Cellular and Molecular Mechanism of Wound Healing Along with Different Plants Used in Wound Healing Potential

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ABSTRACT

Healing a skin wound is a complicated process that needs many types of cells working together at different times. When the skin is hurt, cells in the epidermis, dermis, and subcutaneous tissue must work together perfectly for the area to heal. Changes in the microenvironment, like changes in mechanical forces, oxygen levels, and the production of growth factors, can have a direct effect on the recruitment and activation of cells, which can make repair less effective. Even though wound healing is hard, a lot of work has gone into understanding how wounds heal, making wound care better, and creating new therapies and tools. Herbal medicine has become a good option for many health problems, including wound healing. It has been shown that these natural treatments can help treat ulcers, skin infections, inflammation, and wounds. Traditional herbal medicines are very popular because they are easy to get, don't cost much, and have deep cultural roots. This review talks about how medicinal plants and their derivatives can help heal wounds. It stresses how important herbal medicines are for treating and caring for wounds. These treatments can help clean, remove dead skin, and keep the area wet so that natural healing can happen. However, herbal drugs need to be standardized and their quality must be checked to make sure they are always the same and work as intended. Herbal drugs have a lot of potential to treat and cure a wide range of illnesses. This makes them an interesting choice for wound care and treatment.

Keywords: Herbal wound healing, Cellular and molecular mechanism, Wound Microenvironment, Natural Healing Therapies, wound healing potential.

INTRODUCTION

Indian medicine plants also have a lot of antioxidants, which are known to stop or slow down a number of diseases. At different amounts, the antioxidant protection can be seen.[1] Medicinal plants have been used for centuries to treat skin ailments like cuts, wounds, and burns. Skin diseases, including wounds and burns, are considered significant due to their high mortality rate. Wound healing is a vital process for maintaining skin integrity. Medicinal plants offer alternative or complementary therapies due to their diverse bioactive compounds.[2] Wounds, often caused by infections or injuries, are a significant health concern. Wound dressings are commonly used for protection. Recently, herbal medicines and their derivatives have gained attention for their wound healing properties. These natural agents, such as extracts and essential oils, are valued for their antioxidant and antibacterial properties by researchers and wound dressing manufacturers.[3] Wound healing involves a complex process of cell migration, proliferation, and differentiation, along with biomolecular interactions and ECM synthesis. The dynamic interaction between cells and the ECM, composed of collagen, elastin, fibronectin, etc., guides cell behavior during tissue repair and homeostasis.[4] Healing a wound is a complicated biological process by which the body fixes broken tissue so that it works properly again. Healing wounds is important for your health and well-being, whether they are small cuts or major surgeries. A wound is any damage or disruption to the regular
structure and function of an organ or body part. It can be as easy as a cut on the skin or as serious as damage to the subcutaneous tissue, muscles, tendons, blood vessels, nerves, organs, and even bone. Wounds can be caused by injuries on the outside, diseases, accidents, or deliberate harm on the inside. No matter what caused the wound, it hurts the flesh and changes the environment around it. During normal wound healing, many things happen at the same time, such as bleeding, clotting, inflammation, tissue regrowth, cell migration and proliferation, synthesis of extracellular matrix proteins, tissue remodeling, and collagen deposition. In the end, this process makes the wound stronger and heals any cells that have been cut.\[5\] Wounds that don't heal properly can become chronic, which is very hard on individuals and healthcare systems. In order for a wound to heal normally, inflammation cells, chemokines, cytokines, nutrients, and more metabolic demand must be sent to the wound site. There are three main parts to this process: inflammation, proliferation, and change.\[6\] Hemostasis (which stops bleeding or inflammation), growth, and remodeling are the stages of wound healing. Platelets sticking together and the release of chemokines and growth factors start hemostasis, which lasts for about 72 hours and is then followed by neutrophil and macrophage activity.\[7\]

CLASSIFICATION OF WOUNDS

Wounds are classified as either acute, typically healing within 7 to 10 days, or chronic, where the healing process is slow and disorderly, often extending beyond this timeframe. Several factors contribute to a wound becoming chronic, including underlying diseases, infection, prolonged inflammation, medication use, and oxidative stress associated with aging.\[8\] Wounds are classified based on their cause and healing physiology. Open wounds involve visible bleeding, like incised, lacerations, abrasions, punctures, penetrations, and gunshot wounds. Closed wounds occur when blood remains in the body, including contusions, hematomas, and crush injuries. Acute wounds follow an orderly healing process, resulting in restored anatomical and functional integrity. They heal within the expected timeframe, caused by cuts, burns, or surgical incisions. A common example is a clean surgical incision closed with sutures. Although tissue regeneration is rare, healing usually results in a satisfactory outcome, though not identical to intact skin, except in early fetal healing.\[9\] An acute wound is one that happened not long ago and has not yet gone through the stages of healing. These wounds can be full-thickness skin lesions that only affect the subcutaneous layer of skin or superficial skin lesions that affect the epidermis or superficial dermis. Surgical cuts, thermal burns, abrasions, and lacerations are some examples of these types of wounds.\[10\] Good circulation, a healthy immune system, and a wet environment free of dead tissue or foreign matter are all signs of an acute wound that is healing. These conditions help the cells and molecules that are involved in the repair process work normally. They are wounds that don't heal properly and get in a state of abnormal inflammation. Either these cuts take a long time to heal or they keep coming back. Most chronic wounds are caused by local infections, lack of oxygen, trauma, foreign bodies, and systemic issues like diabetes, poor diet, a weak immune system, or medications.\[11\]

**Fig. 1: Types of Chronic wounds**

Chronic wounds deviate from normal healing stages, resisting treatment and requiring extended healing times. Environmental and host factors like trauma, infection, compromised circulation, and immunodeficiency disrupt healing, causing further tissue damage. Wounds are classified by location, depth, nature, or cause. About 80% of the global population uses traditional health practices, with 85% relying on plant remedies. Natural compounds from plant extracts aid wound healing by reducing scar formation. Plant-derived bioactive compounds, with antimicrobial, antioxidant properties, stimulate blood coagulation, fight infection, and accelerate wound healing.\[12\] Natural compounds offer effective and safe wound healing treatments, often
being more affordable than conventional therapies. Chronic wounds are a global issue, costing millions annually. Microbial complications, including infections and delayed healing, are common. Antimicrobial wound management is challenging, with systemic antibiotics having limited effectiveness against wound biofilms. Antisepsis is preferred for treating germs in wounds.[13]

