's hemostatic capabilities instantaneously cease bleeding through vasoconstriction and platelet aggregation. After then, phagocytosis and vasodilatation occur at the wound site, causing inflammation [13]. The proliferative phase, which lasts for two to three weeks after the inflammatory phase, starts. Collagen fibres build up, and neovascularization takes place during this period. Epithelial tissues are then produced across the wound site when the wound edges are brought together, and the wound site is decreased. Three weeks to two years may pass during the remodelling process. During this stage, the tissue's tensile strength was improved by cross-linking between

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collagen fibres by vitamin C-dependent hydroxylation. Many methods, including the upregulation of VEGF and TGF-, activation of NF-B, activation of interleukin-8, enhanced production of iNOS and alpha-1 type-1 collagen, and anti-oxidant activities, are used by herbal remedies to cure wounds [14]. Herbal remedies are used to clean wounds, remove dead tissue, and provide a moist environment that encourages the emergence of an idea to cure burns, wounds, and cuts [15]. The herbal extracts and fractions efficiently stopped bleeding from recently opened wounds, prevented the growth of bacteria, and sped up the healing process [16]. The antimicrobial and free radical-scavenging qualities of the phytoconstituents present in the extract may be responsible for the enhanced wound-healing capacity that might occur from the individual or combined effects of bioactive molecules. These active components enhance collagen fibrils' viability and collagen fibres' strength by enhancing circulation, reducing cell damage, or boosting DNA synthesis, all of which assist the recovery process of wounds [17]. As a wound is healing, fibroblasts migrate from the borders of the wound to the wound site, proliferate and subsequently produce collagen, the main component in the extracellular matrix [18, 19].

Wound healing uses medicinal plants with a variety of phytoconstituents, with the main components having antibacterial and antifungal activities being Flavonoids, Tannins, Saponins, Terpenes, terpenoids *etc* [20]. 1) Stimulation of Wound healing boosts homeostasis, contains hydroxyproline, increases tensile strength, and is an antioxidant. By the secondary metabolites of plants, such as Tannins, Flavonoids, β- carotene. 2) Plant glycosides decrease the wound closure time; these can increase epithelialization, homeostasis and stimulate granulation of tissues. 3) Vitamins and minerals of plants increase wound healing rate and wound contraction, and these reduce the infection. 4) Natural plant steroids and triterpenes increase epithelialization, increasing wound closure and collagenisation. Carbohydrates as energy sources are used in collagen synthesis (Fig. **1**). Thus, these compounds play an essential function in speeding up the recovery process by upregulating collagen synthesis during the maturation stage [21].

2. METHODS

Many reliable databases, including Google Scholar, PubMed, Science Direct, SciFinder, .www.theplantlist.org, and www.gbif.org, Web of Science, were used to conduct a thorough evaluation of the literature on the applications and bioactivity of different plants in wound healing.

2.1. Versatile Medicinal Plants in Healing Wounds

Herbal products are in huge demand in developed countries due to undue side effects of synthetic products and comparatively safe parameters of herbal products. Indian indigenous groups employ a number of scientifically proven botanicals to regulate wound healing. There have been several new studies on plants (Table **1**) that have potent wound-healing properties, which are illustrated here:

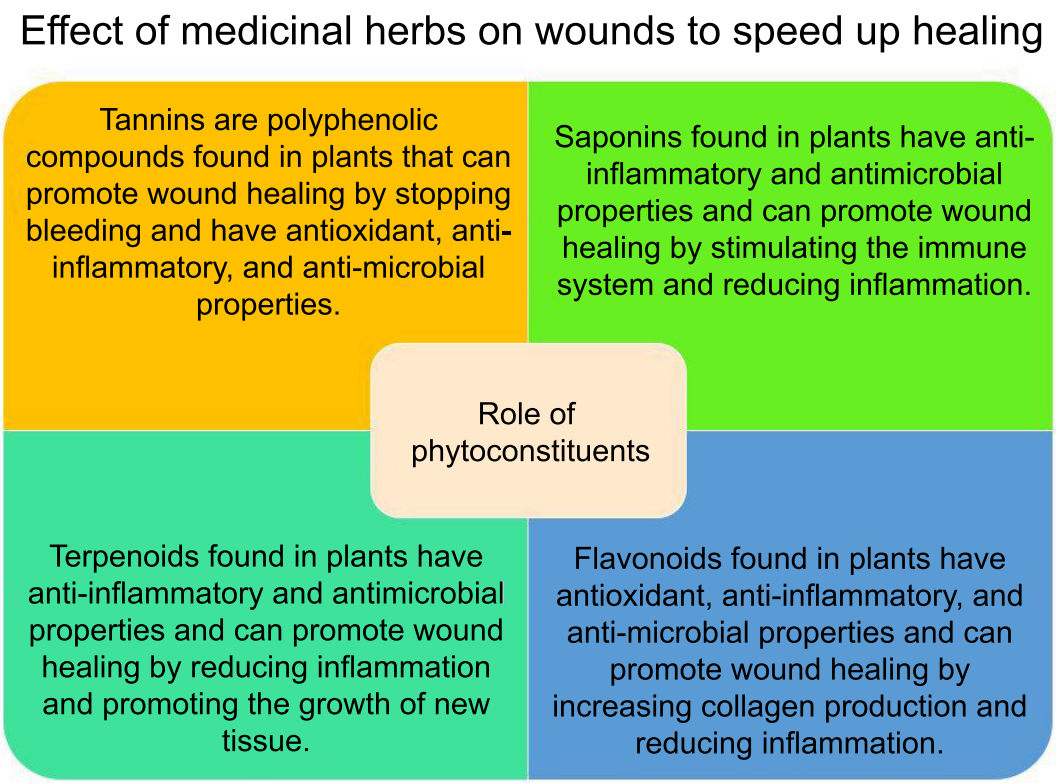

Fig. (1). Role of phytoconstituents in wound healing.

Table 1. List of medicinal plants having wound healing properties.

Plants Used in Wound Healing			
Achillea millefolium L	Candlebush (Cassia alata L.)	Ephedra alata	Morinda citrifolia
Alchemilla mollis and Alchemilla persica	Celosia argentea	Eucalyptus citriodora	Musa sapientum
Alternanthera brasiliana	Citrus tamurana	Flexseed Linum usitatissimum (flax)	Ocimum sanctum Linn.
Allium sativum	Cleoma viscosa	Hibiscus rosa-sinensis	Pentas lanceolata
Aloe vera	Commiphora myrhha	Iris florentina	Pistacia atlantica,
Arnebia densiflora	Curcuma longa (L.)	Ixora coccinea	Quercus infectoria Olivier
Azadirachta indica	Cynodon dactylon	Jatropha curcas,	Rauwolfia serpentina
Caesalpinia ferrea Mart	Delonix elata	Leea macrophylla	Sambucus ebulus
Calendula officinalis	Drypetes klainei	Leucas hirta	Urtica dioica
Calotropis gingantea (L.) R. Br.	Elephantopus scaber Linn.	Melaleuca alternifolia	Vitis vinifera

2.1.1. Achillea millefolium L.

Is a plant that belongs to the Asteraceae family and is usually known as a yarrow. Folk medicine uses yarrow's ethnopharmacological properties to cure inflammation and haemorrhoids, enhance the healing of wounds, and widen blood vessels. The plant has a long history of usage as a potent topical remedy for wounds, cuts, and abrasions. Its leaves are sessile, linear to lanceolate, twice or ternately pinnatifid and up to 25 cm long. Cauline leaves are about 10 cm long and 3 cm wide. Isovaleric acid, salicylic acid, sterols, flavanoids, tannins, and coumarins are the major components of yarrow. *A. millefolium L.'s* ability to cure wounds appears due to its active ingredients, which accelerate the recovery procedure and provide healed wounds breaking strengths by using 5% and 10% w/w alcoholic extract in the form of ointment (0.5 g applied daily for 10 days) [22].

