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Review Article

A review of selected herbs responsible for wound management

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ABSTRACT

Wounds have a significant detrimental influence on the economics of a country's health care system, particularly in developing nations with limited resources. However, there is no effective evidence-based treatment for wounds that may result in evident clinical results. As a result, complementary and alternative medicines (CAMs) such as natural products, which include plant-derived extracts (phytochemicals), and naturally derived substances have intrigued the attention of researchers. Numerous plant extracts and their phytoconstituents are recognized as viable options for wound healing because they possess anti-inflammatory, antioxidant, angiogenic, and cell synthesis-modulating properties. Additionally, using plants with medicinal characteristics to treat wounds has been demonstrated to be effective in combating infection and accelerating wound healing. Thus, this study strives to fill the gaps in the current literature and provides researchers the creation of safe, efficacious, and universally acknowledged herbal medications for a vast array of cuts and wounds.

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1. Introduction

The biggest organ in the body, the skin, forms the live organism's outer cover. It is made up of numerous layers of ectodermal tissues that protect the bones, muscles, and internal organs underneath. It also protects the body against pathogens, light, heat, and harm (Kumar et al., 2007). When the natural function and structure of the skin are damaged, a wound is formed (Tsala et al., 2013). According to the wound healing society (WHS), wounds are physical injuries that produce an opening or break in the skin, disrupting the normal architecture and function of the skin. They cause the epithelium to lose its continuity, with or without the loss of underlying connective tissue. Wounds are a huge burden for individuals and healthcare providers all around the globe. They not only have an impact on the physical and emotional health of millions of people, but they also cost them a lot of money. According to the current estimates, about 6 million individuals suffer from chronic wounds worldwide (Kumar et al., 2007). Inflammatory mediators are continually produced by unhealed wounds, causing swelling and pain at the wound site. Injured patients' recuperation is slowed by wounds, which serve as a breeding ground for infection. Chronic wounds may result in multiple organ failure or patient mortality (Roberts et al., 1998).

The wound healing phenomenon is a complex and necessary controlled sequence of various well-orchestrated cellular and biochemical phenomena that restores the skin's integrity. This process could be divided into four stages, namely hemostatic phase, inflammation, proliferation, and maturation (Pereira and Bártolo, 2016). The materials employed in wound dressings may have a significant impact on wound care and wound healing effectiveness in the occlusion of wounded tissue.

In healthy people, normal or acute wound healing is characterized by the sequential overlap of processes

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that restore skin integrity and function in a coordinated way. Normal wound healing typically takes seven to ten days. Any changes that disturb the timely regulated healing processes will exacerbate tissue damage and lengthen the repair process, hence leading to chronic wound healing (Kurahashi and Fujii, 2015). Chronic wound healing may thus be described as a disturbance of the usual healing route. It may be brought on by underlying disease processes, *e.g.*, cardiovascular disease or diabetes, drugs, *e.g.*, steroids, infections, and aging. Complete healing of chronic full-thickness wounds may take months to years (Baranoski and Ayello, 2008). Delayed wound recovery is regarded as one of the most significant complications associated with type 1 diabetes. In patients with type 1 diabetes, an increase in oxidative stress leads to an increase in the production of reactive oxygen species (ROS), which contributes to delayed wound repair.

Up to the present, drug therapies have been found effective in combating the opportunistic pathologies caused by chronic wounds. However, it remains a challenge to discover an effective treatment to rectify the impaired wound-healing process and surmount the chronic wound state to prevent bacterial growth and severe pain.

Traditional wound healing remedies have been studied experimentally and therapeutically, and various investigations have uncovered a plethora of information regarding their involvement in easing the underlying reasons for nonhealing wounds (Jivad et al., 2016; Devi et al., 2017). Based on a range of active and beneficial components like quercetin, essential oils, flavonoids, phenolic compounds, alkaloids, fatty acids, terpenoids, and so on, medicinal plants may be considered powerful and promising treatments for improving wound healing processes. Because of their reduced side effects, cheap cost, effectiveness, and bioavailability, traditional medicines may be favored over contemporary treatment (Gamit et al., 2017).

Regarding the vital impact of the herbal and medicinal plants on our life (Mohammadhosseini et al., 2019; 2021; 2022) and on the maintenance of our health (Silva et al., 2019; Bailly and Vergoten, 2022; Thagriki and Ray 2022), the current review was organized to comprise a comprehensive description of some selected herbs having a high potential for wound management.

2. Classification of wounds

Undoubtedly, wounds are of prime importance from the medical point of view. In this context, Table 1 summarises the classification of wound involving their types and explanations.

2.1. Stages of wound healing

As maintaining homeostasis is essential for an organism's existence, skin requires and contains a powerful and efficient healing system. The process through which skin heals itself after being injured by trauma, surgery, or burns is known as cutaneous wound healing (Ghahary and Ghaffari, 2007). The healing process has traditionally been split into four stages described below.

2.1.1. Haemostatic phase

Platelets cling to exposed type 1 collagen after an injury and become activated, secreting glycoproteins that cause platelet aggregation. The complex secrete components that interact with one another to promote the intrinsic clotting cascade by producing thrombin, which then encourages fibrin synthesis from fibrinogen. The fibrin mesh and platelets combine to form a stable hemostatic stopper. Blood arteries contract within minutes after damage, lowering the severity of bleeding via many processes that enable hemostasis to be established (Pastar et al., 2014).

2.1.2. Inflammatory phase

The inflammatory phase begins shortly after the injury and lasts between 24 and 48 hours, with rare instances lasting up to two weeks. The hemostatic mechanisms are activated during the inflammatory phase to prevent blood loss from the wound site. As a result of the clinically apparent cardinal sign of inflammation, calor, rubor, dolor, and tumor emerge. This phase is marked by vasoconstriction and platelet aggregation to cause blood clotting, followed by vasodilation and phagocytosis to cause wound inflammation (Li et al., 2007).