Physiology of Wound Healing

In order for a wound to heal, soluble mediators, blood cells, the extracellular matrix (ECM), and parenchymal cells all work together in a complicated way to restore the wound's structural and functional integrity. There are different stages in this process, and each stage is marked by different cellular and chemical events.[14] In traditional medicine, wound healing is split into four stages: stopping the flow of blood, inflammation, cell growth, and tissue reshaping. Even though the procedure is complicated, complications often happen, which slows down mending, raises the risk of illness and death, and results in less-than-ideal cosmetic outcomes. The economic cost of chronic wounds and the mental toll they take on patients are big, but they're hard to measure, so they're often undervalued.[15]

Inflammation, the production of new cells, cellular differentiation, and the organized movement of cells in certain ways to specific locations are all things that help wounds heal. As a wound heals, cells inside and around the damage have to be put back together again. Some of these cells are simple squamous cells, mesenchymal cells that are not doing anything, thrombocytes, and mesenchymal cells that are being controlled by growth factors.[16]

Cellular Mechanism of Wound Healing

Hemostasis

When the skin is hurt, the first thing that happens to stop the bleeding is that the blood vessels get smaller. After that, both primary and secondary hemostasis happen at the same time through routes that are linked to each other. During primary hemostasis, platelets stick together and a platelet plug forms when collagen in the subendothelial tissue is exposed. As part of secondary hemostasis, the coagulation cascade is started, which changes soluble fibrinogen into insoluble fibrin strands that make a fibrin mesh.[17] When the platelet plug and fibrin mesh come together, they form a thrombus. This stops the bleeding, releases complements and growth factors, and gives cells that help the wound heal a short place to live.[18]

During the hemostasis process of wound healing, cells go through a number of important steps:

A: Platelets normally move close to the vessel wall, but anti-thrombotic substances like nitric oxide (NO) and prostacyclin, which are released by endothelial cells, stop platelets from sticking to the endothelium and sticking together.

B: When there is a wound, the cells that are hurt quickly release vasoconstrictors. These chemicals make the smooth muscle tighten automatically, which stops the bleeding for a short time.

C: When a blood vessel breaks, the subendothelial matrix is revealed. Platelets connect to this matrix using G protein-coupled receptors, integrins, and glycoproteins on their surface. Von Willebrand factor (vWF), which sticks to the subendothelial tissue, is also released by platelets. Platelets use their surface receptors to bind to the external vWF, which makes the platelet plug stronger.

D: Both the extrinsic and intrinsic routes turn on Factor X, which changes fibrinogen into fibrin. Cross-linked fibrin sticks to the clumped platelet plug and forms a thrombus. This stops the flow of blood and gives the wound a brief place to heal.[19]

Inflammatory Phase

Injury triggers the initial inflammation response, whether caused by surgery or trauma, starting a sequence of three phases to assist in the ultimate repair process. The initial phase of inflammation readies the area for repair by causing swelling and pain that limits movement. Mast cells release granules containing enzymes, histamine, and other active amines within the first 24 hours post-injury, and this continues for up to 2 weeks in typical wounds. These substances produce the typical signs of inflammation: redness, heat, swelling, and pain around the wound site.[20] These chemokines, named for their chemoattractive properties, play crucial roles in leukocyte trafficking and recruitment during inflammation. The inflammatory response following tissue injury is pivotal in both normal and pathological healing. The innate immune system is swiftly activated post-injury, initiating a local inflammatory response.[21]

Mast cell infiltration increases during the late
inflammatory phase of wound repair, with most mast cells originating from adjacent tissue. As inflammation subsides and leukocyte numbers decline, the wound undergoes a protracted phase of remodeling and resolution. Although inflammation wanes during this phase, its impact on the final wound outcome remains profound. Inflammatory cells accompany every phase of wound repair, depicted as haemostasis (yellow panel), early inflammation (light pink panel), late inflammation (dark pink panel), and resolution/remodeling (blue panel).[22] The relative abundance of the four primary types of leukocytes in wounds—mast cells, neutrophils, macrophages, and T cells—is illustrated. While neutrophils and lymphocytes diminish, a small number of resident mast cells and macrophages persist during the extended remodeling phase.[23] Following tissue damage, the healing process of wounds begins with rapid, non-genomic events. Calcium waves quickly spread across the wound site, commencing at the edges. These waves, in addition to gradients of reactive oxygen species (ROS) and the release of damage-associated molecular patterns (DAMPs) from the damaged cells, act as the primary signals for activating the cells. DAMPs, such as DNA, peptides, components of the extracellular matrix, ATP, and uric acid, function as signals of danger, prompting the recruitment of inflammatory cells, particularly neutrophils. Hydrogen peroxide (H2O2), a notable ROS, plays multiple roles, such as reducing infection, supporting the regeneration of keratinocytes, attracting neutrophils, and even stimulating the creation of new blood vessels through its signaling pathways. Additionally, chemokines, which are small signaling proteins categorized by their cysteine arrangement (CXC or CC), are secreted. CXC chemokines, especially the ELR+ subgroup, have a specific affinity for attracting neutrophils and display properties that promote angiogenesis, further coordinating the initial inflammatory response and tissue repair.[24] Immediately following an injury, mast cells release various mediators like inflammatory cytokines, vasodilation agents, vascular permeability factors, and proteases that aid in attracting immune cells to the wound.[25] As the wound heals, various cells are recruited, and fibroblasts are vital to the production of extracellular matrix and communication with surrounding cells. Astragalus exogenous growth factors and APS2-1 promote wound healing by promoting cell proliferation, migration and cycle progression. Inflammation is reduced and cytokines are secreted, which promote wound healing.[26]

Neutrophils

Neutrophils are quick to respond to tissue injury by receiving signals from platelets and the coagulation cascade. They play a crucial role in fighting infections by engulfing bacteria and clearing out foreign bodies and damaged tissue. The process involves interactions between adhesion molecules on circulating leukocytes and vascular endothelial cells.[27] Neutrophils play a critical role in wound healing by facilitating the penetration of elastase and collagenase through the endothelial cell basement membrane and into the extracellular matrix at the wound site. Additionally, they release TNF-alpha and IL-1, which promote the recruitment and activation of fibroblasts and epithelial cells. Neutrophils also aid in combating bacteria within the wound by utilizing oxygen-free radicals and proteases. However, if bacteria persist in the wound, inflammation can be prolonged as neutrophils continue to be recruited and release proteases, cytokines, and reactive oxygen species. Neutrophils undergo apoptosis within 2 to 3 days in the wound, after which they are replaced by tissue monocytes, further contributing to the healing process.[28]

