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RESEARCH ARTICLE

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A COMPREHENSIVE REVIEW ON TRADITIONAL MEDICINES FOR WOUND HEALING

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ABSTRACT

Wound healing is a critical biological process that restores the integrity of the skin after injuries, which are classified based on depth and severity, ranging from superficial abrasions to complex chronic wounds. The process involves four phases: hemostasis, inflammation, proliferation and remodeling, driven by cellular, enzymatic, and molecular mechanisms. Despite the advancements in medicine, chronic wounds continue to pose challenges because the underlying pathophysiology is one of diabetes or cardiovascular diseases, characterized by prolonged healing, patient discomfort, and high healthcare costs. This review emphasizes the key role that biomaterials, natural and synthetic polymers, bioactive compounds, and innovative dressings play in enhancing wound care. Traditional medicinal herbs like Manuka honey and curcumin, derived from aloe vera plants, and birch tree bark have been reported for remarkable therapeutic potential, partly because of their anti- inflammatory activity, antibacterial activity, and regenerative ability to control inflammation, stimulate neo angiogenesis, and favor the remodeling of the extracellular matrix. Optimization and alignment of drug development and design strategies with translational in vivo models will better suit specific wound indications where imaging-based endpoint assessments prove most useful. It involves integrating the traditional remedy with advanced biomaterials for the better management of chronic wounds by encouraging holistic approaches to wound care and the acceleration of healing processes.

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INTRODUCTION

When the skin's epidermal estate breaks and the dermis beneath is exposed to the air, wounding happens. The skins exposed to the air range from blood vessels to bone, depending on the extent of the skin injury and the affected position.Consequently, injuries are typicallycategorized into three kinds. Awound is considered superficial if it just affects the face of the epidermis. A partial- density wound occurs when the injury affects deeper skin layers, similar as blood vessels, sweat glands, and hair follicles. This occurs when the deeper tissue or bolstering subcutaneous fat rupture in a full- density gash. Cauterization represent common skin trauma that can beget major issues in precluding scarring and restoring function. To launch, the features that distinguish alternate- and third- degree burn injuries are lesions of superficial, partial, and complete thickness.Fourth-degree becks damage the muscles, tendons, ligaments, bolstering tissue, and indeed bone. The nerve endings are torn, and the affected area loses sensation (Jahromi *et al*., 2018). Haemostasias, inflammation, proliferation, and remodeling are the four separate but coextensive stages that make up the wound healing process. The mechanisms of tissue repair involve a range of cell types, enzymes, cytokines, proteins, and hormones (Rajendran *et al*., 2018).

In summary, during the natural healing process, homeostasis is initiated to produce to reduce blood affluence, blood clots and blood highways constrict. Proinflammatory cytokines and growth factors are then secreted (Zha *et al*., 2016). These growth factors thencause inflammation, which is aided by neutrophils, lymphocytes, and macrophages that are drawn in by epithelial cells. Growth factors ultimately lead to angiogenesis, where fibroblast and keratinocyte proliferation leads to reepithelization. Extracellular matrix (ECM) will be deposited as a result of the fibroblasts' posterior sequestration into myofibroblasts (Xue *et al*., 2015). Physicians and technologists must have a thorough understanding of the healing process, implicit polymers and bioactive compounds, and current medical devices for wound management in order to facilitate wound healing. This will allow them to take advantage of biomaterial- supported wound healing. This review's objects are to give a current summary of the eventuality of biomaterials and their uses in wound care and treatment, as well as a structured frame for classifying natural and synthetic polymers and bioactive compounds that will be helpful in the product of biomedical devices that address chronic wound healing. Given the growing number of studies on wound dressings and the dearth of reviews that give the most recent exploration findings, we decided to concentrate on both biomaterials and their application. The potential of sutures, the most constantly used surgical instrument, to promote wound healing is constantly overlooked. We suppose that understanding broader disciplines is necessary to enable the development of new results to the issues brought on by chronic injuries (Ali *et al*., 2022). The body's natural response to tissue damage is wound healing. However, the process of wound healing is not straightforward. Many types of cells and tissues experience many interludes. Diminished and absent cellular structures and tissue layers are replaced throughout the complex and dynamic process of wound healing. Especially, the high expenditure of medical care, patient discomfort, the trouble of bacterial and viral infections, and the cerebral and physiological charges of managing scars each contribute to the strain that injuries place on the healthcare system (V. Coger *et al*., 2019). Acute or chronic wounds are both possible. Depending on its size and depth, an acute wound can heal in around three months. Acute wounds can be cured by only covering them and relying on the body's natural healing process (Sideek *et al*., 2022). However, persistent wounds may lead to sepsis and amputation and create serious issues like pain, discomfort, fluid loss, and unpleasant odours (Eriksson *et al*., 2022). Burns, infections, leg ulcers, pressure ulcers (bed sores), diabetic foot ulcers, venous or arterial ulcers, and other conditions are examples of chronic wounds. Their inability to heal quickly or spontaneously makes them potentially fatal (Sideek *et al*., 2022). Furthermore, infections at the surgical site are thought to be one of the main causes of disease and death in both adult and pediatric patients. Following surgery, surgical site wound infections can develop at the site of the incision or deeper, affecting adjacent tissues, organs, or internal organs. Surgical site wound infections in inpatient surgery will affect 5% of adult patients and 5.4% of pediatric patients by 2022 (Abdelgawad *et al*., 2022).