2.1.3. Proliferative phase

This phase is marked by the widespread activation of fibroblasts, keratinocytes, endothelial cells, and macrophages to coordinate matrix deposition, wound closure, and angiogenesis. Changes in electrical gradients and mechanical tension, as well as exposure to pathogens, H_2O_2, cytokines, and growth factors, activate keratinocytes as early as 12 hours after damage (Shaw and Martin, 2016). Keratinocytes near the wound edge undergo a partial epithelial-mesenchymal transition because of this stimulation, becoming more invasive and migratory. Keratinocytes use integrin receptors to navigate through debris and necrotic tissue in the wound bed, interacting with structural proteins in the early matrix (Santoro and Gaudino, 2005).

After the inflammatory phase, the fibroblastic stage might last anywhere from 2 to 3 weeks. Granulation, contraction, and epithelialization are the three phases of this step. During the granulation phase, fibroblasts produce new capillaries and a collagen bed. Fibroblasts play a key role in wound healing by producing glycosaminoglycans and collagen. The wound edges come together in the contraction stage to eliminate flaws, and epithelial tissues develop over the wound site in the third step (Stadelmann et al., 1998). Driskell et al. (2013) established that skin fibroblasts come from two different lineages, with the top lineage assisting in re-epithelialization and the bottom lineage contributing to ECM deposition in a landmark work (Driskell et al., 2013).

2.1.4. Remodelling phase

Table 1
Depicting classification of wounds.

Sr. Num.	Type	Explanation
1	Open wound	An open wound allows blood to flow out from the body, producing apparent bleeding. Depending on the source of the wound, the open wound may be further divided into several categories.
2	Acute wound	Caused due to surgical incisions or cuts.
3	Closed wound	Blood leaves the circulatory system via closed wounds but stays within the body. It manifests itself in the form of bruises.
4	Chronic wounds	These are the wounds that haven't gone through the typical healing stages and are now at a stage of pathologic inflammation. They need more time to recuperate.
5	Superficial wound	Sliding over a rough surface led to abrasion. Currently, the epidermis, the top layer of skin, is scraped off by abrasion, exposing nerve endings and producing a painful injury.
6	Incised wound	This wound only has little tissue damage and minimal tissue loss. The wounds from sharp objects, like knives or scalpel forms incised wounds.

New collagen is generated during this phase, which is accompanied by improved tissue tensile strength owing to collagen intermolecular cross-linking caused by vitamin C-dependent hydroxylation. This phase is thought to last anywhere between 3 weeks to 2 years (Esimone et al., 2008).

3. Factors affecting wound healing

There are a multitude of factors that might impede wound healing (Table 2). Local and systemic factors may be used to classify the factors that influence repair. Local variables impact the features of the wound directly, while systemic factors affect the individual's general health status, affecting their capacity to recover.
According to recent research, an increase in the enzyme 11-hydroxysteroid dehydrogenase-1 (11-HSD-1) may have a deleterious impact on the growth of keratinocytes and fibroblasts during the healing of cutaneous wounds (Demling et al., 1999). According to the literature, DM patients' fibroblasts are less receptive to growth factors, which results in lower fibroblast proliferation and poor wound tensile strength (Rasik et al., 2000; Itoi et al., 2013). All of these factors are crucial in accelerating the healing of wounds.
One of the main causes of several age-related processes, including slow wound healing in postmenopausal women, is estrogen deficiency (Hall et al., 2005). Changes in skin morphology and physiology brought on by menopause-induced estrogen deprivation include a loss of elasticity and an increase in fragility, as well as a reduction in thickness, collagen, and water content. Wound healing is further hampered by lower estrogen levels brought on by menopause. Menopause has a detrimental influence on wound healing in particular because it results in weak skin that is prone to stress and easily bruises and rips (Brincat et al., 2005).

4. Traditional herbs

Plants have been used to cure and prevent illnesses for millennia in both traditional and popular medicine. Plants are used in "Ayurveda," which has been practiced in India for over 5000 years as a natural therapy technique to prevent and heal ailments. Traditional Chinese medicine is at least 3000 years old and uses a variety of plant species across Eastern Asia (Garodia et al., 2007). Animal research on a variety of plant species has shown encouraging findings. *Leea macrophylla*, for example, offers therapeutic properties. It boosts antioxidant production, collagen synthesis, cell proliferation, and lowers proinflammatory levels (Joshi et al., 2016). The cicatricial process was hastened by *Pereskia aculeata*, which increased collagen deposition and blood flow. *Wrightia tinctoria* showed healing activity by increasing the pace at which produced lesions contracted. Antioxidant activity was found in *Cynodon dactylon*, which also enhanced collagen production and repair. *Struthanthus vulgaris* ointment accelerated granulation tissue development, lesion closure, and collagen fiber proliferation and organization (dos Santos Gramma et al., 2016). *Caesalpinia mimosoides* caused the epidermal layer to re-epithelialize and the lesions to shrink (Bhat et al., 2016).
A large number of plant extracts display remarkable wound healing properties which are most probably due to their potential to manipulate the inflammatory pathways. Fig. 1 depicts the pathway of the wound healing mechanism.
Plant species that have historically been used to treat ailments have been intensively investigated in contemporary science to find their bioactive ingredients and produce novel medications. Some of the potential medicinal plants representing wound-healing activity are described below.

4.1. *Aloe vera*

For over 5000 years, *Aloe vera* (Fig. 2) has been used for ulcers, and surgical wounds by the Romans, Egyptians, and indigenous people of Asia, Africa, and America (Garcia-Orue et al., 2017). It includes several naturally occurring bioactive chemicals, such as pyrocatechol, polysaccharides, anthraquinones, saponins, acemannan, oleic acid, glycosides, and phytol (Salehi et al., 2018). The primary mucopolysaccharide (mesoglycan) of *Aloe vera*, acemannan, stimulates the production of proinflammatory mRNAs (including nitrous oxide, IL-

Table 2
Depicting various factors affecting wounds.