Macrophages

Activated macrophages are pivotal for proper wound healing. Originating from circulating monocytes, they arrive at the wound site approximately 24 hours after injury. There, they differentiate into tissue macrophages in response to various signaling molecules. These macrophages play a dual role, patrolling the wound area to eliminate bacteria and clearing damaged tissue while also facilitating the transition from the inflammatory phase to the proliferative phase of healing. They achieve this by releasing a range of growth factors and cytokines that recruit and activate fibroblasts, promoting the synthesis and organization of new tissue matrix and angiogenesis. Macrophages regulate proteolytic tissue destruction and exhibit a high degree of plasticity, adapting to their environment throughout the healing process.[29]

Fibroblast Migration
Fibroblasts are attracted to wounds by signals released by platelets and macrophages. They move within the extracellular matrix by interacting with specific components of the matrix. Normally inactive, fibroblasts become active and numerous in the provisional matrix and granulation tissue at the wound site. Their movement and accumulation require changes in their shape and the release of enzymes to clear a path in the extracellular matrix. Fibroblasts bind to matrix components such as fibronectin, vitronectin, and fibrin through integrin receptors. They extend projections from their cytoplasm to find new attachment points, using their cytoskeletal network to propel themselves forward and migrate into the wound site.\[30\]

Collagen and Extracellular Matrix Production

The extracellular matrix (ECM) is a complex network consisting of collagen and elastic fibers suspended in a substance rich in glycosaminoglycans, proteoglycans, and connective tissue glycoproteins. Cellular calcium processing plays a crucial role in controlling collagen production, impacting keratinocyte differentiation, ECM composition, collagen synthesis, and wound healing. Studies have shown that calcium channel blockers like nifedipine and amlodipine can enhance skin strength, accelerate wound contraction, and partially reverse steroid-induced impairment of wound healing in rats. Hydroxyproline, an essential component of collagen, maintains its stable structure. Insufficient hydroxyproline, seen in conditions like scurvy, alters collagen structure and accelerates its breakdown. Therefore, measuring hydroxyproline levels is crucial for assessing collagen production and metabolism in experimental studies.\[31\]

Fibroblasts are crucial for synthesizing collagen and other components in granulation tissue. PDGF and TGF-β are key growth factors regulating fibroblast activity. TGF-β, produced by platelets and macrophages, controls extracellular matrix deposition by stimulating gene transcription for matrix proteins and inhibiting matrix degradation enzymes. CTGF mediates many of TGF-β's effects on matrix synthesis.\[32\]

Fibroblasts are crucial players in the process of normal wound healing. A variety of extracellular matrix (ECM) constituents, including collagens, fibrin, fibronectin, proteoglycans, glycosaminoglycans, and matricellular proteins, can be viewed as powerful advocates for fibroblast survival, movement, and metabolism.\[33\] Skin's capacity to shield against harm depends on cells that safeguard its seamless structure and drive repair following injury. Cutaneous wound healing in adult mammals unfolds as a multifaceted journey involving stages like blood clotting, inflammation, re-epithelialization, granulation tissue formation, neovascularization, and remodeling. Epidermal renewal typically commences promptly post-injury, advancing over days until the epithelial layer fully recuperates through basement membrane restructuring. This intricate process hinges on diverse signaling cues and cellular interactions within the epidermis and surrounding tissues. Numerous elements, including growth factors, cytokines, matrix metalloproteinases, cellular receptors, and components of the extracellular matrix, play crucial roles in orchestrating regeneration. This exploration zooms in on how extracellular matrix proteins shape epidermal rejuvenation during the wound healing process.\[34\]

In pulmonary fibrosis, fibroblasts found in Masson bodies and fibroblastic foci demonstrate the presence of vimentin and alpha smooth muscle actin. The presence of actin filament bundles within a fibronectin-containing matrix indicates that fibroblast contractions likely play a role in lung remodeling.\[35\] Collagen remodeling continues for months after wound closure and the tensile strength of the repaired tissue increases to about 80–85% of normal tissue if all processes proceed without any perturbations.\[36\] NF-κB's role in macrophage signal transduction and polarization is particularly pertinent to wound healing. During the initial inflammatory phase, macrophages are recruited to the injury site where they release cytokines, chemokines, and growth factors, orchestrating the inflammatory response and tissue repair. NF-κB activation in macrophages regulates the expression of these molecules, influencing immune cell recruitment and pathogen clearance. Dysregulated NF-κB signaling can lead to prolonged inflammation and impaired wound healing, as observed in chronic wounds.\[37\] The Wnt/β-catenin pathway is like a conductor in the orchestra of wound healing, guiding inflammation, cell growth, and rebuilding the skin's supportive structure. Because of its importance and malfunctions in many diseases, scientists are looking at ways to use tiny molecules to activate this pathway as a
treatment. Over the past few years, promising small molecules have been discovered that can turn on Wnt/β-catenin in lab experiments. While we're still figuring out exactly how these activators work, some studies are pinpointing the proteins involved. However, despite the potential benefits, developing these Wnt activators into safe and specific drugs remains a challenge.[38]

**Dendritic Cells**

Dendritic cells, which include Langerhans cells in the epidermis, are crucial for kickstarting T-cell responses by presenting antigens. First identified by Paul Langerhans in the 1800s and later named dendritic cells by Ralph Steinman in 1973, these cells were initially thought to have neurological functions due to their shape. During skin infections, both Langerhans cells and dermal dendritic cells move to the lymph nodes draining the skin. Macrophages, on the other hand, act as scavengers, engulfing debris and pathogens, though their antigen-presenting abilities are not as potent as dendritic cells'. When dendritic cells encounter antigens, they display them to T cells in the dermis before migrating to lymph nodes, where they further activate T-cell responses. T cells play crucial roles in wound healing.[39]