2.1.2. Alchemilla mollis and Alchemilla Persica

Are annual plants in the Rosaceae family that are commonly called Lady's mantle. Alchemilla species have been employed to treat dermatitis, skin rashes, oral and tongue irritation, dysmenorrhea, and gastrointestinal problems. Traditional uses for *A. mollis* include the therapy of sores and excessive periods [23]. Moreover, *A. mollis* has been discovered to have antiviral, astringent, diuretic, antispasmodic, and antioxidant activities because of the existence of phenolic content such as tannins and flavonoids [24]. *A. mollis* areial and root aqueous-methanol extract pharmaceutical formulations (ointment) were tested on Wistar rats using circular and linear wound models to determine their ability to repair wounds; by using the (20:80) hydroalcoholic extract in ointment base (applied daily for 9 days). In comparison to control rats, the ointment raised the rate of wound contraction and tensile strength substantially. A histological examination revealed the development of fibroblasts, epithelization, collagen synthesis, and neovascularization; similar results were also seen with *A. persica's* salve [25, 26].

2.1.3. Alternanthera Brasiliana Kuntze

Is a perennial plant of the family Amaranthaceae. In Brazilian traditional medicine, it is employed to treat dysentery, coughs, and inflammatory conditions [27]. Due to their astringent and antibacterial effects, terpenoids are widely recognised for speeding the process of wound healing [28]. Animals administered a 5% w/w ointment of *A. brasiliana* methanolic extract on the diabetic lesion had considerable progress in wound healing. Compared to the control group and standard groups, the percent wound shrinkage (89.76%,) on day 8 in the extract-treated group was considerably higher. Its methanolic extract demonstrated a speedier wound closure rate and wound healing by interleukin-8 stimulation, an inflammatory chemokine that effects the function and placement of different inflammatory cells, fibroblasts, and keratinocytes, which may be the cause of this. It might boost granulation tissue development and gap junctional intracellular signalling in cultured fibroblasts [29].

2.1.4. Allium Aativum

Also called garlic, belongs to the Amaryllidaceae family. It has about 8 to 20 cloves in subglobular compound bulbs that are 3 to 5 cm wide and cloves are ovoid and have three to four sides. Many phytochemicals, including sulfur-containing compounds like E and Z ajoenes, thiosulfinates (allicin), vinyldithiins, and sulphides, are present in the bulbs of *A. sativum*. It is used as a spice and condiment in foods. It serves as anticancer, antiviral, and antidiabetic, renalprotective, anti-atherosclerotic, antibacterial, and antifungal effects. Garlic also has carminative, antipyretic, sedative, aphrodisiac, antioxidant and diuretic actions, and it has been utilised in conventional medicine to address heart disease, indigestion, lung infections, and urinary tract infections [30]. Several animal studies have shown that garlic extracts can both hasten healing wounds and prevent infection. Allicin stimulates fibroblasts, which promotes faster and more effective wound healing. Fibroblasts are essential for the healing of wounds [31]. The injured area's increased antioxidant levels hasten the recovery procedure. Anti-inflammatory substances, however, in addition to antioxidants, also serve critical roles in quickening the recovery process. *A. sativum* accelerates the recovery procedure by promoting dynamic healing. Therefore, topical treatment with *A. sativum* extract boosts the carbohydrate ratio in dermal and epidermal cells, supporting these cells' energy needs and supplying the first substrate required for the creation of structural components, thus aiding in the healing process. The high flavonoid and phenol contents of *A. sativum* were found to promote wound healing at the concentrations of 1%, 5%, 10%, and 15% methanolic extract mixed with skin lotion

(painted twice daily for 6 days) in a rat model, mitigated the degenerative effects of inflammation. Also, it dramatically sped up the recovery procedure by lowering inflammatory response, improving mast-cell distribution, raising the ratio of intracellular carbohydrates, and encouraging angiogenesis [14, 32].

2.1.5. Aloe Vera

It is sometimes referred to as kumari (Hindi) of the Liliaceae family. This plant is used as a treatment for burns, wounds, peptic ulcers, skin irritation, diabetes, asthma, and other conditions [33]. Transforming growth and vascular endothelial growth factor (VEGF) factor-1 (TGF-1) expression is raised in the Wistar rat when type 2 diabetes is treated with oral *A. vera* mucilage, increasing the pattern of wound healing by inducing fibroblasts to rebuild extracellular matrix [34]. The research found that a male rat model with a circular wound was used to assess the consequences of *A. vera* gel. It was shown that *A. vera* gel significantly decreased wound thickness when contrasted with the control team and when changed with neutrophil, macrophage, and fibroblast cells [35]. The amount of new blood vessels grew substantially after taking aqueous extract while significantly reducing the number of lymphocytes and macrophages [36]. In a separate study, streptozotocin-induced diabetic Wistar rats were given an oral dose of an ethanolic extract of *A. vera* gel (300 mg/kg/day) for nine days. This therapy significantly raised DNA and glycosaminoglycan levels, reduced blood glucose levels, and improved plasma insulin levels. Additionally, the extract greatly raised the incision model's tensile strength. According to studies, *A. vera* has the ability to cure wounds when made into an ointment for use in tropical climates [37].

2.1.6. Arnebia Densiflora

It belongs to the family Boraginaceae; known as egnik by red dye was made by locals and used to tint carpets and rugs. Its butter-soaked roots are utilised in the local treatment of wounds. This plant's roots have reportedly been found to contain alkannin derivatives, namely β, β-dimethylacrylalkannin, teracrylalkannin and isovalerylalkannin + α-methyl-n-butylalkannin. As per the study conducted by using *A. densiflora*, root extracts ointment applied tropically in rat intra oral wound to full- thickness skin incision in rats for 7 days reduced oedema, accelerated collagen fibre production, and increased epithelium thickness [38]. Rats given *A. densiflora* root extract for scalpel wounds demonstrated quicker histological recovery than the control group. Healing occurred on the 14th day after wounding, but healing started in the control group on day 21 by using the concentration of 16% solution in medicated olive oil (applied twice daily for 26 days). Wound closure and collagen formation were also quicker in the healing group. Its root extract accelerated wound healing and collagen fibre formation, in particular [39, 40].