Types of Wounds

Acute wounds: Tissue damage or injury in acute wounds often goes through a systematic, time-reparative phase that leads to a sustainable restoration of the anatomical and functional integrity. Usually, cuts or surgical incisions result in acute wounds.

Chronic wounds: Chronic wounds are those that have reached a state of pathologic inflammation because they have not undergone the normal healing phases. They require more time to heal (Nagori*et al*., 2011).

Closed wounds: When wounds are closed, blood leaves the circulatory system but remains inside the body. Bruises are one way that it manifests.

Open wounds: An open wound allows blood to escape from the body, and the bleeding is easily observed. Depending on the cause of the wound, the open wound can be further classified into several groups.

Incised wounds: This wound has only moderate tissue damage and no tissue loss. Sharp objects like knives and scalpels are the main cause of it.

Tear or laceration wounds: This non-surgical injury causes tissue loss and damage when combined with other forms of stress.

Puncture wounds: These are brought on by an item that punctures the skin, such as a nail or needle. There is a high risk of infection because dirt can get deeply into wounds.

Abrasive or superficial wounds: Abrasion is caused by sliding slide into a rough surface. This time, the epidermis, the top layer of skin, is scraped off, exposing nerve endings and causing a painful injury.

Penetration wounds: The main source of penetration wounds is an item, such as a knife, entering and exiting the skin.

Gunshot wounds: They are typically produced by a bullet or other object that enters or passes through the body.

Phases of Woundhealing: Tissue reconstitution is the outcome of an ordered series of overlapping processes that characterize wound healing. haemostasias, inflammation, proliferation, and the development of mature scar tissue are all steps in this process.

Haemostasis: Haemostasis starts as soon as the damage occurs. Vascular condensation, platelet thrombus development, coagulation waterfall propagation, clotting termination, andfibrinolysis are the styles used to control bleeding from injuries (Janis *et al*., 2016). Blood flows to the crack point when the vascular endothelium is damaged, exposing the rudimentary lamella. After actuated platelets attach to the exposed collagen, a variety of growth factors, seditious intercessors, and cytokines are released. In order to stop fresh blood loss, a fibrin clot forms a seal and the natural and foreign coagulation pathways are touched off (Broughton *et al*., 2006). Following their release during the haemostasis phase, cytokines contribute to angiogenesis, chemotaxis, extracellular matrix deposit, and epithelialization. These correspond of platelet- deduced growth factor, fibroblast growth factor, epidermal growth factor, transubstantiating growth factor- beta, and vascular endothelial growth factor (Janis *et al*., 2016).