**T Cells**

Human skin primarily contains αβ+ T cells in the dermis, while murine epidermis is mainly populated by γδ+ T cells, specifically known as dendritic epidermal T cells (DETCs) due to their unique morphology. DETCs originate in the fetal thymus and migrate to the epidermis, where they persist and slowly proliferate in response to interleukin signals, particularly IL-15, maintaining steady levels. Positioned in the basal layers of the epidermis, DETCs extend dendrites into the suprabasal layers, actively surveilling for signs of epidermal stress, like infections or abnormal cell presence. Unlike other skin T cells, DETCs are non-migratory. They are particularly relevant in wound healing research for several reasons: they are the only T cell subset capable of secreting cytokines and growth factors vital for keratinocytes and wound re-epithelialization; mice lacking DETCs show significant delays in wound closure; and DETCs possess a unique T-cell receptor, Vγ3Vδ1, exclusive to skin T cells.[40]

**Proliferative Phase**

Angiogenesis is regulated by chemical mediators like vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), along with the extracellular matrix, metabolic gradients, and physical forces. Chemical mediators promote endothelial cell migration, proliferation, and tube formation, while the extracellular matrix provides a scaffold for vessel development.[41] Angiogenesis, the growth of new capillaries from pre-existing blood vessels, is a complex process involving multiple cellular events resulting in neovascularization. It is essential in various physiological processes such as fetal development, tissue repair post-surgery or trauma, and is a hallmark of wound healing, the menstrual cycle, cancer, as well as ischemic and inflammatory diseases.[42] The recognition that tumor growth correlates with the formation of new blood vessels prompted investigations into the chemical factors that mediate angiogenesis, expanding our understanding of pathological processes and offering new avenues for disease diagnosis and treatment. Subsequently, the proteolysis of basement membrane matricellular components becomes essential to promote the invasion of ECs into the stroma of neighboring tissue. As migrated ECs advance, they initiate lumen formation, resulting in the development of a multicellular structure.[43]. During wound healing, angiogenic capillary sprouts infiltrate the fibrin/fibronectin-rich wound clot and organize into a microvascular network throughout the granulation tissue. As collagen accumulates to form scar tissue, the density of blood vessels decreases. Specific endothelial cell ECM receptors, particularly αvβ3, play a crucial role in morphogenetic changes in blood vessels during wound repair.[44] During the proliferative phase of wound healing, mechanical forces emerge as important regulators of cell and tissue function. Endothelial cells, critical for angiogenesis, exhibit proliferation in response to tissue stretch, while the mechanical properties of the environment dictate the direction and growth of capillary sprouting. Considering the vascular network's pivotal role in both physiological processes and diseases, the control of vascularity through mechanical forces presents promising avenues for innovative therapeutic strategies. This shows the potential for leveraging mechanical
Manipulation to influence vascular development and function, offering new opportunities for therapeutic intervention in various medical conditions during the proliferative phase of wound healing.[45] Angiogenesis is stimulated by local microenvironmental factors like low oxygen tension, low pH, and high lactate levels. Hypoxia-inducible factor (HIF) is a key transcription factor activated by low oxygen levels, promoting the transcription of genes like VEGF that promote angiogenesis. During the proliferative phase of wound healing, granulation tissue serves as an intermediary between the initial wound and eventual scar formation. It differs from normal dermis by exhibiting a dense network of blood vessels and capillaries, increased cellular density of fibroblasts and macrophages, and disorganized collagen fibers.[46] Rigorous characterization of dermal fibroblast heterogeneity is challenging, but distinct populations have been elucidated, with different functions and behaviors.[47]

**Epithelialization in Skin Wound Healing**

The formation of new epithelial tissue is essential for wound healing during the proliferation phase, as it involves the movement and growth of epithelial cells to seal the wound and reconstruct the protective layer of the skin.[48] Cytokines and growth factors play a crucial role in promoting the migration and growth of keratinocytes, which are important for the healing process of re-epithelialization. If not properly regulated, this process can result in the development of chronic wounds.[49] Epithelialization involves epithelial cell detachment, migration, proliferation, and differentiation. Growth factors such as EGF, KGF, and TGF-α encourage both migration and proliferation. Basal epithelial cells detach, flatten, and move over granulation tissue, multiplying around the edges of the wound. Leading edge cells produce MMPs to penetrate scab or necrotic tissue. Migration continues until epithelial cells form a confluent sheet, re-establishing stratified epidermal layers and barrier function. TGF-β accelerates epidermal maturation, and Intercellular desmosomes and attachments of hemi-desmosomes to the basement membrane are being restored.[50]

**Remodeling and Scar Formation Phase in Skin Wound Healing**

Remodelling is the last stage of healing, where granulation tissue matures into scar tissue, improving the strength of the tissue. During the turnover of collagen and extracellular matrix, there’s a notable reorganization and realignment taking place. As maturation advances, there’s a decline in cellular density and metabolic function.[51] Nonetheless, this is counterbalanced by alterations in collagen composition, quantity, and arrangement, leading to an improved tensile strength of the tissue. Initially, type III collagen is synthesized, but it undergoes a gradual substitution with type I collagen. While the tissue doesn't fully restore its original strength, it typically achieves around 80% of its normal strength within several months.[52]

**Molecular Mechanism of Wound Healing**

Restoring the skin barrier in both acute and chronic wounds requires intricate molecular mechanisms. These mechanisms coordinate cellular turnover, enzyme functions, and neurovascular responses. Genetic and epigenetic pathways are pivotal in orchestrating the complex processes involved in physiological wound healing.

**Genetic Background of Skin Repair**

Involves transcription-independent diffusible damage signals, individual variability, epigenetic mechanisms, controlled qualitative traits, post-translational modifications, antioxidants, nutrients, DNA modifications, bacterial activation, mitochondrial activity, and oxidative stress.

**Molecular Targets in Wound Healing**

Employing target-specific drugs aims to hinder molecular targets pivotal to the disease mechanism. Research traditionally focuses on molecular signaling pathways, immune cell responses, and epithelial cell activity during both acute and delayed wound healing processes. The primary objective behind employing target-specific drugs in wound healing is to hinder the molecular targets pivotal to the disease mechanism. Traditionally, research on wound healing medications has concentrated on molecular signaling pathways, immune cell responses, and the activity of epithelial cells during both acute and delayed wound healing processes. Fibroblasts, keratinocytes, immune cells, extracellular matrix, Cytokines, growth factors, reactive oxygen species, and an array of...
inflammatory mediators play important roles in the inflammatory reaction and repair processes during wound healing. Cellular processes in wound healing commence during the coagulation phase following injury. Platelets release soluble mediators such as PDGF, IGF-1, EGF, FGF, and TGF-β, which draw inflammatory cells to the injury site. Drugs that reduce bleeding time suggest a positive effect on blood vessel integrity or platelet involvement in forming the hemostatic plug.[53] Several drugs stimulate fibroblasts and keratinocytes, enhancing wound healing. Keratinocytes differentiate to form the skin's barrier function.[54]

Several signaling pathways and molecules regulate these cellular processes throughout the different phases of wound healing.