2.1.7. Azadirachta Indica

Also called neem of maliaceae, family Neem Leaves have medicinal compounds like nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl 7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol [41, 42]. Aqueous leaf extracts of Neem leaves increase the rate of wound healing through increased inflammatory response at the concentration of 5% methanolic leaf extract (applied daily for 15 days) and neovascularization in mice. Research in the field of dentistry has demonstrated the effectiveness of neem extract in root canal and endodontic procedures. Many active substances, including azadirone, azadiractin, and flavonoids, have been discovered to have medicinal promise [43 - 45].

2.1.8. Caesalpinia Ferrea Mart

It belongs to the Caesalpinioideae family. It is a leguminous plant that may be found throughout Brazil. This plant's bark is utilised in conventional therapy to cure cancer, rheumatism, enterocolitis, and wounds. *C. ferrea* bark aqueous extract was evaluated for its analgesic, antibacterial, anti-inflammatory, anticancer, and antiulcer effects [46]. The efficacy of an ointment produced from *C. ferrea* bark powder along with vaseline for skin wound healing was examined in mongrel goats. This ointment decreased the affected area and completed epithelialization on the 21st day. Wistar rats' wound healing time, leukocyte infiltration, vascular permeability, and angiogenesis were all shown to be decreased by the polysaccharide-rich extract of *C. ferrea* stem bark. Moreover, it promoted the growth of fibroplasias and epithelial layers at the concentration of 0.025-1% aqueous bark extract (applied daily for 21 days). It also reduced the synthesis of myeloperoxidase, total protein, malondialdehyde (MDA), prostaglandin E2, tumour necrosis factor (TNF), and interleukin-1 (MPO). Additionally, it boosted the expression of TGF and Inos [11, 47, 48].

2.1.9. Calendula Officinalis

Called pot marigold, of the Asteraceae family, has a long history of use in ethnopharmacology and has been cultivated throughout Europe for millennia [49]. Calendula flower-derived medications have a long history of use for the external management of inflammation and wounds [50]. In comparison to the control group, the ethanolic extract of *C. officinalis* flowers significantly reduced the presence of fibrin and hyperemia in a cutaneous wound model in Wistar female rats at days 4 and 7 after surgery. Additionally, collagen deposition increased in the ethanolic extract; at the concentration of 2% and 10% ethanolic extract in gel/ointment form (applied daily for 21 days). An immunohistochemical study revealed that the dermis expressed VEGF and had more blood vessels [51]. It has been established that *C. officinalis* tincture stimulates the spread of Swiss albino mice fibroblast human primary dermal fibroblast (HDF), cells (NIH-3T3), and human Caucasian fibroblast-like foetal lung cells (WI38). According to the findings, NIH-3T3, HDF, and WI38 cells migrated as per the experiment. The effects of n-hexane, ethanolic, and aqueous extracts of *C. officinalis* flowers were investigated on human immortalised keratinocytes and dermal fibroblast cells were used to do research on the inflammatory stage of wound healing. It was demonstrated that in human immortalised keratinocytes, the n-hexane extract boosted the activity of the transcription factor NF-B and the chemokine (Interleukin-8) [9, 52].

2.1.10. Calotropis Gingantea (L.) R. Br

Also called Sweta arka of the Asclepiadaceae family is indigenous to Malaysia, China, and other nations. The main active phytoconstituents that are extracted from plants include flavonoids, triterpenoids, phenolic compounds, tannins, alkaloids, steroids, glycosides, saponins, terpenes, enzymes, alcohol, resin, fatty acids, and esters of calotropeols [53]. The efficiency of topical *C. gigantea* therapy in healing excision wounds was assessed. Incision wounds included more hydroxyproline, and it was demonstrated that the dead space wound model increased the proportion of wound contraction by using the 180 mg/kg-200 mg/kg methanolic extract of leaves (applied daily for 13 days) [54, 55].

2.1.11. Cassia Alata L.

It is usually referred to as a candle bush or ring warm plant, and it has a very high therapeutic value historically and internationally. It is used as an antidote and bactericide in rheumatism, skin disorders, snakebites, stomachaches, and venereal diseases. The candlebush methanolic extract of leaves may aid in the healing of wounds *in vivo*; this action may be brought on by the antibacterial or modulatory characteristics of the bioactive components [56, 57]. Candlebush leaf extract contains 3,4 dihydroxycinnamic acid, which has antibacterial properties against both Gram-positive and Gram-negative bacteria according to an *in vitro* test, which also shows its antibacterial action against *Bacilus subtilis* and *Staphylococcus aureus*. This plant's flavonoids, terpenoids, tannins, and other phenolic substances modulate keratinocytes and fibroblasts. Another family of bioactives, fatty acids having modulatory impacts on the healing of wounds; in particular n-9, boost the reparative response in living organisms while reducing inflammation in the lesion at the dose of 125mg/kg-500 mg/kg ethanolic extract of leaves (applied daily for 21 days). Oleic acid, a different kind of fatty acid, accelerates the inflammatory response to promote wound healing [58, 59].

2.1.12. Celosia Argentea

It is sometimes known as “troublesome weed” and is a member of the Amaranthaceae family, used in ulcers, sores, and hemorrhagic disorders, among other diseases, in addition, to being hypothermic, antibacterial, antiprotozoal, and hepatoprotective [60, 61]. In order to heal wounds, *C. argentea* leaves have been employed in traditional Chinese and Indian medicine. The alcoholic fraction promotes recovery from injuries caused by burn, the probable mechanism by decreasing inflammatory response, increasing the flow of blood at the site and reducing infection. The chemical elements of the *C. argentea* extract, including celosia, flavonoids, phenolic compounds, and vitamins, may promote healing by triggering antioxidant enzymes and scavenging free radicals. Early wound healing at the concentration of 10% w/w methanolic extract in ointment form (applied daily for 15 days) and less post-burn complications may be caused by certain chemical elements present in the alcoholic extract of *C. argentea* leaves [10, 62 - 64].

2.1.13. Citrus Tamurana

In the past, people have used this citrus crop from Miyazaki, Japan, which belongs to the Rutaceae family, as an agent to enhance appetite and digestion, lessen flatulence, prevent stomach distention, and help with respiratory problems. It has been shown that *C. tamurana* peel extract inhibits human midazolam 1-hydroxylase activity, Cytochrome P450 3A, and prevents bone loss [65 - 67]. The growth of *C. tamurana* peels' aqueous extract was utilised to assess skin fibroblasts (TIG-119). While the extract showed linear and, depending on time and TIG-119 cell proliferation at lower doses (0.1, 0.25, 0.50, and 0.75 mg/mL) inhibited the increased TIG-119 cell proliferation concentrations (>1 mg/mL). The extract increased cell migration to the wound site in a model for healing of scratch wounds at the concentration of 0.1, 0.25, 0.50, and 0.75 mg/mL aqueous extract of peel (*in-vitro* study for 1 day). The effects of the extract (0.8 mg/mL) on the G2 and M stages of the cell cycle were also favourable. Cdk-1 and 2 (cyclin-dependent kinase 1 and 2), Rac-1, Rho-A, Cdc-42, and other genes were expressed more often as a result of the extract. Cdk-1 and protein levels, however, did not increase [68].