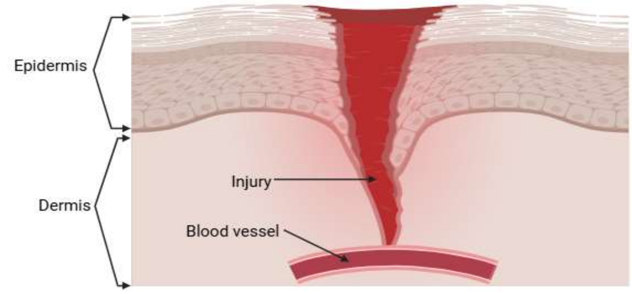

Figure 1. Haemostasis Process

Inflammation: In the initial days after injury, platelet activation is followed by the migration of inflammatory cells to the wound site. In order to facilitate migration, mast cells emit vasoactive cytokines including prostaglandins and histamine, which raise capillary permeability and encourage local dilatation. The majority at first are neutrophils, which are drawn to the wound bed by bacterial products. After the first 48 to 72 hours, neutrophils absorb the bacteria and any dead tissue, resulting in the pus that is visible in wounds. Monocytes then develop into macrophages, which further debride the wound by removing fibrin, wasted neutrophils, and other cell debris from the matrix. The majority of inflammatory cytokines, including fibroblast growth factor, platelet-derived growth factor, epidermal growth factor, and transforming growth factor-beta, are also released by macrophages. Because of these functions, macrophages are necessary for effective wound healing; when their function is inhibited, wound healing is delayed (Janis *et al*., 2016; Broughton *et al*., 2006).

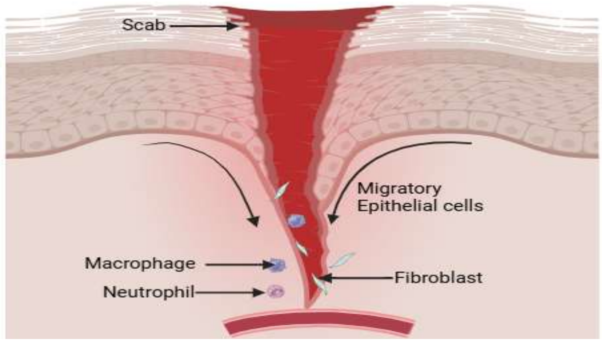

Figure 2. Inflammation Process

Proliferation: A sufficient number of fibroblasts move to the site within two to three days following the original injury, signaling the start of the proliferative phase, which can extend up to three weeks in a healed cutaneous lesion. Fibroblasts are essential during this stage because they produce a lot of immature type III collagen and disorganized collagen into this temporary matrix (Landen *et al*., 2016).Under the impact of certain cytokines, fibroblasts recruited to the wound may change into myofibroblasts, which may ultimately cause the wound to contract and produce more collagen (Desmouliere *et al*., 1993; Finnson *et al*., 2013). Numerous signaling mechanisms, including but not limited to angiotensin II and TGF-β via both canonical and noncanonical signaling pathways, were discovered to be involved in regulating the wound healing process (Finnson *et al*., 2020; Murphy *et al*., 2015).

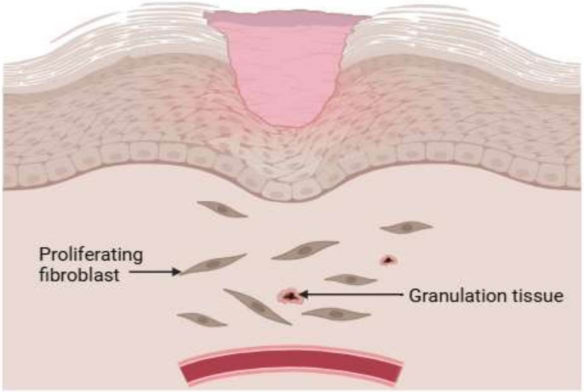

Figure 3. Proliferation Process

Maturation and Remodeling Phase: In the final remodeling stage of wound healing, granulation tissue is replaced by permanent scar tissue. Over the course of the following year, type I fibrillar collagen progressively replaces type III reticular collagen following four to five weeks of continuous net collagen synthesis (Diegelmann *et al*., 2003; Carlson *et al*., 2004). Zinc-dependent endopeptidases, commonly known as matrix metalloproteinases, are secreted by epidermal cells and are essential for tissue remodeling (Broughton *et al*., 2006; Velnar *et al*., 2009). As collagen production increases, wound tensile strength continues to increase, increasing from 3% in week one to 20% in week three. Three months following injury, intact skin's tensile strength peaks at 80% but never reaches 100% (Lindstedt *et al*., 1975; Levenson *et al*., 1965). Each of these phases—hemostasis/inflammation, proliferation, and remodeling—is necessary for the wound healing process to be successful (Janis *et al*., 2014).