**Transforming Growth Factor-Beta (TGF-β)**

Scarring remains a persistent challenge in wound management and fibrotic disorders. Insights from the TGF-β superfamily offer potential intervention strategies. TGF-β3, in particular, stands out for its ability to promote scarless healing, holding promise for therapies aimed at reducing scarring and alleviating complications associated with fibrosis in both acute and chronic wounds. The TGF-β superfamily, integral to tissue repair, comprises various isoforms, each exerting different effects on wound healing that may vary depending on the context. While TGF-β1 is implicated in fibrosis in adult wounds, TGF-β3 has shown efficacy in promoting scarless healing during fetal development and reducing scarring in adults. Consequently, TGF-β3 emerges as a potential therapy for minimizing scarring in acute and chronic wounds as well as fibrotic disorders.[55]

**Platelet-Derived Growth Factor (PDGF)**

Particularly PDGF-BB, stimulates fibroblast Cellular Proliferation and Migration, promoting granulation tissue formation and accelerating collagen accumulation essential for tissue repair. PDGF-AA is less effective in this regard.[56]

**Epidermal Growth Factor (EGF) and Fibroblast Growth Factor (FGF)**

In cancer biology, the epidermal growth factor receptor (EGFR) shares similarities with the v-erbB oncogene. Although mutations akin to v-erbB are rare, EGFR overexpression is common in many cancers. EGFR's activation extends beyond EGF to include ligands like TGF-alpha and vaccinia virus growth factor, revealing its multifaceted roles in cellular transformation. Understanding EGFR's structural nuances is crucial for unraveling its diverse functions and regulatory pathways in both normal and pathological contexts. Hypoxia-inducible factor 1-alpha (HIF-1α) regulates angiogenesis in low-oxygen conditions at wound sites. The cyclometalated iridium(III) complex 1α enhances HIF-1α levels, leading to increased expression of genes linked to HIF-1α, such as Vascular Endothelial Growth Factor (VEGF) and Glucose Transporter 1 (GLUT1). This accelerates wound healing, particularly in diabetic wounds.[57] EGF and FGF-2 activate neural precursor cells in different brain areas, but their lineage connection remains uncertain. In E14 mouse striatum cultures, 12% of cells responded to FGF-2, consisting of 75% neurons and 25% nestin-positive precursors. Over six days, cells responsive to both EGF and FGF-2 emerged, suggesting FGF-2 primes cells for EGF sensitivity during development.[58] Epidermal keratinocytes, crucial for skin health, respond to growth factors like EGF and FGF by promoting proliferation, while TGF-β and Vitamin D inhibit it. These cells play roles in immune responses and inflammation, impacting various skin conditions.

**Medicinal Plants with Significant Wound Healing Activity**

Traditional herbal medicines are widely embraced globally, offering accessible and culturally embedded primary healthcare solutions at low costs. Despite their effectiveness in managing various health issues, there's a pressing need for standardization to ensure consistent quality and efficacy. In wound care, conventional methods like disinfection, debridement, and creating a moist healing environment prevail. These practices, rooted in herbal wisdom, have demonstrated effectiveness in treating cuts, wounds, and burns, emphasizing the importance of traditional herbal medicine in healthcare.[59-60]

*Arctium lappa. (Burdock)*

The research investigated the healing properties of burdock leaf extract on skin lesions in rats. Extracted using hydroethanolic methods, the extract underwent analysis for proteins, phenols, antioxidants, and other phytochemicals. Incorporated into a gel for application on rat
wounds, the extract revealed the presence of proteins, phenols, phenolic compounds, and antioxidants. Rats treated with the burdock extract gel displayed improved wound healing compared to both control and fibrinase-treated groups. These findings suggest the potential of burdock extract as a herbal remedy for skin healing, likely due to its antioxidant properties.\[61\]

*Astragalus propinquus (Astragalus, Huang Qi) and Rehmannia glutinosa (Chinese Foxglove, Di Huang)*

These roots, commonly utilized in Traditional Chinese Medicine (TCM), have shown considerable promise in expediting wound healing, especially in diabetic rats. Researchers have observed that extracts derived from these roots can enhance the development of new blood vessels and reduce tissue damage caused by harmful molecules. Additionally, they seem to activate a cellular pathway that encourages the production of new skin components. This discovery could have significant implications for the treatment of diabetic foot ulcers and similar conditions.\[62\]

*Ampelopsis japonica (Japanese Ampelopsis)*

Researchers conducted an investigation into the influence of varying geographical regions and altitudes on the antioxidant capacity and polyphenolic composition of Ampelopsis grossedentata, commonly referred to as vine tea—a revered botanical indigenous to southwestern China. Their meticulous analysis revealed notable disparities in the chemical composition of vine tea across different locales and altitudes. These not only shed light on the nuanced intricacies of vine tea but also provide valuable insights into the ways in which geographical factors and elevation can modulate its biochemical properties.\[63\]

*Andrographis paniculata (King of Bitters, Kalmegh)*

Andrographis paniculata, commonly known as green chiretta, has been a traditional remedy for fever, infections, wounds, and various other ailments in China, India, and Southeast Asian countries. Extracts derived from A. paniculata demonstrate a wide range of pharmacological activities, including antioxidant, anti-inflammatory, antidiabetic, anticancer, antimicrobial, antiviral, antimalarial, hypotensive, immunostimulatory, and hepatoprotective effects. In rat studies, wound closure was significantly improved following treatment with a 10% aqueous leaf extract of A. paniculata. This treatment led to decreased inflammation and scarring, along with increased angiogenesis and collagen fiber formation in healed wounds. Andrographolide, a compound isolated from A. paniculata leaves, has been clinically evaluated and shown positive effects on autoimmune disorders.\[64\]