2.1.14. Cleoma Viscosa

Hul hul is the name given to native Indian healers of the Cleomaceae family. It is an annual plant that thrives in wastelands and in grassy places. It is a hairy plant with white, yellow and pink flowers. Traditional uses for the plants' leaves, bark, roots, and seeds include stimulant, anthelmintic, antiscorbutic, carminative, stomachic, laxative, diuretic, anti-inflammatory, anti-tumor, and antileprosy properties. The leaves are also used topically on ulcers and sores [69, 70]. The methanolic extracts of *C. viscosa* at the concentration of 5% w/w methanolic extract of whole plant and leaf in simple ointment (applied daily for 22 days) for wound healing activities were used to measure the changes in the wound region at various points, including 4 days, 8 days, 12 days, 16 days, and 22 days after the wounding. Compared to the control group, animals in the treatment groups had epithelization for 22 days instead of 30 days. Comparing the plant *C. viscosa* to the control group, it showed good wound-healing activity, which supported its use in traditional medicine [71, 72].

2.1.15. Commiphora Myrrha

Often referred to as Guggul, of the Burseraceae family, the deciduous prickly tree can reach heights of 5 metres and a width of 1.5 metres. There are three leaflets per oblong to oval leaf. Myrrh contains resin, gum, and volatile oil [73]. The disulphide is mostly to blame for the oil's unpleasant odour. In addition to being utilised locally to treat boils, wounds, and mouth ulcers, myrrh is widely used in oral preparations. It is the best herbal remedy for treating gingivitis, mouth ulcers, and sore throats. It works well as a treatment for boils, acne, and other mildly inflammatory skin conditions because of its mild astringency [74]. Aromatherapists utilise an essential oil extracted from the resin as a natural antiseptic to treat oral and skin conditions. It serves as stomachic, digestive, carminative, bacteriostatic, intellect-promoting, aphrodisiac, diuretic, deodorant, and ophthalmic. Topical application of 4% (v/w)

essential oil and 5% (w/w) resin is used for its wound healing abilities. At the doses used, 0.5% w/w aqueous extract of myrrh in ointment (applied daily for 9 days), the ointments were proven to be non-irritating, but they also showed a significant (p 0.05–0.001) influence on the healing of wounds, as shown by a faster rate of wound contraction, shorter time for epithelization, and a higher skin breaking strength when contrasted with control. Similar to ciprofloxacin, the oil and resin both displayed significant antibacterial action against different types of Gram-negative bacteria [75, 76].

2.1.16. Curcuma Longa L.

Called haldi (Hindi) of the Zingiberaceae family, and its main rhizomes are ovate, oblong, or pear-shaped, averaging around 3 cm in diameter and 4 to 5 cm long, with transverse annular leaf scars. Curcuminoids, a mixture of curcumin, demethoxycurcumin, and bisdemethoxycurcumin, make up 3-6% of turmeric's chemical constituents. The curcuminoids, which give turmeric its bright yellow colour, are accountable for the volatile oil's scent. Its oil contains hundreds of different compounds, but pharmacologically important ones are ar turmerone, -turmerone, and -turmerone [77, 78]. In multiple bioassays for curcumin administration at the wound area, the ability of curcumin to lower reactive oxygen species, which promote collagen synthesis, stimulate the development of granulation tissue, and finally speed up wound contraction, were all demonstrated at the dose of 40 mg/kg hydroalcoholic extract orally (daily for 11 days). Cholagogue increases the liver's production of bile and the gallbladder's excretion of bile, which improves the body's ability to digest fats [79]. Moreover, it affects several phases of the body's natural wound-healing cycle to speed up healing. Curcumin can lessen the body's normal reactions to cutaneous wounds, including oxidation and inflammation. Recent research on the compound's wound healing abilities may provide more support for curcumin's capacity to promote collagen deposition, tissue remodelling, granulation tissue production, and wound contraction [80, 81].

2.1.17. Cynodon Dactylon

The family Poaceae includes the perennial grass *C. dactylon*. Farmers have long used the crushed plant's leaves to cease bleeding tiny wounds since it has many more medicinal applications. The plant's roots are consumed as a paste with water to alleviate fever [82]. Dysentery is treated using the aqueous fluid extract of the rhizome, which also functions as an anti-inflammatory, diuretic, antiemetic, and purifying agent. The anti-diabetic, anti-ulcer, diuretic, anti-microbial, hepatoprotective, cardioprotective, and immunomodulatory effects of this plant have also been demonstrated [83]. An excision wound model in Wistar rats treated topically with carbopol gel containing aqueous and alcoholic extracts of the *C. dactylon* plant exhibited quick wound healing. A gel formulation of aqueous and ethanolic extracts improved the tensile strength in an incision wound model at the concentration of 250 gm of aqueous and 250 gm of alcoholic extract (10% & 20% w/w) of leaf in gel formulation (applied daily for 16 days) [84]. Wistar rats that had applied an ointment with a hydromethanolic extract of the *C. dactylon* plant had increased collagen deposition and decreased necrosis and inflammatory cell infiltration at the 21st post-surgery day. Another investigation revealed that Swiss albino mice's wounds could be healed by *C. dactylon* flavonoid fraction. This fraction was discovered to rise tissue levels of collagen, protein, and hexosamine while lowering lipid peroxidation [85, 86].

2.1.18. Delonix Elata

The plant is 10-15 m tall and has many branches and an umbrella-shaped crown. It is a member of the Fabaceae family, subfamily Caesalpinioideae. Its bark and leaves are used in order to treat arthritis, joint stiffness, and discomfort [87]. It possesses many phytochemicals, *viz*. saponins, alkaloids, carotene, hydrocarbons, phytotoxins, flavonoids, tannins, steroids, carotenoids, galactomannon, lupeol, β-sitosterol, terpenoids, glycosides and carbohydrates, in leaves, flowers, bark and roots. The plant shows diverse therapeutic prospective, such as antifungal, antibacterial, antioxidant, wound healing, antiemetic, larvicidal, hepatoprotective, anti-diarrhoeal, anti-inflammatory, antimalarial, anthelmintic, antiarthritic and anticarcinogenic potential [88]. In an excision, incision, and dead space wound model in Wistar rats, the efficacy of a simple 5 and 10% ointment of hydro-ethanolic (70%) and aqueous extract of *D. elata* flowers was examined at the concentration of 40 mg/kg of alcoholic extract of flowers and leaves (5% & 10% w/w) in gel formulation (applied daily for 15 days). In the incision wound model, both extracts significantly increased tensile strength; in the excision wound model, wound contraction and epithelialization; and in the dead space wound model, the development of granuloma tissue with high hydroxyproline content. According to an examination of the histology, the dermis included inflammatory cells and a hair follicle, as well as a thin epidermis [12].