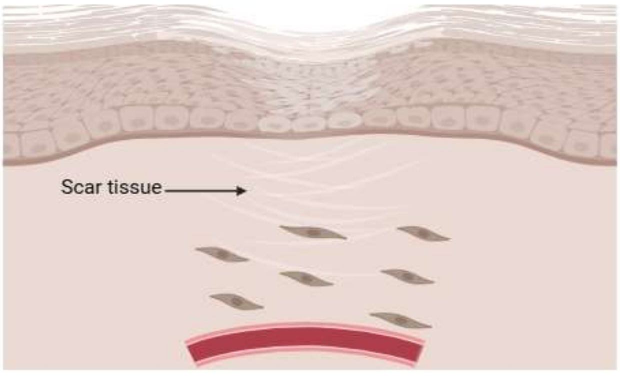

Figure 4. Remodeling Process

Key Factors for Enhancing the Development of Drugs for Wound healing: Throughout the development of the clinical contender ILP100-Topical (emilimogenesigulatibac), from idea through non-clinical progress and clinical proof of concept, three essential components that support the successful development of treatment for wounds have been found (Vagesjo *et al*., 2021).

Explain how the candidate medication works in translational in vivo research utilizing relevant endpoints for the intended wound indication: It is better to know the exact intended-to-treat wound indication before creating the translational program because the aetiology of wounds to the skin has a big influence on the wound-healing cascade. Age and underlying conditions such as diabetes and cardiovascular illnesses, for example, have a significant impact on immune system components and the wound microbiome. These factors impact the ability of the wound to heal, which in turn affects the result (Ohnstedt *et al*., 2019; Phillipson *et al*., 2011; Gould *et al*., 2015). Since the wound ecology and healing capabilities may differ significantly for different wound indications, non-clinical models should be developed to as accurately mimic all aspects of the underlying diseases or conditions of non-healing wounds of varied aetiologies as possible. This increases the possibility that the identified mechanism of action (MOA) will also be relevant for the specific wound indication being targeted and ensures that the translational in vivo program is well-designed. The % body surface area can be used to scale the wounds of different species in order to align the wound volume and size under study. An unappreciated component is matching the assessment of nonclinical research with endpoints that have been verified for the specific wound indications specified in the current or proposed criteria for the relevant market. When looking through the scientific literature on medication candidates being studied during preclinical development, many other components are also missing. These include the following: a description of the safety profile and risk/benefit; an evaluation of the candidate drug in conditions associated with impaired in vivo healing; variance reported in the control groups; time to full healing; and a MOA also confirmed in human tissues (Vagesjo *et al*., 2021).

Locate, utilize, and confirm pertinent endpoints for the selected wound indicators: Regulatory requirements pre-set the primary and some secondary goals while defining the clinical research strategy. For instance, the European Wound Management Association and the FDA both recognize that full wound closure is the most clinically significant endpoint in their 2006 Guidance to Industry (Price *et al*., 2014). There are other factors that are pertinent and crucial for patients, even though total wound closure can be the ultimate goal. Therefore, in 2014, the Wound Experts/FDA Clinical Endpoints Project (WEFCEP) was established as a joint effort with the goal of identifying and validating primary endpoints that are patient-centered and clinically significant. Twelve more endpoints were consequently found to have unmet needs in wound patients (Driver *et al*., 2019), and the FDA consented to discuss five additional primary endpoints with sponsors in 2020: 1) a decrease in the percentage of wound area; 2) a decrease in infection; 3) a decrease in pain or the need for analgesics; 4) an improvement in physical function and ambulation; and 5) quality of life, in addition to the assessment and validation of the tools used to measure the
aforementioned.

Use a comprehensive and verifiable evaluation of wound healing in addition to patient and clinicalvalue: Although the investigators clinical appraisal of wound healing is obviously significant, it may no longer be the stylish option for main endpoint evaluation for a variety of reasons. We support the use of imaging grounded endpoint assessments in confluence with the standardization of dazed and traceable evaluations. The imaging datasets allow for thorough detailed assessments of both tolerability parameters and wound healing, as well as for traceability and reevaluation at any point in time by one or multiple external assessors and validators who are ignorant of the case's medical history andunknown /unconscious impulses also, it may be delicate to estimate the final time points for the endpoint assessment in the early stages of clinical exploration; these should be applicable and significant in light to demonstrate the impact of the investigational medicinal product (IMP) with little influence from confounding variables (Vagesjo *et al*., 2021).