*Angelica sinensis (Dong Quai)*

Angelicae Sinensis Radix (ASR), sourced from the root of Angelica sinensis, is a fragrant perennial herb indigenous to China, Japan, and Korea. Within traditional Chinese medicine (TCM), it holds esteemed status for its acclaimed abilities to replenish blood, boost vitality, alleviate discomfort, and promote intestinal hydration. A wealth of literature showcases the isolation of numerous chemical components from ASR, spurring both preclinical and clinical inquiries into their therapeutic significance.\[65\] Angelica sinensis, commonly known as Dong Quai or female ginseng, contains various bioactive compounds including polysaccharides, ligustilide, ferulic acid, essential oils, coumarins, and flavonoids. These constituents contribute to its medicinal properties such as immunomodulation, anti-inflammatory effects, neuroprotection, and antioxidant activity, making it a valuable herb in traditional Chinese medicine.\[66\] Danggui, or Angelica sinensis (Oliv.) Diels from the Apiaceae family, has a rich history in Chinese medicine, particularly for treating menstrual disorders. Over 70 compounds have been extracted and characterized from Danggui, with notable examples including ferulic acid, Z-ligustilide, and n-butylidenephthalide. These components show diverse biological activities, ranging from anti-inflammatory and anti-cancer properties to neuroprotective effects.\[67\]

*Blumea balsamifera (Ngai camphor, Sambong)*

Blumea balsamifera, also referred to as sambong, holds a place in traditional medicine across Southeast Asia due to its healing properties, especially in wound care. Extracts from this plant are known to accelerate the healing process of skin wounds by promoting the regeneration of capillaries, collagen deposition, granular tissue formation, and wound contraction. Moreover,
sambong demonstrates various additional bioactivities, such as anti-tumor, hepatoprotective, antioxidant, antimicrobial, and anti-inflammatory effects.[68]

**Boswellia sacra (Frankincense)**

The study evaluated the antimicrobial and wound-healing properties of various concentrations of BC extract and its combination with penicillin–streptomycin. Antimicrobial activity was assessed using agar well diffusion, while wound healing was evaluated using an infected wound model in albino rabbits.[69]

**Calendula officinalis**

Calendula flower extracts were studied for their impact on different phases of wound healing, including inflammation, tissue formation, and granulation tissue formation. Calendula officinalis, commonly known as pot marigold, is highly regarded for its versatility in treating various skin conditions, thanks to its array of properties such as anti-inflammatory, antioxidant, antibacterial, antiviral, antifungal, and anticancer effects. It facilitates fibroblast migration and proliferation through PI3K-dependent mechanisms. In mice with excisional wounds, Calendula enhances granulation tissue formation by modulating the expression of CTGF and α-SMA. Moreover, it stimulates angiogenesis, demonstrated in studies using chicken chorioallantoic membrane and rat cutaneous wound healing models.[70]

**Camellia sinensis (Tea plant)**

Topical application of Camellia sinensis extract accelerated wound healing by enhancing fibroblast growth and collagen synthesis while reducing inflammation duration.[71] Studies consistently show that green tea extract, particularly its compound epigallocatechin-3-gallate (EGCG), can prevent skin tumor formation and has anti-inflammatory effects. In mouse skin models, EGCG has successfully countered the oxidative stress and immune suppression induced by UVB radiation. While human studies are limited, there is a growing interest among cosmetic and pharmaceutical companies in incorporating green tea extracts into skincare products. EGCG has been found to stimulate the proliferation and differentiation of keratinocytes, reduce scar formation by influencing TGF-β signaling, and inhibit keloid growth by suppressing STAT3 signaling. Additionally, extracts from Camellia sinensis, the plant source of green tea, have been shown to increase fibroblast proliferation and collagen synthesis, promoting wound healing and angiogenesis in various animal models, including those with diabetes.[72]

**Carthamus tinctorius (Safflower)**

Safflower, one of the earliest cultivated crops, has a long history of traditional cultivation on a small scale. Every part of this plant serves multiple purposes, including oil production, culinary uses, flavoring, coloring, dyeing, and medicinal applications. Safflower is known for its ability to thrive in conditions of salinity and drought. Various methods, from mechanical to supercritical fluid extraction, are used to extract oil from safflower seeds. The resulting oil is notably high in oleic and linoleic acids. Safflower is valued for its functional benefits, which include its use in treating conditions such as atherosclerosis, menopausal symptoms, skin infections, and bone-related disorders.[73]

**Celosia argentea (Cockscomb)**

The wound healing efficacy of an alcohol extract of *C. argentea* formulated in a 10% w/w ointment was evaluated using a rat burn wound model. Results confirmed the positive effect of the *C. argentea* extract on wound healing, possibly due to its ability to promote the proliferation and migration of dermal fibroblasts. *C. argentea* is recognized as one of the medicinal plants with wound healing properties in India, along with others like *Aloe vera*, *Azadirachta indica*, *Carica papaya*, *Cinnamomum zeylanicum*, *Curcuma longa*, *Ocimum sanctum*, and *Nelumbo nucifera*.[74]

**Centella asiatica (Gotu Kola, Indian Pennywort)**

Centella asiatica, commonly known as Asiatic pennywort, has been used for centuries to aid wound healing. Extracts from *Centella asiatica* enhance the healing of chronic ulcers and acute radiation dermatitis wounds in animal models. Asiaticoside, a compound isolated from *Centella asiatica*, boosts collagen deposition and epithelialization. Triterpenes from *Centella asiatica* enhance collagen remodeling and glycosaminoglycan synthesis. Madecassoside from *Centella asiatica* promotes collagen synthesis and angiogenesis when orally administered in animal wound models.[75]
**Cinnamomum cassia (Chinese Cinnamon)**

Cinnamomum cassia, commonly used as a spice, has various medicinal properties. It is part of the Shexiang Baoxin pill, used for chest pain and coronary artery disease. Cinnamomum cassia demonstrates anti-inflammatory, anticancer, and antidiabetic activities. Cinnamaldehyde, a bioactive compound in Cinnamomum cassia, acts as an insecticide, antimicrobial, and neuroprotective agent. It activates signaling pathways like PI3K/AKT and MAPK, increases VEGF expression, and promotes angiogenesis. Additionally, cinnamaldehyde improves wound healing in zebrafish.\[76\]