2.1.19. Drypetes Klainei

Drypetes (Putranjivaceae) plants are employed in traditional Asian and African drugs for treating a range of conditions, including typhoid, gonorrhoea, rheumatism, sinusitis, and tumours [89]. It is frequently used as a treatment of burns, wounds 70% hydroalcoholic extract of stem bark (at the concentration of 5% & 10% w/w) in ointment (applied daily for 15 days), headaches, urethral problems, fever in young children, and other ailments. *D. roxburghii* (Asian species) cures many diseases because of the existence of terpenes, steroids, and some thiocyanates. Applying a fine powdered stem bark to skin wounds or ingesting it; both options [90]. To support the Baka Pygmies' traditional use of *D. klainei*, aqueous, dichloromethane, and methanolic stem bark extracts were examined for their capacity to treat injuries. Each of the three extracts raised the vitality and migration of human and murine fibroblast cells using a scratch assay, and the most active extract was the methanolic one [91, 92].

2.1.20. Elephantopus Scaber Linn.

belongs to the Asteraceae family and is a tropical species of flowering plant. It is native to tropical Africa, Eastern Asia, and India. It has phytoconstituents like sesquiterpene lactones, such as elescaberin, isodeoxyelephantopin, deoxyelephantopin, isoscabertopin, and scabertopin as the primary bioactive

components identified from ethanolic extract of the plant. Deoxyelephantopin, a substance derived from ethanolic leaf extract, and aqueous leaf extract were both tested for their ability to heal wounds at the dose of 250 g/kg & 500 g/kg of the extract applied daily for 16 days by Singh *et al.*, in animals given deoxyelephantopin, which demonstrated improved wound healing [93].

2.1.21. Ephedra Alata

Called Alanda of the Ephedraceae family, a perennial genus with a maximum height of more than one metre, has a strong pine odour and an astringent taste. It is a small, stiff, perennial shrub, and its dioecy is light green and thickly branched. A decoction of the stems of *E. alata* was employed as a stimulant, a treatment for cancer, bronchial asthma, circulatory system irregularities, and renal health problems. Chewing the plant stems helps to treat bacterial and fungal disorders, especially infections of the mouth. Ephedra species were located utilising the alkaloids and phenolic compounds present in them, including trans-cinnamic acid, catechin, epicatechin, symplocoside, flavonol-3-O-glycosides, and proanthocyanidins. It is also used to treat diabetes mellitus. An *E. alata* extract-based ointment was tested on hamsters using an excision and burn wound model to assess its potential for healing wounds at the concentration of 1.5 g of alcoholic extract of the whole plant in ointment form (applied daily for 15 days). The cream was discovered to induce fibrosis, encourage the deposition of collagen fibres, and speed up wound ulcer healing, but it had no same beneficial effects on burn wounds. Excision wound ulcers became more fibrotic as a result of the ointment [94, 95].

2.1.22. Eucalyptus Citriodora

It is a member of the Myrtaceae family and is known as lemon-scented gum, blue spotted gum or lemon eucalyptus. From ancient times, this substance has been utilised as an anti-inflammatory, analgesic, antibacterial, antipyretic, and support against respiratory infections, nasal congestion, and it has antioxidant qualities. It is well recognised for its essential oils with vital properties as citronellal, cineole, and citronellic acid [96]. Eucalyptol has been shown to decrease the production of cytokines and chemokines in inflammatory cells, including TNF-a, IL-1, leukotriene B4 and thromboxane B2. Eucalyptus citriodora leaf extracts in ethanol and tetraacetic acid (200 mg/kg) were efficacious in all models of wound healing. Its extract promoted wound contraction while reducing epithelization and scar area at the concentration of 0.1 mg/ml of 50% alcoholic extract of leaves in ointment form (for 1 day). The wounds in the treated group completely healed, and the collagen and reticulin structures were nearly normal. Substantial improvement in skin-breaking strength, which was a result of increased collagen levels and collagen fibre cross-linking.

Moreover, an increase in the dry granulation tissue's weight revealed a higher protein content. Studies have demonstrated that flavonoids provide therapeutic effects because of their anti-inflammatory, anti-fungal, antioxidant, and wound-healing properties. Flavonoids are also known to endorse methods for healing wounds primarily owing to their antimicrobial and astringent qualities that cause wound constriction and a faster rate of epithelization. Tannins and polyphenolic flavonoids are said to speed up the healing process [97].

2.1.23. Linum Usitatissimum

(Flax/Flexseed) is an annual plant that is frequently found in the Mediterranean and warmer climatic zone. It is a member of the Linaceae family. It is one of the earliest agricultural plants used for oil and fibre production. Furthermore, there is a report that flax products are also recommended for treating skin disease due to their antibacterial, antifungal, antiviral and antioxidant properties. One of the best sources of linoleic acid (l-LA) is flax oil, which also contains secoisolariciresinol diglucoside (SDG), 15 to 29% linolenic acid, and 13 to 29% oleic acid. Although both linolenic acid and -linolenic acid are necessary for the structural integrity of the cell membrane, they work together to help keep wounds intact and hasten the healing process [98]. By assisting the natural process of wound clearing by macrophages, which is stimulated by the high antioxidant content (such as phenolic acids), this bandage may ensure the ideal environment for efficient healing. This can stop fibromas from forming and maintain the ideal humidity needed for epithelial cells to migrate at the dose of 2% flaxseed oil in ointment form (applied daily for 12 days) [99, 100].

2.1.24. Hibiscus rosa-sinensis

(Malvaceae), called china rose, of the family, is an unbranched shrub traditionally used for its anti-tumor, anti-hypertensive, anti-oxidant, and antiammonemic capabilities. The flowers and leaves promote hair growth and the recovery of ulcers. Flowers have also been shown to be efficient in the therapy of arterial hypertension and have antifertility properties [101]. In Sprague Dawley rats, the ability of *H. rosa-sinensis* flower ethanolic extract to hasten the healing of excision, incision, and dead space wound models was investigated. When the extract was diluted in water and given at a dosage of 120 mg/kg/day, the epithelization and wound contraction increased. The extract further demonstrated enhanced granulation tissue, hydroxyproline content, and skin-breaking strength at the concentration of 5% & 10% w/w alcoholic extract of flower in ointment (applied daily for 15 days) [102, 103]. Wistar rats were used in a different investigation to examine the therapeutic potential of an ethanolic extract of *H. rosa-sinensis* leaf. In models of burn wounds and excision wounds, the extract improved wound contraction and epithelialization. The incision wound model's wound-breaking strength was improved. After histological analysis of the removed wound, the normal architecture of the skin was revealed to have been restored [104]. Epithelialization, fibroblast distribution, and collagen distribution were clearly visible using the Masson's trichrome and hematoxylin and eosin staining techniques. The proteins transforming growth factor-1 (TGF-1) and vascular endothelial growth factor (VEGF), which are involved in angiogenesis and the synthesis of collagen fibre, were found to be expressed more often in an immunohistochemical investigation [105].