Traditional Medicinal Plants used in Wound Healing: Significant progress has been made in the treatment of chronic wounds over time, especially with better surgical wound bed preparation (Schultz *et al*., 2003; Kim *et al*., 2023), and improved treatments for wounds (Su *et al*., 2023). Novel biomaterials incorporated into wound dressings (Da *et al*., 2023) changing the fluid balance (Brumberg *et al*., 2021), by altering the wound environment's pH (Haverkampf *et al*., 2017; Schreml *et al*., 2011) have significantly enhanced the results for individuals with persistent wounds. Crucially, underlying pathophysiology frequently causes chronic wounds, and improvements in diabetes care (Von Scholten et al., 2021; Tahrani *et al*., 2016) with insufficient blood flow (Stanek *et al*., 2023) are among the most effective strategies to lessen the burden of long-term injuries. Here, we look at the advancements made in creating treatments meant to promote the healing of chronic wounds and their suggested mode of action.

Manuka Honey *(Leptospermum scoparium)*: Throughout history, honey has been utilized in medicine; the Egyptians were the first to utilize it in surgical dressings to promote wound healing. Honey provides extra pro-healing properties in addition to its well-known antibacterial properties when it comes to wound care (Lee *et al*., 2011). The inflammatory phase is believed to be aided by medical honey, which is known to increase the synthesis of prostaglandin E2, IL-1β, IL-6, and pro-inflammatory cytokines TNF-α. Additionally, honey can raise TGF-β and MMP-9, which aids in the remodeling and proliferative phases (Hadagali *et al*. 2014). Manuka honey is one kind of therapeutic honey that is frequently used to treat wounds. Glucose oxidase is one of the enzymes in manuka honey that catalyzes the conversion of glucose to gluconic acid and H2O2. The pH is lowered by glutaconic acid, and the H2O2 has antibacterial properties. Protease activity at the wound site decreases as a result of this pH shift, which also causes haemoglobin to release more oxygen, which in turn stimulates fibroblast and macrophage activity. Furthermore, the H2O2 promotes the synthesis of VEGF. Additionally, honey contains flavonoids, which are ROS scavengers that neutralise free radicals and promote healing (Tashkandi *et al*., 2021). The FDA has approved a number of Manuka honey dressings, with variations in the amount of Manuka honey used on the wound. Robson*et al*. report that 90% of their chronic wound patients were successfully closed, highlighting Medi honey's effectiveness in their clinical environment (Robson *et al*., 2009). Additionally, Biglari *et al*. showed that Medihoney significantly shortened the healing period for individuals with persistent pressure ulcers (Biglari *et al*., 2012). Although the effectiveness of medical honey as an antibacterial in wounds is well established, more research is necessary to determine whether medical honey is promoting healing physiologically rather than merely lowering bacterial contamination and facilitating better healing (Patenall *et al*., 2024).

Curcumin *(Curcuma longa)*: Turmeric is a polyphenol that is extracted from the rhizome of the plant. Because of its anti-inflammatory, antioxidant, antibacterial, and anti-cancer qualities, curcumin has long been utilized in herbal medicine all over the world for wound care and other ailments. Curcumin regulates the proliferative, remodeling, and inflammatory stages of wound healing (Akbik *et al*., 2014). TNF-α and IL-1, two important cytokines in causing inflammation, have been shown to be inhibited by it through NF-κBsignalling (Wang *et al*., 2009; Aggarwal *et al*., 2013). Furthermore, during the proliferative stage of wound healing, curcumin scavenges ROS, reducing oxidative stress and boosting collagen and hydroxyproline synthesis (Akbik *et al*., 2014; Gopinath *et al*., 2004). Gadekar *et al*., demonstrated that administering transdermal curcumin patches to rats' excisional wounds accelerated angiogenesis and wound contraction, which shortened the healing period (Altoe *et al*., 2019). Phan *et al*., investigated this effect further in vitro, showing that curcumin administration resulted in successful repair using an H2O2 model of damage on human fibroblasts and keratinocytes (Phan *et al*., 2001). It has also been demonstrated that curcumin contributes to the proliferative phase of healing. When Gopinath et al. administered curcumin-loaded chitosan sponges to injured rats, they observed improved granulation tissue alignment in comparison to a control group (Gopinath *et al*., 2004). Thus, by reducing the inflammatory phase and promoting proliferation and remodeling, curcumin can hasten the healing of wounds. Curcumin is more frequently applied topically due to its hydrophobicity, which impairs oral absorption (Akbik *et al*., 2014).