Sr. Num.	Factors	Mechanism
1	**Local factors**	
	Infection	Both bacteria and endotoxins released from them may extend the inflammatory phase by causing an increase in pro-inflammatory cytokines like TNF-α and interleukin-1β (IL-1β).
		Increases the amount of matrix metalloproteases as well.
	Oxygenation	It inhibits infection, boosts keratinocyte migration, differentiation, and re-epithelialization, and stimulates wound contraction. It also increases collagen production and fibroblast proliferation.
2	**Systemic factors**	
	Stress	At the wound site, stress increases glucocorticoids (GCs) while decreasing pro-inflammatory cytokines TNF- α, IL-1β, and IL-6.
	Age	Delay in collagen synthesis, re-epithelialization, and angiogenesis due to altered inflammatory response, like chemokine production changes, delayed T-cell infiltration into the wound region, and decreased macrophage phagocytic capability.
	Diabetes	Delay in repair owing to faulty T-cell immunity, phagocytosis, chemotaxis, and bactericidal capability abnormalities in fibroblast and leukocytes, and epidermal cell dysfunction.
	Medications	Inhibit clotting or platelet function, as well as inflammatory and cell growth.
	Obesity	Leads to skin wound dehiscence, infection, seroma development, hematoma, pressure ulcer, and other wound complications.
	Alcohol intake	In response to an inflammatory stimulus, it inhibits the production of pro-inflammatory cytokines.

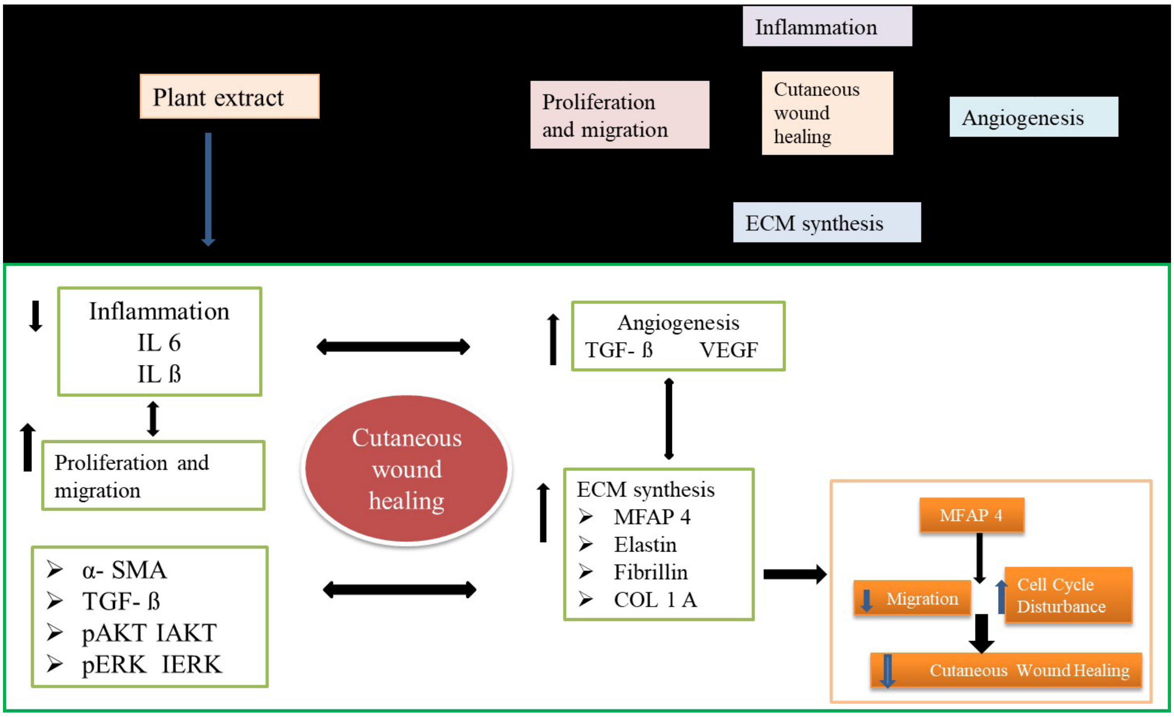

Fig. 1. Pathway of the wound healing mechanism.

Fig. 2. *Aloe vera* (https://www.goodhousekeeping.com/home/gardening/g19682442/aloe-plant-care/).

1α, TNF-α, and PGE2) and serves as a powerful activator of T-cell and macrophage activity (Ali et al., 2014).
Due to the molecule glucomannan's abundance in polysaccharides like mannose, the plant has regenerating capabilities. Glucomannan's impact on fibroblast growth factor receptors increases their activity and proliferation, which in turn promotes the production of collagen. *Aloe vera* gel may improve wound healing by boosting the amount of collagen in wounds, changing its chemical composition, and enhancing collagen cross-linking. Because the gel remarkably consists of water (99%), many reports have suggested that it could make the skin more flexible and less brittle (Ghaffarzadega et al., 2013). Table 3 summarises some of the recent reports evaluating the wound-healing efficacy of *Aloe vera*.

Table 3
Some recent studies evaluating the wound-healing efficacy of *Aloe vera*.