2.1.25. Iris Florentina

Belongs to the Iridaceae family, found in Iran, India, and China all contain large populations of this plant. The gorgeous blossoms have a violet-like smell that distinguishes them. From Eurasia to North America, the plants may be found in moderate climates across the Northern Hemisphere. Several iris species are attractive flowers utilised in conventional remedies to cure cancer, bacterial and viral infections, inflammations, and other illnesses. Extensive phytochemical study has led to the isolation of several isoprenoids, flavonoids, and isoflavonoids and their glycosides, xanthones, quinones, and stilbene glycosides from the species [106]. Recent studies have shown that a 10% hydroalcoholic flower extract and its cream can hasten female Wistar rats' wound healing. In this study, an excision wound model was analysed using the histo-morphometrical technique to assess the fibroblast population, collagen synthesis, and vascularization. The cream and ointment demonstrated enhanced collagen production, fibroblast proliferation and vascular density at the dose of 10% w/w hydroalcoholic extract of different plant parts in ointment form for 15 days [107].

2.1.26. Ixora Coccinea L.,

A member of the Rubiaceae family, is a small-medium evergreen shrub widely cultivated throughout Southeast Asian regions and beneficial for treating various ailments, such as chronic ulcers, hypertension, menstrual irregularities, sprain, and skin diseases. Its leaf extract has proven to be successful in combating Staphylococcus aureus while its methanolic leaf extracts are effective antioxidants, anti-inflammatory agent, fibroblast proliferative, and stimulate collagen production at 2.5% w/w with the pace of wound contraction greater than gentamicin sulphate (0.01% w/w) in both *in vivo* and *in vitro* research applied topically once daily for 21 days. *I. coccinea's* antibacterial action was caused by its active components, including terpenoid, flavonoid, coumarin, alkaloid, and phenolic groups [108]. The preformulated hydrogel had an average pH of 3.13 and was honey-colored, sweet-smelling, smooth, homogeneous, and acidic in nature. It included 2.5% of methanolic leaf extracts from *I. coccinea*. The study found that an alkaline pH state slows the course of wound healing. Additionally, a more acidic environment promotes wound healing by reducing infection, changing protease activity, releasing oxygen, and fostering angiogenesis and epithelization [109].

2.1.27. Jatropha Curcas Linn.

It is a kind of flowering plant of the Euphorbiaceae family. Historically used as an antibacterial, it also helps digestive issues, mouth ulcers, and toothaches. Polyphenols, flavonoids, alkaloids, saponins, triacontanol, alpha-amirin, cholesterol, beta-sitosterol, 7-keto-beta-sitosterol, stigmasterol, stigma-5-en-3-beta-7-alfadiol, vitexin, and cyanide acid are among the compounds found in jatropha. The seeds contain lots of compounds, including saponins and the toxic protein kursin (the amounts of toxins will diminish when cooked). In the study, mice were given the sap from Jatropha leaves, and then the wounds were incised for the wound study. On the first day after the wound was incised, the wound started to heal, and on the second and third days, the skin was totally dry. The povidone-iodine treatment caused the incision wounds to begin healing on the second and third day and finish healing on the fourth and fifth day. Wound drying started in the control group on the third and fourth day and was completed on the fifth and sixth day at the concentration of 500 mg/kg ethanolic extract of Jatropha sap (applied daily for 7 days). After the wound dries up, it develops a scab that will peel off in one to two weeks. The final stage of the incision, the potential wound healing procedure to be observed using the sap of Jatropha leaves, is wound closure [110].

2.1.28. Leea Macrophylla (Lelaceae)

It is an edible plant by the name of Hastikarnapalasa of the Vitaceae family. The herb is used for sores and wounds and is reputed to be effective against ringworm and guinea worm in the past. This plant's pharmacological effects on inflammation and urolithiasis have been demonstrated. It was looked into whether L. macrophylla roots' ethanolic extract might heal wounds [111]. Topical treatment of bioadhesive gel (5% w/v applied daily for 20 days). and ethanolic extract (500 mg/kg p.o. daily for 20 days) significantly enhanced reduced glutathione (GSH) levels and lowered lipid peroxidation (LPO) in addition to enhancing wound breaking strength. Myeloperoxidase production was also reduced. The levels of VEGF and pro-inflammatory cytokines, such as tumour necrosis factor, interleukin-1, and interleukin-6 were also positively impacted by topical gel therapy [112].

2.1.29. Leucas Hirta

A seldom plant of the Labiateae family that is found in the Deccan Peninsula and Western Ghats. In the initial phytochemical investigation, leaf extract consists of flavonoids, alkaloids, tannins, saponins, glycosides, steroids, and triterpenoids. The study's findings demonstrated that *L. hirta* leaf extract in methanol has a higher potential for wound healing than aqueous extract, as shown by the faster rate of wound contraction, shorter time for epithelialization, and increased collagen deposition, breaking strength, and hydroxyproline in granulation tissue at the concentration of 5% w/w methanolic extract of leaves in ointment gel (applied daily for 18 days); and 35 mg/ml orally of aqueous and methanolic extract of leaves daily for 18 days). The phytoconstituents of this plant, such as flavonoids, alkaloids, tannins, saponins, glycosides, steroids, and triterpenoids, may be responsible for healing wounds [113].

2.1.30. Melaleuca Alternifolia

It is called the tea tree of the Myrtaceae family; a tiny tree with a bushy crown and pale, papery bark that can reach a height of around 7 m. Leaves are organised alternately, occasionally whorled or dispersed. They are smooth and velvety. They have large glands and are also oil-rich. Its oil is a colourless to light yellow, transparent, and mobile liquid, which is made up of several monoterpenes, including 1,8-cineol, limonene, sabinenep-cymene, -terpineol, -pinene, terpinolene, and -terpinene. Its oil is frequently used medicinally to treat small wounds, burns, athlete's foot, vaginal yeast infections, mild fungal nail infections and lung issues, as

it has antimicrobial, analgesic, antiviral, antibacterial, antifungal and antiprotozoal activities [114]. To address the wound healing processes, melaleuca essential oil was applied topically using a mouse model at the concentration of 10% v/v viscous film-forming solution (applied topically as a film for 14 days). The injured region was topically treated for 10 days with either *M. alternifolia* oil-based cream, silver sulphadiazine (positive control), or cream base (negative control) after the whole thickness of the mouse skin was excised. The amount of wound contraction was measured with ImageJ software from digital photographs. With complete wound closure occurring in the melaleuca-treated mice within 10 days after the excision, it could be concluded that the skin rejuvenation process was likely advancing favourably as a result of melaleuca's anti-inflammatory, antioxidant and antibacterial properties [115].