Aloe Vera *(Aloe barbadensis miller)*: Originating from the cactus-like shrub Aloe barbadensis, aloe vera has been used for a very long time; the Egyptians were the first to employ it about 4000 B.C. (Sung *et al*., 2006; Lee *et al*., 2006). Aloe vera has been demonstrated to lessen discomfort and speed up the healing process when used to treat burns and ulcers (Eshghi *et al*., 2010). Aloe vera's phenolic component content encourages ROS scavenging, which lowers inflammation (Liang *et al*., 2021; Davis *et al*., 1994), and it is also known to lower TNF-α and IL-1 (Kang *et al*., 2014; Ozsoy *et al*., 2009). Furthermore, polysaccharides included in aloe vera, like mannose-6-phosphate, bind to and promote fibroblast activity and proliferation, increasing the formation of collagen (Liang *et al*., 2021).

Birch Bark *(Betulaalba)*: The Native American Ojibwe tribe was the first to employ Betulaalba (birch bark) in wound treatment, wrapping their wounds in it to hasten the healing process (Erichsen *et al*., 2013). Birch bark has been used in traditional medicine throughout the northern hemisphere. Since then, the therapeutic benefits of birch bark have been demonstrated in clinical settings utilizing n-heptane dry extract from the birch's outer bark; pentacyclic triterpenes make up 97% of the extract (Scheffler *et al*., 2019) [68], and botulin is the triterpene that promotes wound healing (Emricg *et al*., 2022). Triterpenes, which are mediated by IL-6 and signal transducer and activator of transcription 3 (STAT3) signaling, have been shown by Ebeling et al. to significantly increase wound healing in an ex vivo porcine healing model. They also showed improved migration and skin barrier when applied to human keratinocytes (Ebeling *et al*., 2014).

Ginseng *(Panax ginseng)*: In Eastern Siberia, China, Japan, and Korea, it is among the most widely used medicinal plants. Recollection is also thought to improve physical agility, immunity, and fatigue levels. Consequently, Panax ginseng is used to treat chronic fatigue, anxiety, and depression. Vasodilatation, blood lipid regulation, inflammation reduction, and the provision of antioxidant, anti-cancer, antibacterial, anti-allergic, anti-aging, and immunomodulatory properties have all been demonstrated to be attributed to Panax ginseng (Xiong *et al*., 2019). There are numerous bioactive chemicals in Panax ginseng, but the most powerful active ingredient is a family of saponins known as panaxosides by Russian scientists and ginsenosides by Asian researchers. It has been demonstrated that extracts from Panax ginseng roots protect the skin from acute UVB irradiation and greatly accelerate wound healing after laser burning and excision. Research shows that Panax ginseng extracts promote keratinocyte migration, stimulate proliferation, and raise collagen synthesis in human dermal fibroblasts in vitro.However, it has also been demonstrated that ginsenoside Rb2, which is isolated from Panax ginseng, promotes the growth of the epidermis in raft culture by raising the expression of fibronectin and the receptor, keratin and collagenase I, and epidermal growth factor and receptor, all of which are essential for wound healing (Lee *et al*., 2014).

Neem *(Azadirachta indica)*: It was widely recognized for its anti-ulcer, antifungal, antibacterial, antiviral, anticancer, and antioxidant properties in wound dressings (Phan *et al*., 2001). A study investigated neem-incorporated collagen bio composite films for their anti-inflammatory, nitric oxide scavenging, and antioxidant properties. Films with 1000 µg/mL neem extract demonstrated significant nitric oxide reduction (10 µg/mL), while films with 400 µg/mL extract showed an 80% increase in DPPH scavenging activity and maintained over 80% cell viability in MTT assays using RAW 264.7 cell lines. Additionally, the electrospinning potential of various plant extracts, including Azadirachta indica (neem), Indigofera aspalathoides, Memecylon edule (ME), Myristica andamanica, and PCL, was explored for skin tissue engineering. Among them, M. edule-integrated PCL nanofibers showed enhanced cell proliferation, with 31% higher performance than PCL alone over nine days. F-actin staining revealed strong cell-to-cell interaction, and collagen staining confirmed extracellular matrix secretion, supporting epidermal differentiation of human adipose-derived stem cells (ADSCs) on these nanofibers (Altoe *et al*., 2019).