No.	Study	Study type	Dose given	Result	Reference
1	Investigating the wound healing activity of Aloe vera	*In-vitro* study	Various concentrations	The findings indicate that A. vera promotes wound healing by boosting the migration and proliferation of keratinocytes and fibroblasts and by preventing the preservative-induced mortality of keratinocytes.	Teplicki et al. (2018)
2	Evaluate the potential healing and mutagenic effects of the aqueous extract of A. vera (AEAV) in mice	*In-vivo* animal study	10 and 50 mg/kg for 7 days	At a concentration of 50 mg/kg, the aqueous extract of A. vera demonstrated substantial healing capability in mice.	Rodrigues et al. (2018)
3	A novel alginate dressing containing Aloe vera gel was produced, and Wistar rats with surgical wounds were utilized to examine its cutaneous healing efficacy	*In vivo* animal study	25% of the Aloe vera gel in aloe-alginate films	The assessment of collagen fibers revealed a reduction in type III fibers and an increase in type I fibers in the group treated with aloe-alginate film, indicating wound healing activity.	Koga et al. (2018)
4	To investigate the impact of topical Aloe vera treatment on skin wound healing	*In-vivo* animal study	1% and 2% aloe vera cream	The capacity of 1 percent and 2 percent Aloe vera cream to enhance the ratio of CD4+/CD8+ lymphocytes in the wound region confers wound healing potential.	Prakoso and Kurniasih (2018)
5	This study assessed the feasibility of producing a topical gel formulation of Aloe vera with insulin-loaded nanoemulsions, as well as the gel's ability to promote wound healing in diabetic rats	*In-vivo* animal study	0.2 g formulation with 1.6 g of Aloe vera	Aloe vera with insulin-loaded nanoemulsion has shown a synergistic impact on wound healing in diabetic rats and might be a promising and successful therapy for diabetic individuals with wounds.	Chakraborty et al. (2021)

4.2. *Azadirachta indica*

Azadirachta indica (Fig. 3), often known as Neem, is a multipurpose Indian plant that has been used for over 2000 years with a broad range of medical properties. Nimbin, nimbidine, nimbolide, and sodium nimbidate were shown to have antipyretic, antibacterial, and anti-inflammatory activities when extracted from the oil of the seed kernels (Biswas et al., 2002). In male Albino rats, Purohit et al. (2013) tested the wound-healing efficacy of an ethanolic extract of *A. indica* leaves. Some recent findings evaluating the wound-healing efficacy of *Azadirachta indica* have been also summarized in Table 4.

Fig. 3. Neem (https://www.britannica.com/plant/neem-tree).

Table 4
Some recent studies evaluating the wound healing efficacy of neem.

No.	Study	Study type	Dose given	Result	Reference
1	Formulate aqueous topical creams comprising varying doses of aqueous extract of Azadirachta indica leaves (AEAIL) as bioactive components and assess their stability and wound healing capabilities in male Wistar rats using hydroxyproline (HXP) as a biochemical marker.	*In-vivo* animal study	1.0, 1.5, 2.0 and 3.0 % w/w of leave extract in creams	The extract of *Azadirachta indica* leaves produced as an aqueous cream was stable and maintained its wound-healing properties.	Ugoeze et al. (2021)
2	The effects of topical A. indica extract on excisional lesions in hyperglycaemic rats were examined.	*In-vivo* animal study	20 mL of hydroalcoholic extract	The topical administration of *A. indica* extract to excisional wounds of hyperglycaemic rats hastens wound healing through antioxidant, anti-inflammatory, fibrogenic, and angiogenic actions.	Silva et al. (2021)
3	In the Bundelkhand area of India, the paste made from the stem bark of *Azadirachta indica* (AI) is historically applied to wounds and scars to promote speedy healing.	*In-vivo* animal study	15 (w/w%) dried extract in ointment	The substantial wound-healing qualities of the stem bark of AI justify its historic usage.	Maan et al. (2017)

4.3. *Calendula officinalis*

Calendula officinalis (Fig. 4), sometimes known as pot marigold, is a widespread plant that has been used for a long time to treat several skin ailments, like burns, wounds, and dermatitis (Nicolaus et al., 2017).

Fig. 4. *Calendula officinalis* (https://en.wikipedia.org/wiki/Calendula_officinalis).

Calendula officinalis has various pharmacological properties involving anti-inflammatory, antioxidant, antiviral, antibacterial, anticancer, and antifungal properties (Chandran and Kuttan, 2008). However, the precise processes involved in its wound-healing effects remain unclear. It is been reported that the extracts prepared from the flowers of *Calendula officinalis* flower induce granulation tissue development in excisional wounds of mice by changing the expression of connective tissue growth factor (CTGF) and α-smooth muscle actin (α-SMA) *in vivo* (Dinda et al., 2016). A parallel study revealed that an extract of *Calendula officinalis* stimulates the migration and proliferation of fibroblasts in a PI3K-dependent way (Dinda et al., 2015). Using a cutaneous wound healing model in rats and the chicken chorioallantoic membrane (CAM) test, it has been established that *Calendula officinalis* stimulates angiogenesis *in vivo* (Parente et al., 2012).

4.4. *Calotropis procera*

Calotropis procera (Ait) R. Br. (Asclepiadaceae) (Fig. 5), also known as Milkweed, Apple of Sodom, or Swallowwort, is a tiny, pubescent, resistant, upright, evergreen, and compact shrub that grows to a maximum height of 4.5 m and is coated with cottony tomentum.

Fig. 5. *Calotropis procera* (https://en.wikipedia.org/wiki/Calotropis_procera).

It produces huge amounts of milky sap when it is cut. This herbal species grows naturally in tropical Africa, southeastern Asia, including India, Afghanistan, and Pakistan, Morocco, Indochina, and Senegal, mostly in drier, warmer climates up to 1,050 m on alkaline and sandy soils (Rais et al., 2020). The roots of this plant are frequently used to cure asthma, anasarca, bronchitis, ascites, cutaneous disorders, cough, leprosy, and intestinal worms (Mhaskar et al., 2000).