**Leptadenia pyrotechnica (Forsk) Decne**

The stem and root of Leptadenia pyrotechnica (Forsk) Decne, commonly referred to as "Jivanti" or "Dodi," have been subject to pharmacognostical and quality control analysis. This plant, belonging to the Asclepiadaceae family, has a history of traditional use in various medicinal applications, including potential wound healing properties. While specific scientific studies focusing on its wound healing effects may be limited, its traditional use suggests it may contain compounds beneficial for this purpose. Leptadenia pyrotechnica is believed to possess anti-inflammatory, antimicrobial, and antioxidant properties, which are often associated with promoting tissue repair and reducing inflammation, both essential components of wound healing.\[77\]

**Daphne genkwa (Lilac Daphne)**

A traditional Chinese herb, Daphne genkwa, boasts a long history for pain relief and coughs. But its potential goes beyond that. Recent research suggests extracts from its flowers might speed up wound healing. These extracts seem to influence skin cell activity (fibroblasts) and collagen production, both essential for repair. This exciting discovery adds to Daphne genkwa's diverse properties, including anti-inflammatory and skin-lightening effects.\[78\]

**Ganoderma lucidum**

Ganoderma lucidum, known as “the mushroom of immortality,” is used in Traditional Chinese Medicine to enhance the immune system. Research suggests it can modulate the immune system, reduce inflammation, fight infections, protect the heart and blood vessels, and even lower cholesterol levels. Clinical studies show promise for its use in reducing tumors, viral loads, and high blood pressure. Interestingly, extracts from Ganoderma lucidum rich in polysaccharides have been linked to improved wound healing in diabetic rats. This effect may be due to the mushroom's ability to stimulate the growth and movement of skin cells, promote new blood vessel formation, and reduce cell damage caused by free radicals. Some researchers believe these benefits might be connected to Ganoderma lucidum's established ability to strengthen the body's antibody-based immune response.\[79\]

**Ligusticum striatum (Szechuan Lovage)**

Ligusticum striatum, a rootstock used in Traditional Chinese Medicine (TCM), has a long history of promoting heart and brain health. It's commonly used for problems like blood flow issues, menstrual irregularities, and headaches. This versatile herb contains over 170 identified compounds, with phthalide lactones and alkaloids being the most prominent and thought to be responsible for its medicinal effects. Interestingly, recent studies suggest that essential oils extracted from Ligusticum striatum may help prevent scar formation on the skin.\[80\]

**Lonicera japonica (Japanese Honeysuckle)**

Honeysuckle (Lonicera japonica) boasts a long history of use in traditional Asian medicine for treating infections. Research conducted in the 1980s revealed a range of potential benefits in the plant, including fighting microbes, inflammation, fever, and free radicals. It also showed promise against cancer, liver damage, and high cholesterol. More recent studies suggest that extracts from the flowering parts of honeysuckle, specifically those made with ethanol, can aid various stages of wound healing on the skin. These stages include the formation of new skin cells (reepithelization), the growth of new blood vessels (angiogenesis), the development of granulation tissue (important for wound repair), and wound contraction. It's important to note, however, that consuming high doses of honeysuckle may lead to neurological issues.\[81\]

**Paeonia suffruticosa (Tree Peony)**
Paeonia suffruticosa, known as moutan peony, boasts over 1000 distinct cultivars developed over millennia. Its root bark is a rich source of bioactive compounds for traditional Chinese medicine. Pharmacological studies reveal its antioxidant, neuroprotective, antitumor, anti-inflammatory, and antidiabetic properties. Commonly used for cracked skin, the dried root of Paeonia suffruticosa aids healing and relieves pain. In vitro studies demonstrate its ability, at low concentrations ($\leq 10 \mu g/mL$), to enhance the viability and proliferation of human primary dermal fibroblasts and HaCaT keratinocytes, suggesting its potential for wound healing therapy.[82]

**Panax ginseng (Asian Ginseng)**

Ginseng, a popular herb in Eastern medicine, boasts an impressive range of benefits. It's known for improving memory, boosting immunity, and fighting fatigue. Studies even suggest it can combat depression and chronic fatigue. But ginseng's talents extend beyond the brain. The root extracts can shield skin from sun damage and speed up wound healing. In lab tests, ginseng extracts helped skin cells move and multiply, while also boosting collagen production, a key component for healthy skin. One specific compound in ginseng, Ginsenoside Rb2, even appears to promote the formation of the skin's outer layer, further aiding wound healing.[83]

**Cordia dichotoma Linn.**

Cordia dichotoma Linn. bark may have potential relevance to wound management. In traditional medicine systems, including Ayurveda, this plant has been utilized for various medicinal purposes. Cordia dichotoma, a tree native to tropical and subtropical regions like India and Nepal, is rich in essential phytoconstituents such as carbohydrates, alkaloids, glycosides, flavonoids, tannins, and saponins found in its leaves, roots, seeds, bark, and fruit. Studies have shown its diverse pharmacological activities, including immunomodulatory, antidiabetic, anthelminthic, antulcer, antilarvicidal, and hepatoprotective effects, making it promising for medicinal use.[84]

**Lithospermum erythrorhizon (Purple Gromwell)**

A plant native to northeast China called Lithospermum erythrorhizon has some interesting properties that could be useful for medicine. The root extracts have anti-inflammatory, antibacterial, and even anti-cancer effects. One specific compound, shikonin, can actually kill cancer cells and prevent scar tissue from forming excessively. Another compound, arnebin-1, seems to work well with the body's natural healing signals to improve wound healing in diabetic rats.[85]

**Salvia miltiorrhiza (Chinese Sage, Danshen)**

Salvia miltiorrhiza, or red sage, is prized in traditional Chinese medicine for its root, known for treating cerebrovascular and cardiovascular diseases. Extracted salvianolic acids possess potent antioxidative, hepatoprotective, neuroprotective, antimicrobial, anti-inflammatory, and anticaner properties. These acids promote cardiac angiogenesis, inhibit ischemia, and hypoxia, offering cardiovascular protection. A certain wound healing tea made with water-soluble extracts seems to speed up healing by helping skin cells multiply and build collagen, a key building block for healthy skin. Conversely, cryptotanshinone from Salvia miltiorrhiza ameliorates fibrosis and scarring by downregulating collagen expression and reducing scar-derived fibroblast migration and contraction.[86]