2.1.31. Morinda Citrifolia

Called Indian mulberry of the Rubiaceae family, Traditional healers are said to have utilised the fruit in treating conditions, including digestive problems, skin irritation, infection, mouth sores, fever, contusions, and sprains. Plant fruit shows the presence of phytoconstituents like Glycosides, lipids, alkaloids, flavonoids, tannins, cardenolides, triterpenes, polyphenols, steroids, and resins. When streptozotocin-induced diabetic rats received mulberry juice orally sooner than the animals in the control group, the wound area was reduced [116]. The experimental group of animals had smaller wounds, lower blood glucose levels, and healed more quickly. Researchers were able to demonstrate the combined effects of transforming growth factor-1 and fibroblast growth factor on biochemical markers of wound healing and the recovery of the tensile strength deficit in diabetic wounds. *M. citrifolia* seems to promote speedier wound healing and lessen the quantity of dead tissue around the wound at the dose of 0.25 ml of essential oil with cream (applied topically daily for 10 days). The excision wounds' increased hydroxyproline concentration in the granulation tissue, which suggested that the wounds were healing quickly due to fast collagen turnover [117]. Due to their astringent and antibacterial qualities, *M. citrifolia* triterpenoids and tannins may have a role in wound contraction and increased rate of epithelialization, as well as in stimulating the wound-healing process. An enhanced blood flow that, by limiting vasoconstructive chemicals, enhances the oxygen supply to the wound, a larger migration of epidermal cells and a significant reorientation of collagen fibres brought on by a stronger cross-linking. When diabetic animals ingest *M. citrifolia* extract, this sort of pro-healing effect boosts and accelerates the quicker lay down of collagen fibres than the untreated diabetic control wound [118].

2.1.32. Musa Sapientum

Also called plant banana of the Musaceae family thrives in tropical humid low- to highland regions. It is considered to have ulcer healing activity through its predominant effects on mucosal defensive factors promoting mucosal cell proliferation and enhanced DNA synthesis without any carcinogenic/mutagenic effect. Collagen, which gives the tissue matrix strength and stability, is the predominant extracellular protein in the granulation tissue of a healing wound and is created quickly in the wounded area immediately after the injury. The amount of this hydroxyproline, which is produced when collagen is broken down, has been utilised as a measure of collagen turnover. Sapientum including sitoindisides I–IV, sterylacylglycosides, and flavonoids (leucocyanidin), were the major chemical components of *M. sapientum.* Sitoindoside IV, a main constituent, may mobilise and activate peritoneal macrophages as well as improve DNA and [3H]-thymidine absorption. Flavonoids are known to increase vascularity and decrease lipid peroxidation in addition to minimising or delaying the onset of cell necrosis. Hence, it is hypothesised that any medicine that inhibits lipid peroxidation will improve collagen fibril survival by increasing collagen fibre strength, improving circulation, minimising cell damage, and promoting DNA synthesis by using 100 ml/kg of fruit juice orally (for 10 days daily). Due to their astringent and antibacterial properties, which appear to be responsible for wound contraction and an increased rate of epithelialization, flavonoids are also known to aid wound healing at the concentration of 4.5-5% w/w of aqueous and methanolic extract of fruit (applied daily for 21 days) and 50, 100, 200 mg/kg aqueous and methanolic extract of fruit daily for 21 days) [119].

2.1.33. Ocimum Sanctum Linn

often known as Tulsi, is a plant native to India and other countries that is a member of the Labiaceae family. Many ailments, such as bronchitis, bronchial asthma, malaria, diarrhoea, dysentery, skin problems, rheumatoid arthritis, severe eye infections, persistent fever, and bug stings have been treated using Tulsi. It has been shown that eugenol (1-hydroxy-2-methoxy-4-allylbenzene), the active component in *O. sanctum* L., is largely to blame for the therapeutic properties of tulsi [120]. It possesses qualities that are antibacterial, analgesic, stimulate the immune system, anti-inflammatory, and scavenge free radicals. The ability of plant flavonoids to scavenge free radicals promotes wound healing. *O. sanctum* aqueous leaf extract was examined to see if it may aid in the topical healing of wounds using Wistar albino rats as a model for an excision wound. The ability of an *O. sanctum* cold aqueous extract to heal wounds and its effect on tumour necrosis factor (TNF) were evaluated at the dose of 500 mg/kg of drug suspension in distilled water and ointment (prepared with simple ointment base) daily for 28 days. Rats given *O. sanctum* extract were shown to heal wounds more quickly than control rats due to enhanced TNF- production [121].

2.1.34. Pentas Lanceolata

It comes under the Rubiaceae family and consists of iridoid glucosides, including seven of them. Together with the conventional Rubiaceae iridoids asperuloside and asperulosidic acid, five unique iridoids were also found, including tudoside (1), 13R-epi-gaertneroside (2), 13R-epi-epoxygaertneroside (3), and a compound made up of E-uenfoside (4) and Z-uenfoside (5). Using an excision wound model, the effects of an oral 150 mg kg-1 day-1 administration of *P. lanceolata* flower ethanolic extract on wound healing in rats were investigated. Granulation tissue weight, tensile strength, hydroxyproline, and glycosaminoglycan content all increased significantly. The level of protein increased somewhat. In

comparison to the controls, the test group's measurement of the wound area was much lower. In addition to better alignment and maturation, greater collagen deposition may also contribute to effective prohealing action [122].

2.1.35. Pistacia Atlantica

It is the dioecious herb of the Anacardiaceae family. The pistachio fruit, which is rich in oil, is used widely by the locals as a stomachic, an anti-diarrheal, and a component of cattle feed. Due to their antioxidant action and other health advantages, sterols are crucial. They also have activities like astringent, anti-inflammatory, antipyretic, antibacterial, antiviral and stimulant in eczema, throat infections, kidney stones, asthma, and stomach aches [124]. These plants contain phenolic chemicals, triterpenoids, and flavonoids. *P. khinjuk* fruit extract may have contributed to the faster healing in excision wounds compared to control groups and faster wound contraction rate since it contains flavonoids, which are regarded to be one of the most important components of wound healing, at the dose of 4.5-5% w/w of aqueous and methanolic extract of fruit (applied daily for 21 days) and 50, 100, 200 mg/kg aqueous and methanolic extract of fruit daily for 21 days [124].

2.1.36. Quercus Infectoria Olivier

It is a little tree from the Fagaceae family; Traditional uses include treating toothaches, gingivitis, and inflammatory diseases due to its astringent, anti-diabetic, anti-tremorine, local anaesthetic, larvicidal, antiviral, antibacterial, and antifungal characteristics. The main components of *Q. infectoria* galls are tannin (50–70%) and trace amounts of free gallic acid and ellagic acid. In a study using the excision wound model, animals treated with the ethanol extract of *Q. infectoria* had a significantly shorter time for epithelization, as evidenced by the shorter time for the fall of eschar when compared to control at the dose of 3ml in 30% and 60% concentration of oral suspension of hydroalcoholic extract orally for 21 days; 1g in 30% and 60% concentration of hydroalcoholic extract's topical cream applied tropically daily for 21 days. This resulted in a significant improvement on the tenth post-wounding day, and the treated group saw an increase in skin tensile strength. The results of this investigation show that the use of *Q. infectoria* accelerates wound healing and restoration. This was demonstrated by the dermis having developed scar tissue while an orderly epidermis completely covered the area of the incision. The plant's (Tannin) capacity to scavenge free radicals and the increased level of antioxidant enzymes in granuloma tissues may be the reason for the enhanced wound healing [125].