In an excision wound model, topical administration of *Calotropis procera* enhances the percentage of wound contraction and reduces scar area and epithelization time. It enhances the breaking strength of wounds and hydroxyproline in incision and dead space wounds. The tensile strength of the tissue is increased when freshly generated collagens are deposited at the location of the wound. The astringent and antibacterial qualities of phytochemical components like triterpenoids and flavonoids, which seem to be responsible for wound contraction and an enhanced rate of epithelialization, have been proven in recent research to improve the healing process of wounds (Mali et al., 2020). The results of some of the recently published reports on the wound-healing efficacy of *Calotropis procera* have been represented in Table 5.

Table 5
Some recent studies evaluating the wound healing efficacy of *Calotropis procera*.

No.	Study	Study type	Dose given	Result	Reference
1	Wistar rats were used to assess the wound-healing properties of an aqueous extract of *Calotropis procera* (AECP) leaves.	*In-vivo* animal study	25 and 50 mg/kg, p.o.	Compared to control groups, AECP was associated with a significant (p<0.05) increase in breaking strength and percentage wound contractions with a reduced epithelization duration.	Patil and Makwana (2015)
2	Assess the antioxidant capacity and wound healing impact of the ethanolic extract of Calotropis procera's bark.	*In-vitro* and *In-vivo* animal study	50 mg g/ wound	This research demonstrated the exceptional potential of *C. procera*. The presumed mechanism of action on cutaneous wound healing involves increased collagen deposition and decreased inflammation.	Tsala et al. (2015)
3	In the current research, the wound-healing efficacy of *Calotropis procera* root bark on diabetic rats was examined. The root bark was extracted using the Soxhlet technique from an ethanolic extract.	*In-vitro* and *In-vivo* animal study	100 and 200 mg/kg oral	The extract has a positive impact on diabetic wounds, which heal more quickly than with the regular component. The findings of this investigation indicate that this extract is useful for diabetic wounds.	Mali et al. (2020)

4.5. *Centella asiatica*

Centella asiatica (Fig. 6), often known as Asiatic pennywort belongs to the family Apiaceae and has been used to enhance wound healing for centuries (Somboonwong et al., 2012).According to some reports, extracts from the aerial portions of the plant ameliorate the breadth, depth, and duration of chronic ulcers in Sprague-Dawley rats. It has been shown that wounds linked with acute radiation dermatitis in rats healed faster when treated with *C. asiatica* extracts compared to the control group that received no therapy (Chen et al., 1999). Prostaglandin E2, tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and

Fig. 6. *Centella asiatica* (https://en.wikipedia.org/wiki/Centella_asiatica).

cyclooxygenase-2 (COX-2) levels have been decreased in response to *C. asiatica*, as well (Wan et al., 2013; Pakdeechote et al., 2014). Additionally, it has been implied that *C. asiatica* inhibits lipoxygenase activity and decreases proteinase activity, preventing protein denaturation, to minimize inflammation. Furthermore, *C. asiatica* increases the tensile strength of the newly produced skin on the wound (Gunathilake et al., 2018). Some aspects relating to the wound-healing efficacy of *Centella asiatica* have been shown and summarized in Table 6.

Table 6
Some recent studies evaluating the wound healing efficacy of *Centella asiatica*.

No.	Study	Study type	Dose given	Result	Reference
1	Determine the effectiveness of an asiaticoside-rich hydrogel formulation in rabbits in vivo.	*In-vivo* animal study	24 mg of extract in hydrogel	The asiaticoside-rich hydrogel produced by the freeze-thaw technique proved successful in accelerating wound healing in rabbits.	Taher et al. (2019)
2	Conducting an *in vivo* examination of wound healing efficacy in diabetic rabbits	*In-vivo* animal study	2% extract ointment	Similar to the usual treatment, pegagan extracts-based ointment and its combination was able to reduce erythema, edema, and wound scores in diabetically-induced rabbits.	Sutrisno et al. (2018)
3	Evaluated the effect of asiaticoside on human gingival fibroblasts	*In-vitro* study	0.25 mg/mL	As determined by the scratch test, asiaticoside substantially accelerated wound healing (p<0.05).	Suriyah et al. (2021)

4.6. *Curcuma longa*

Curcuma longa (*C. longa*) (Fig. 7), often known as turmeric, is a ginger family member (Zingiberaceae). It has been used as a condiment and dye since antiquity.

Fig. 7. *Curcuma longa* (https://en.wikipedia.org/wiki/File:*Curcuma_longa*_roots.jpg).

C. longa has been taken regularly in Asian nations for generations with no reports of its harmful impacts (Ammon and Wahl, 1991). Curcumin (diferuloylmethane), the main curcuminoid present in *C. longa*, is thought to be the most active component. Demethoxycurcumin and bisdemethoxycurcumin are two more curcuminoids identified in turmeric (Akram et al., 2010). Apoptosis, proinflammatory cytokines, NF-κB, COX-2, 5-LOX, prostaglandin E2, prostate-specific antigen, transforming growth factor-β, phosphorylase kinase, creatinine, ET-1, AST, and ALT, and heme oxygenase-1 have been found as some of the targeted biochemicals (Gupta et al., 2013).
The capacity of curcumin to heal wounds is assumed to be a result of its biochemical features, such as its anti-inflammatory, anti-infectious, and antioxidant actions. Curcumin has also been shown to facilitate the healing of cutaneous wounds by enhancing collagen deposition, granulation tissue growth, and tissue remodeling. Numerous investigations have shown that topical curcumin application enhances vascular density, stimulates fibroblast activity, and supports epithelial regeneration (Thangapazham et al., 2013).
Using a mouse model, Jagetia and Rajanikant (2012) concluded that the improvement in wound healing brought on by curcumin therapy was partly caused by an increase in NO. Additionally, curcumin promotes wound contraction. TGF-β is a crucial cytokine that plays a role in collagen deposition, chemotaxis, and wound healing. Numerous cells, including fibroblasts are responsible for releasing TGF-β (Jagetia and Rajanikant, 2012). When compared to untreated wounds, wounds treated with curcumin consistently had more fibroblasts that stained positively for TGF-β (Jagetia and Rajanikant, 2012). The literature available data on wound-healing efficacy of *Curcuma longa* have been summarized in Table 7.