German chamomile *(Chamomilla recutita)*: Researchers evaluated nanofibrous membranes of electro spun polycaprolactone/polystyrene (PCL/PS) incorporated with chamomile (C. recutita) extract for active wound dressing applications. Chamomile's therapeutic properties are attributed to its phenolics and flavonoids, particularly apigenin, which significantly aids wound healing. Antibacterial and antifungal tests showed the nanofibers' efficacy against S. aureus and C. albicans with inhibition zones of 7.6 mm. MTT assays confirmed cell adhesion and mesenchymal stem cell viability on the nanofibers. Membranes with 15% chamomile extract demonstrated up to 99% wound healing after 14 days in a rat model, accompanied by reepithelialization, collagen deposition, and absence of necrosis in the dermis tissue (Sung *et al*., 2006).

Table 1. Some Medicinal plants used for treating different types of wounds

S.No.	Medicinal plants	Part used	Metabolites	Medicinal Uses	Reference
1.	Turmeric *(Curcuma longa)*	Rhizomes	Curcumin, vitamin A, proteins	Chronic wound healing	Jain *etal*., 2007
2.	Liquorice *(Glycyrrhiza glabra)*	Roots	Glycyrrhizin, glycyrrhetinic	Acute/chronic wound healing	Ameri *etal*., 2013
3.	Centella *(Centella asiatica)*	Leaves	Asiatic acid, asiaticoside madecassoside, madecassic acid	Incision wound healing	Shukla *etal*., 1999; Chen *et al*., 1999
4.	Carbonal *(Mimosa tenuiflora)*	Stem	Mimosine (an alkaloid), sitosterol, amino acids, linoleic acid, tannins, polyphenols and oleic acid	Chronic wound healing	Kumarasamyraja*et al*., 2012
5.	Honey *(Apis mellifera)*	Secretion from hive	5- Hydroxyimidacloprid, 4,5-dihydroxyimidacloprid, desnitroimidacloprid, 6-chloronicotinic acid, olefin	Acute wound healing	Georgescu *et al*., 2017
6.	Theaceae *(Camellia pubipetala)*	Leaves	Flavonoids, theanine and caffeine	Excision wound healing	Yang *et al*., 2014
7.	Forest Champa *(Spermadictyon suaveolens)*	Roots	Triterpenes, sesquiterpenes, alkaloids	Chronic wound	Rani S *et al*., 2016
8.	Neem *(Azadirachta indica)*	All portions	Azadirachtin, azadirone, nimbin,	Open wound healing	Osunwokeemek *et al*., 2013
9.	Sesame *(Sesamum indicum L)*	Seeds	Metronidazole, E and C vitamins, sesamolinol, sesamol, sesaminol, sesamolin	Acute/chronic wound healing	Kiran *et al*., 2008
10.	Trumpet tree *(Cecropia peltate)*	Leaves	Flavonoids, terpenes phenols, alkaloids, sterols, waxes, fats, tannins, gums, resin acids	Closed wound healing	Sapna *et al*., 2016
11.	Kencur *(Kaempferia galanga)*	Rhizomes	Amino acids, protein, carbohydrate, alkaloids, steroids	Incision wound healing	Himesh *et al*., 2012
12.	Maidenhair *(Ginkgo biloba)*	Leaves and seeds	Flavonoids, lactones, and ginkgolic acid	Closed wound healing	Muhammad *etal*., 2015
13.	Indian mulberry *(Morinda citrifolia)*	Leaves and fruit	Anthraquinones, steroid, phenol, tannin, and terpenoids	Closed wound healing	Nayak *et al*., 2007
14.	Club Moss *(Lycopodium serratum)*	Spores and whole fern	Alkaloids, steroids, tannins	Acute/chronic wound healing	Manjunatha *et al*., 2007
15.	Asthma Weed *(Euphorbia hirta)*	Leaves	Saponins, tannins, flavonoids, alkaloids, glycosides	Chronic wound healing	Mittal *et al*., 2013
16.	Madagascar periwinkle *(Catharanthus roseus)*	Leaves	Monoterpenoids alkaloids, vinblastine, vincristine	Acute/chronic wound healing	Nayak *et al*., 2006
17.	Red sandalwood *(Pterocarpus santalinus)*	Bark wood	Santalin A and B, savinin, calocedrin, pterolinus K and L, and pterostilbenes	Acute/chronic wound healing	Yogesh *et al*., 2013
18.	Lawsonia alba *(Lawsonia inermis)*	Leaves and roots	Coumarins, naphthoquinone, flavonoids, sterols, triterpene, and xanthones	Chronic wound healing	Chaudhary *et al*., 2010
19.	Bay *(Sphagneticolatrilobata)*	Leaves	Flavonoids, terpenoids, alkaloid, and saponin	Incision wound healing	Balekar *et al*., 2012; Govindappa *et al*.,2011
20.	Papaya *(Caricapapaya)*	Latex, fruit	papain	Diabetic, burn, soft tissue wounds	Mahmood *et al*., 2005