2.1.37. Rauwolfia Serpentine

It is commonly called Indian snakeroot, belonging to the Apocynaceae family. More than 80 alkaloids have been isolated from the 0.7–2.4% total alkaloidal bases found in it, such as Reserpine, rescinnamine, -reserpine, rescidine, raubescine, deserpidine, Ajmalinine, ajmaline, ajmalicine (8-yohimbine), serpentine, serpentinine, tetrahydroreserpine, raubasine, reserpinine, isoajamaline, and yohambinine are the other alkaloidal components. The other ingredients include phytosterols, fatty acids, unsaturated alcohols, and sugars. Tannins from *R. serpentina* have a healing effect on wounds. The tannins gallic acid and diagallic acid are in charge of preventing oxidation and hastening the healing of wounds and inflamed mucous membranes. Because *R. serpentina* has a high saponin concentration, it can be used to heal wounds and halt bleeding. Other nutrients found in high concentrations in the *R. serpentina* plant include ascorbic acids, riboflavin, thiamin, and niacin. As ascorbic acid promotes proper wound healing and inhibits the body's intercellular components from forming correctly when it is absent, it is crucial for physiological function at the dose of 200 mg/kg body wt. hydroalcoholic extract orally (for 15 days daily) [126]. Moreover, the ability of triterpenoids and flavonoids to scavenge free radicals and aid in the healing of wounds. By preventing or postponing the onset of cell necrosis and by promoting vascularity, both of these phytoconstituents can reduce lipid peroxidation. Hence, it is hypothesised that any drug that inhibits lipid peroxidation improves the longevity of collagen fibrils, which in turn improves collagen fibre strength by boosting circulation, lowering cell damage, and promoting DNA synthesis. The enhancement of collagen production, which greatly helps in better and more efficient healing, may be the cause of the increase in tensile strength [127].

2.1.38. Sambucus Ebulus

Called danewort of the Caprifoliaceous family is abundantly present in Iran. In Iranian traditional medicine, it is used to relieve arthritic pain and inflammation and is beneficial for managing Paederus dermatitis. According to pharmacological research, it has been proven that this plant's antibacterial and antioxidant properties are helpful for healing burns, wounds, eczema, rash, inflammation, and rheumatism. Sprague Dawley rats and Swiss albino mice were used to test the wound-healing properties of ointments made from n-hexane, ethyl acetate, and methanol extract of *S. ebulus* leaves and extracted quercetine 3-O-glucoside. The 1% methanolic extract ointment demonstrated significant wound healing efficacy [128]. In a replica of a circular excision wound, the ointment increased the tensile strength of the wound. The isolated substance quercetine 3-O-glucoside shown significant wound healing abilities in all animals. A histological investigation revealed collagen accumulation at the location of the excision [129]. Different research used Wistar rats to examine the efficacy of an ointment (5%) containing methanolic extract of *S. ebulus* fruits in treating wounds. Granulation tissue, collagen, epithelialization, and wound healing were all accelerated by it at the dose of 1%, 2%, & 5% w/w of methanolic root extract in ointment (applied for 21 days daily) [130].

2.1.39. Urtica Dioica

It iscalled stinging nettle of the Urticaceae family, a temperate-zone-dwelling perennial herbaceous flowering plant that is abundant in North Africa, Asia, America, and Europe [131]. Nasal bleeding and excessive menstrual flow have traditionally been treated using this plant's powdered leaf extract. It is used in rheumatism, arthritis, anaemia, and prostate issues [132]. In rats at intervals of 7, 14, and 21 days,

researchers examined the effects of a 2 and 5% ointment of a 70% methanolic extract of a combination of leaves, areals, and roots of *U. dioica* on wound healing. Angiogenesis, fibrogenesis, granulomatous tissue, and epidermal thickness were all generated by the creams [133]. Wistar rats were used to study the effects of the hydroalcholic extract of *U. dioica* leaves on hemostasis and wound healing. The extract sped up the healing of the excision wound at the dose of 2%, 5%, & 70% w/w of methanolic extract of the plant in the form of root ointment (applied for 21 days daily). The tissue also had more hydroxyproline than usual. Epithelial regeneration, neovascularization, fibroblasts, and a considerable number of inflammatory cells were discovered during a histological study. Moreover, the extract significantly prolonged the bleeding duration. This is because the plant contains a variety of phytoconstituents, primarily phenolics, flavonoids, and saponins [134, 135].

2.1.40. Vitis Vinifera Linn

It is a popular grape plant of the Vitaceae family, a variety from western Asia and southern Europe. Among the many active compounds present in grape's skin and its seed are flavonoids, polyphenols, anthocyanins, proanthocyanidins, procyanidines, and the stilbene derivative resveratrol. It has a variety of activities, including anti-oxidative, anti-inflammatory, and antibacterial activities, as well as cardioprotective, hepatoprotective, and neuroprotective benefits [136]. Re-epithelialization, angiogenesis, granulation, keratinocyte differentiation and fibroblast proliferation are signs of wound healing. Multiple growth factors and intricate cell interactions are needed for the intricate wound healing processes in which TGF- is involved. *V. vinifera* seed extract is the most significant factor that influences all stages because it improves TGF-beta 1 expression, restores wound healing, and influences all stages [137]. Also, the high *in vitro* antioxidant activity of V. vinifera seed extract, together with two identified components (ursolic acid and -sitosterol-3-O-glucopyranoside) that are ascribed by its SOD and H_2O_2 scavenging activity, can remove ROS and consequently boost its wound-healing activity, by using the 250 mg of hydroalcoholic extract of seeds in the form of cream (applied for 15 days daily). Its antioxidant activity may be supported by the extract's phenolic component [138].

CONCLUSION

Plants naturally heal wounds through their phytoconstituents *via* different mechanisms of actions. This review uncovered the cellular mechanisms of recently discovered medicinal plants with wound-healing properties. These findings may be applicable to clinical practise and the development of innovative drugs for treating human wounds. Wound-healing properties of numerous medicinal plants were investigated, and it was shown that plants may be quite beneficial in promoting the wound-healing process. Many studies have demonstrated the benefits of using plant-based medicines, and many industrialised countries employ herbal treatments for a variety of uses in addition to the treatment of wounds. This review also focused on a number of research where various formulations were created using plant extract, and productive results were obtained. Flavonoids, tannins, glycosides, vitamin C, and carbohydrates are the main phytoconstituents that provide plants with their capacity to heal wounds, according to this review. Using plants that have these phytoconstituents for their ability to heal wounds is safe. These compounds primarily function by promoting haemostasis, collagenization, epithelialization, and tensile strength. New research paths in the treatment of wounds will be made possible by improved quality control methods for the identification, screening, and measurement of herbal components as well as by carefully organised pre-clinical and clinical trials.

LIST OF ABBREVIATIONS

MDA	=	Malondialdehyde
TNF	=	Tumour necrosis factor
VEGF	=	Vascular endothelial growth factor
HDF	=	Human primary dermal fibroblast

CONSENT FOR PUBLICATION

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