4.7. *Mimosa pudica*

Mimosa pudica Linn (Fig. 8), also known as touch-me-not plant belongs to the Leguminaceae family and is an attractive perennial plant. It is native to Tanzania, the Americas, Southeast Asia, and several Pacific Islands, all of which get regular precipitation. It is a sub-erect or semi-erect shrub with delicate, grey-green leaves, and velvety, recurved thorns. The plant exhibits nyctynastic movement and its leaves shut in response to stimuli like heat, touch, and shaking. These distinctive bending actions have given this plant the position of curiosity.

Table 7
Some recent studies dealing with the wound healing efficacy of *Curcuma longa*.

No.	Study	Study type	Dose given	Result	Reference
1	A composite of ZnO and *C. longa* nanoparticles (nano ZnO/CUR composite) was developed as topical ointments.	*In-vivo* animal study	1% w/w skin ointments	The research indicated that nano ZnO/CUR combination ointment would treat third-degree burn lesions more quickly than solus alone application.	Bhutta et al. (2021)
2	Determined the impact of turmeric extract (*Curcuma longa*) on white rat wound healing.	*In-vivo* animal study	3%, 5%, 7% 7% turmeric ethanol extract cream	The turmeric ethanol extract preparation is comparable to Bioplacenton® in its capacity to heal wounds in mice.	Ling et al. (2022)
3	Electrospinning was used to effectively create a unique multicomponent nanofibrous mat from a solution of honey, polyvinyl alcohol, and *Curcumin longa* (turmeric) extract for possible use as a wound dressing material.	*In-vitro* study	1.0 g of turmeric extract	The created nanomats have the potential to be employed in tissue and as wound dressings.	Shahid et al. (2021)
4	Evaluate the efficacy of yellow turmeric infusions of 5 and 10 percent on the healing of grade II perineal wounds.	*In-vivo* human study	5% and 10% Turmeric infusa	It has been shown that turmeric reduces edema, inflammation, and perineal wound healing time.	Mutia et al. (2021)
5	Determine the number of new blood vessels that form during the wound healing process when *C. longa* rhizome extract and zinc oxide are used as a wound dressing.	*In-vivo* animal study	0.3 g *C. longa* rhizome liquid extract	The combination of *C. longa* and zinc oxide extract in a wound dressing may improve the number of neovascular in the wound healing process, with 14 days being the optimal period of administration.	Faiga et al. (2018)

In addition to its decorative purpose, *Mimosa pudica* is a common plant used by traditional healers to cure a variety of ailments (Ahmad et al., 2012). Table 8 summarises some valuable information concerning the wound-healing efficacy of *Mimosa pudica*.

Fig. 8. *Mimosa pudica* (https://en.wikipedia.org/wiki/*Mimosa_pudica*).

4.8. *Panax ginseng*

Panax ginseng Mey. (Fig. 9) belonging to the family Araliaceae is a perennial plant. A literature survey demonstrates that *Panax quinquefolius* (American ginseng), *Panax ginseng* (Asian ginseng), and *Panax notoginseng* (Chinese notoginseng or Sanqi) are the most often utilized species (Yun, 2001). Ginseng has been used as a tonic and restorative in China for over 4000 years, boosting health and treating impotence, bleeding, infections, and anorexia. The most important bioactive phytochemicals in *P. ginseng* are ginsenosides, which are triterpene saponins of the dammarane type with distinct sugar moiety attachments at C-3 and C-20. The wound-healing action of fermented black ginseng in human umbilical vein endothelial cells was demonstrated to be regulated by angiogenesis via the MAP kinase pathway, with migration in HaCaT cells and enhanced tube formation in HUVECs. HaCaT cells may be stimulated to phosphorylate p38 and extracellular signal-regulated kinase by fermented black ginseng.

Fig. 9. *Panax ginseng* (https://www.researchgate.net/Fig. /*Panax-ginseng*-CA-Meyer-photo_fig4_352956543).

Additionally, mice administered with 25 mg/mL demonstrated quicker wound healing in an experimental model of cutaneous wounds (Park et al., 2018). *Panax ginseng* has been found some valuable wound-healing and therapeutic properties in the relevant information has been shown in Table 9.

Table 8
The results of some of the recently reports on the wound-healing efficacy of *Mimosa pudica*.

No.	Study	Study type	Dose given	Result	Reference
1	Assessed the wound-healing properties of *Mimosa pudica* root extract.	*In-vivo* animal study	5, 7.5, and 10% w/w) methanolic extract in ointment	A pharmaceutical formulation ointment containing *Mimosa pudica* root extract reinforced with povidone-iodine revealed superior wound healing effectiveness compared to a commercially available povidone iodine ointment.	Singh et al. (2021)
2	In this work, ethanol-extracted *Mimosa pudica* was inserted into the silk-PCL (Polycaprolactone) nanofibrous mat was created using an electrospinning process.	*In-vitro* study	2.5% of the Mimosa pudica herbal extract in nanofibrous mat	This research demonstrated that the silk-PCL electrospun mat containing *Mimosa pudica* has tremendous potential for use in wound healing.	Lakshmipriya et al. (2019)
3	To discover the active constituents and pharmacological properties of the root and shoot extracts of *Mimosa pudica* Linn.	*In-vivo* animal study	100 mg of extract	In comparison to the conventional medicine gentamicin, the *Mimosa pudica* root methanolic extract (MRME) and the *Mimosa pudica* shoot methanolic extract (MSME) showed superior wound healing efficacy.	Kannan et al. (2009)
4	To assess wound healing efficacy of ethanolic leaf extract of *M. pudica* L. (EMP) was evaluated in Streptozotocin-induced diabetic rats (55 mg/kg, i.p.).	*In-vivo* animal study	2.5% & 5% of the extract	In comparison to the diabetic control group, wound-breaking strength and epithelialization increased significantly (p<0.01) in the EMP 2.5% and EMP 5% groups.	Kumar et al. (2017)
5	Assess the wound healing activities of ethyl acetate and ethanolic extracts of *Mimosa pudica* seeds in rats with diabetes induced by streptozotocin.	*In-vivo* animal study	100, 200, and 400 mg/kg body weight	The findings demonstrate that *Mimosa pudica* has significant anti-diabetic and wound-healing properties in diabetic rats.	Saini and Verma (2019)