Burdock (Arctium lappa): This perennial weed is commonly grown and is commonly called burdock. In North America, Europe, and Asia, Arctium lappa is used to heal sore throats and skin conditions like boils, rashes, and acne. Arctium lappa was found to have hepatoprotective, antiviral, anti-inflammatory, anti-diabetic, antibacterial, and antioxidant properties in a clinical experiment. Root extract from Arctium lappa has been demonstrated to significantly improve dermal ECM metabolism, influence glycosaminoglycan turnover, and reduce evident in vivo wrinkles in human skin. Additionally, it has been documented that Arctium lappa regulates gene expression and cell adhesion in canine dermal fibroblasts, impacting the Wnt/β-catenin signaling pathway, which is a crucial regulator of wound healing. Human first and second degree burn suffering and healing were reported to be managed more effectively with Arctium lappa burns and wounds topical ointment (B&W) than with the control treatment in a pilot trial (Ramnath*et al*., 2012).

Centella *(Centella asiatica)*: This was also referred to as Asian pennywort and was used to promote wound healing. According to reports, extracts from Centella asiatica aerial sections can help the chronic ulcers heal in terms of their size, depth, and distance. In a punch-type wound, it has been demonstrated that Asiaticoside, which is extracted from Centella Asiatica, promotes collagen deposition and epithelialization. Glycosaminoglycan production and collagen remodeling are enhanced by the isolated triterpenes from Centella astica. Furthermore, oral administration of Centella asiatica's madecassoside has been demonstrated to stimulate angiogenesis and collagen synthesis at the wound site (Kishore *et al*., 2011).

Silver cock's comb *(Celosia argentea)*: In traditional drug, celosia argentea, generally appertained to as tableware incline’s comb, is used to cure mouth ulcers, skin blisters, eruptions, other skin conditions (Priya *et al*., 2004). This factory’s splint excerpts have hepatoprotective (Wu *et al*., 2013), antidiabetic (Hamzah *et al*., 2018), antioxidant (Malomo *et al*., 2011), and antibacterial (Wiart *et al*., 2004) parcels. By raising the quantum of collagen and hexosamine in granulation towel injuries, Priya et al. showed that an alcohol excerpt of Celosia argentea speeds up the mending of burn injuries in rats. Likewise, primary rat dermal fibroblasts motility and proliferation were enhanced by the excerpt (Priya *et al*., 2004).

CONCLUSION

The thorough analysis of wound healing emphasizes the complex mechanisms at play, including as haemostasis, inflammation, proliferation, and remodeling, as well as the application of conventional therapies to promote these mechanisms. It illuminates the possibilities for cutting-edge wound care products that address both acute and chronic wounds by investigating natural and synthetic biomaterials. By highlighting their function in fostering angiogenesis, collagen synthesis, and epithelialization, this work emphasizes the significance of utilizing bioactive chemicals and polymers to create novel wound dressings and medical devices. Through the modulation of inflammatory responses and the enhancement of tissue repair mechanisms, medicinal plants such as curcumin, aloe vera, and manuka honey show promising benefits in speeding wound healing. The research also highlights the difficulties in managing wounds, including excessive healthcare costs, infection risk, and patient discomfort. In order to create successful treatment plans, it necessitates a multidisciplinary strategy that combines conventional therapies with contemporary biomedical developments. Validating the therapeutic potential of these biomaterials, investigating patient-centred objectives, and improving medication formulations should be the goals of future research. All things considered, this work bridges the gap between ancient knowledge and modern medical procedures by offering a crucial framework for creating targeted therapeutics to address chronic wound issues.

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