4.9. *Polygonum cuspidatum*

Polygonum cuspidatum (Fig. 10) root is often used to treat hepatitis, coughs, amenorrhea, jaundice, arthralgia, leukorrhea, snake bite, and burns when combined with numerous additional components (Peng et al., 2013).

Fig. 10. *Polygonum cuspidatum* (https://en.wikipedia.org/wiki/*Reynoutria_japonica*).

It is believed that polydatin, resveratrol, and anthraquinones are responsible for *Polygonum cuspidatum's* estrogenic, anti-aging, antitumor, cardioprotective, and neuroprotective properties (Jiao et al., 2018). *Polygonum cuspidatum* contains novel anthraquinones which have been shown to inhibit the enzyme tyrosinase, the rate-limiting enzyme that regulates the formation of melanin (Liu et al., 2013). In a recent *in vivo* investigation on wound healing in rats, *Polygonum cuspidatum* extracts were shown to dramatically promote granulation tissue development, reepithelization, angiogenesis, and collagen production (Wu et al., 2012).

4.10. *Schinus mole*

Schinus molle L., (Fig. 11) often known as pink pepper, pepper tree, or Brazilian pepper belongs to the family Anacardiaceae.

Fig. 11. *Schinus mole* (https://en.wikipedia.org/wiki/*Schinus_molle*).

Table 9

Some recent studies dealing with the wound healing efficacy of *Panax ginseng*.

No.	Study	Study type	Dose given	Result	Reference
1	The effects of red g1 ginseng extract on a diabetic wound model were investigated.	*In-vivo* animal study	10 mg/kg	The red ginseng extract stimulated the synthesis of the wound-healing proteins VEGF and TGF-1.	Lim et al. (2021)
2	To investigate the wound healing benefits of Korean black ginseng hot water extracts taken orally (KBG).	*In-vivo* animal study	100 and 200 mg/kg	The findings indicate that KBG possesses wound-healing properties in mice due to its anti-inflammatory and antioxidant properties.	Kim et al. (2022)
3	The modulatory potential of Korean red ginseng (KRG) on keratinocytes was examined.	*In-vitro* study	100 and 200 µg/mL	KRG had a direct modulatory impact on keratinocytes, and these modulatory effects may be beneficial to skin health when KRG is utilized as a nutricosmetic or cosmeceutical element.	Kim et al. (2022)

It is a tiny evergreen tree or shrub that may reach a height of 10 meters and has thin leaves, berry-like fruits that range in color from pink to scarlet, and white-yellow flower clusters (Kramer, 1957). Originating in Peru, S. *molle* is present in several Central American and South American nations. The historic usage of this plant as an anti-bacterial, anti-inflammatory (Yueqin et al., 2003), and anti-fungal agent (Ibrahim and Al-Naser, 2014) with antioxidant qualities (Bendaoud et al., 2010) is supported by a large number of reports. The wound-healing capacity of this plant is given special consideration, as shown by *in vitro* tests (Gomes et al., 2013; Eryigit et al., 2017).

Aboalhaija et al. (2021) have examined the wound healing ability of alcoholic and aqueous extracts of *Schinus molle* L. using human fibroblast cell proliferation and scratch testing. In this relation, *in vitro* wound healing studies were conducted. Based on the encouraging findings obtained, the aqueous extracts were subsequently evaluated using an *in vivo* wound model in rats. Two strengths of a hydrogel formulation containing a plant aqueous extract were administered to animals (2% and 5%). Fibrosis, re-epithelialization, and neovascularization of the epidermis and sub-epidermal cells were found in the regenerated tissue, along with an increase in the tensile strength of the skin in rats. The findings significantly support the topical use of *Schinus molle* aqueous extracts for wound healing (Aboalhaija et al., 2021).

4.11. *Urena lobata*

Plants are a prospective source for a range of natural compounds with wound-healing properties, but they have been relatively understudied. *Urena lobata* (Fig. 12), often known as Congo jute or Caesarweed, is a member of the Malvaceae family (Roul, 2009).

Fig. 12. *Urena lobata* (https://en.wikipedia.org/wiki/Urena_lobata).

Caesarweed is also often referred to as aramina, hibiscus bur, bur mallow, pink Chineseburr, cadillo, grand cousin, malva, carrapicho do mata, cousin petit, mahot cousin, jut africain, cousinrouge, dadangsi, and cooze mahot. *Urena lobata* is one such plant historically used to treat various skin conditions, including burns and wounds. Traditional practitioners prescribe a decoction of the leaf for lowering blood pressure and alleviating rheumatic discomfort, and body aches. Root and leaf extract of *U. lobata* is also recommended for the treatment of hematemesis, gonorrhea, fever, malaria, diarrhea, toothache, nephritis, gastritis, pneumonia, bronchitis, inflammation, and menorrhagia (Sajem and Gosai, 2006). According to some pharmacological investigations, *U. lobata* possesses amoebicidal, antibacterial, and analgesic effects (Adeloye et al., 2007; Yang et al., 2017).

In a recent preclinical study, Rathinam et al. (2021) evaluated the efficacy of ointment formulations containing ethanolic extract (EO) of *Urena lobata* (5%) and nanosized extract (NO) of *U. lobata* (5%)

for their wound healing activity by evaluating tensile strength, wound contraction, catalase, superoxide dismutase, hydroxyproline, myeloperoxidase, and lipid peroxidation in open wounds of Swiss Albino rats. In addition, qualitative and quantitative estimates of the formulation's active ingredient, quercetin, were derived through HPLC experiments. Accordingly, in contrast to the control, topical administration of EO and NO formulations enhanced catalase activity, and GSH, SOD, and hydroxyproline levels promoted faster wound contraction, re-epithelialization, and maximum tensile strength, while decreasing lipid peroxidation and myeloperoxidase. Compared to the control group, histopathological examinations demonstrated decreased inflammatory cell proliferation, degeneration, and considerable fibroblast proliferation and collagen maturation. The obtained results also reveal that both NO and EO formulations were superior to the usual povidone ointment for the treatment of wounds (Rathinam et al., 2021).

4.12. *Zanthoxylum bungeanum*

Zanthoxylum bungeanum (Fig. 13), also known as the Da Hongpao Huajiao, is extensively spread in China's Shanxi, Hebei, Gansu, Sichuan, and Shandong provinces, as well as certain Southern Asian nations (Yang et al., 2013). It belongs to the *Zanthoxylum* genus of the Rutaceae family.

Fig. 13. *Zanthoxylum bungeanum* (https://en.wikipedia.org/wiki/*Zanthoxylum_bungeanum*).

Apart from its usual use as a seasoning to add taste to meals, each portion of *Z. bungeanum* possesses a variety of therapeutic properties. Recent research has revealed that it can also be used as a cosmetic ingredient and it also shows cardiovascular, antimicrobial, antioxidant and anti-inflammatory activity (Huang et al., 1993; Artaria et al., 2011; Tezuka et al., 2001; Xia et al., 2011), and lifting skin wrinkles. The relaxation of subcutaneous muscles when administered topically to the skin reduces skin wrinkles, attracting the attention of cosmetic makers (Lan et al., 2014). According to Li et al. (2017), *Zanthoxylum bungeanum* seed oil (ZBSO) shows promising wound healing abilities in the skin of experimentally scalded rats. The increased antioxidant properties as indicated by the decrease in MDA level and the rise in SOD level, accelerated collagen synthesis via the decrease in MMP-2 and MMP-9 expressions, and anti-inflammatory action via the NF-κB signaling pathway in ZBSO-treated wounds could all be linked to early re-epithelialization and faster wound closure. ZBSO's improved wound healing activity might also be related to its phytoconstituents, which could be owing to their activity or a synergistic impact (Li et al., 2017).

5. Recent approaches

Biopolymers, or polymers made by living microbes, are often used to treat wounds. However, it seems that certain polymers get more attention than others when they come to be used as wound dressings. The purpose of wound dressings should be to aid and speed up the healing process. This may be done by shielding the wound from potential healing-delaying or -impairing factors such as pollution and moisture loss. Films, sponges, fibers, or hydrogels made of natural and synthetic polymers alone or in combination are utilized as wound dressing components. However, it is most critical that the ideal wound dressing replicate the structural and biological properties of the skin's extracellular matrix (ECM).

Although photosensitive polymers are a promising class of materials for *in situ* hydrogel formation, they still have concerns with local heating, which may harm the nearby cells and tissues. Antibiotic-loaded wound dressings not only hasten wound healing but also cause microorganisms to become resistant. Dressings for wounds include antibiotics toxicity and depigment of the region around the wound. Plants and their metabolites are a major source of novel bio-molecules in the hunt for new treatment solutions. In comparison to their pure form, plant extracts are natural antimicrobials with limited compatibility in hydrogel polymeric solutions and lower release and efficacy in hydrogel films. More effective healers than humans, plants can naturally treat wounds.

Although it may be regarded as being relatively new, the use of nano and solid lipid microparticles as delivery vehicles for topical, dermal, and transdermal usage has been significantly increasing the number of innovative formulations in the fields of dermopharmacy and cosmetics. Due to its benefits over polymeric systems, the utilization of lipid particles for this purpose is gaining popularity (Khater et al., 2021).

Cárdenas et al. (2008) looked into how chitosan films with oleic acid or linoleic acid and glycerol could be used in medicine. The researchers tried the chitosan films on human participants who had wounds and sores. The findings showed that films with glycerol stuck together better than films that didn't have glycerol. Tests on people have shown that the films help in good epithelialization of the skin healing within 12 to 15 days (Cárdenas et al., 2008). Altiok et al. (2010) looked into how to make mending dressings out of chitosan strips with thyme oil. Accordingly, thyme oil was picked because it calms inflammation, kills bacteria, and fights free radicals. The results showed that the films with more than 1.2% thyme oil have antibiotic activity and that as the oil percentage goes up, the film's antioxidant activity goes up (Altiok et al., 2010).

The generation of lipid particles for topical application using the spray cooling method is still a mostly unexplored field of study. For active substances that may be used topically, several investigations have focused on the viability and effectiveness of producing solid lipid micro/nanoparticles using the spray colling approach.

6. Concluding remarks

Since prehistoric times, medicinal herbs have been used as the first line of defence against trauma, infection, sickness, and damage. Over centuries, people have learned to detect and convert the local environment's botanical resources into food and medicine as they are cost-effective and safer to use. It has been proven that plant secondary metabolites are major sources of potential drugs owing to their various pharmacological activities that influence the different phases of wound healing. Modulations of immune cell function, the proliferation of skin cells (keratinocytes and fibroblasts), collagen and other ECM proteins, angiogenesis, and cytokines and/or growth factors are among the proven targets of these natural compounds. Since relatively few clinical studies have been conducted to definitively demonstrate the bioavailability, safety, and therapeutic potential of natural wound healing chemicals, more research should be focused on reaching this objective.

Conflict of interest

The authors declare that there is no conflict of interest.

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