**Portulaca oleracea**

Groups administered with POL extract showed enhanced wound healing have increased formation of new blood vessels, collagen deposition, and re-epithelization, along with reduced iron accumulation and inflammatory infiltration. Our findings indicate that POL extract promotes muscle repair following ischemia–reperfusion injury, underscoring its potential in diabetic foot ulcer (DFU) treatment.[87]

**Angelosorba officinalis (Common Burnet)**

Great burnet (Sanguisorba officinalis), a native of cool climates in Asia, Europe, and North America (and part of the rose family!), has some impressive hidden talents. The roots of this plant pack a punch with various health benefits. They can potentially stop bleeding, fight free radicals, regulate the immune system, reduce inflammation, and even combat allergies. Traditionally used to manage bleeding disorders and treat various skin conditions, including burns, allergic dermatitis, and eczema, Sanguisorba officinalis root extracts have been found to suppress mast cell degranulation and
inhibit inflammatory pathways. In mouse studies, polysaccharides from Sanguisorba officinalis promoted wound healing by enhancing wound contraction, reepithelization, collagen synthesis, and angiogenesis, while also increasing levels of IL-1β and VEGF.88

**Drypetes Roxburghii Leaves**

Plants from the Drypetes genus, belonging to the Putranjivaceae family, play a significant role in traditional medicine across Sub-Saharan Africa and Asia. They are renowned for their versatility in treating a broad range of ailments, spanning dysentery, gonorrhea, malaria, rheumatism, sinusitis, and tumors. Additionally, Drypetes plants are highly valued for their effectiveness in wound healing, headache relief, managing urethral problems, and reducing fever in children. Certain species of Drypetes are also utilized for food preservation against pests and serve various purposes such as aphrodisiacs, stimulants or depressants, rodenticides, and fish poisons. Furthermore, they provide protection against insect bites, aid in conception, and are esteemed for their general healing properties. The widespread and diverse utilization of Drypetes plants underscores their profound significance in traditional healing practices across different cultures.89

**Stemona tuberosa (Baibu)**

Stemona tuberosa, a key herb in Traditional Chinese Medicine, is renowned for its insecticidal properties and used to treat impetigo, scabies, and lice. It's also a mosquito repellent and insect infestation deterrent for stored cereals. Compounds from its root exhibit anti-inflammatory, antibacterial effects, while promoting wound healing.90

**Wedelia trilobata (Creeping Oxeye)**

A tropical plant called Wedelia trilobata, also known as Sphagnetica trilobata, has been used in traditional medicine for a long time, particularly for wound healing and joint pain. Although it can be invasive in some areas, this plant holds promise for modern medicine too. Compounds found in its leaves, like luteolin, have been shown to protect brain cells, fight cancer, and reduce inflammation. Interestingly, luteolin also seems to help wound healing by promoting the growth and movement of the skin cells involved in repair.91

**Zanthoxylum bungeanum (Sichuan Pepper)**

Zanthoxylum bungeanum, known as Sichuan pepper, is valued for its culinary and medicinal properties. Rich in various compounds, it exhibits diverse biological effects such as analgesic, anticancer, antioxidant, and anti-inflammatory properties. Traditionally used for pain relief, it's also employed in Traditional Chinese Medicine for skin infections, wound healing, acne, and eczema.92

**Costus speciosus**

Costus speciosus, recognized for its medicinal and ornamental value, demonstrates a diverse range of pharmacological activities, including antibacterial, antifungal, antioxidant, anti-inflammatory, analgesic, and antipyretic effects. Its rhizomes exhibit bitter, astringent, and cooling properties, and are revered for their aphrodisiac, purgative, and febrifuge qualities. Historically, these rhizomes have been utilized to address various ailments such as pneumonia, rheumatism, urinary diseases, and jaundice, while the leaves have been employed in managing mental disorders. However, due to excessive utilization and insufficient propagation methods, Costus speciosus is now categorized as a threatened plant species, facing the peril of extinction. Consequently, there is a pressing need for conservation efforts, with biotechnological methods like tissue culture emerging as promising solutions to safeguard its genetic diversity.93

**Haworthiopsis limifolia (Fairies Washboard)**

Haworthiopsis limifolia previously classified under Haworthia, belongs to the Asphodelaceae family. It shares morphological traits with Aloe species and is used as a spiritual remedy and treatment for various ailments.94 Ethnopharmacological studies confirm its traditional use by different ethnic groups for treating coughs, skin rashes, burns, and other conditions.95

**Zantedeschia aethiopica**

Zantedeschia aethiopica, commonly known as the "white arum lily," is a South African aquatic plant with a distinctive white spathe. While traditional uses are documented, scientific research on its biological activity is limited. It exhibits pharmacological properties like antibacterial, antifungal, antithrombotic, and anticoagulant
effects, although its chemical profile is not fully characterized.\[96\]

**Herbal Medicine: Natural Alternative for Health and Food Preservation**

There's a growing interest in exploring the efficacy of plants in traditional medicine due to their affordability and minimal side effects. Synthetic preservatives, commonly used in food, pose health and environmental risks. Spices and herbs like garlic, cinnamon, and ginger are replacing synthetic preservatives, offering natural, effective, and non-toxic alternatives. Despite their increasing popularity, herbal medicines lack regulation for purity and potency, posing potential risks to consumers. Herbal therapeutics are integral to global primary healthcare, offering accessible and cost-effective solutions rooted in cultural beliefs. While herbal remedies are popular due to their affordability and availability, their standardization and quality control remain a concern. Despite their potential in treating various illnesses, including ulcers, wound healing, and skin infections, caution is necessary as some herbal medicines can be toxic or interact negatively with synthetic drugs. Consulting healthcare professionals before use is advised.

**Table 1: Medicinal Plants Having Wound Healing Activity**

<table>
<thead>
<tr>
<th>Botanical Name</th>
<th>Family</th>
<th>Use</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirsium sinense CBC</td>
<td>Asteraceae</td>
<td>Root crushed and applied as a poultice for wound treatment</td>
<td>97</td>
</tr>
<tr>
<td>Cirsium veratum</td>
<td>Asteraceae</td>
<td>Application of root paste directly to wounds, similar to this method.</td>
<td>98</td>
</tr>
<tr>
<td>Cissampelo s pareira</td>
<td>Menispermaeae</td>
<td>Topical application of leaf extract for external use</td>
<td>99</td>
</tr>
<tr>
<td>Cleome viscosa L.</td>
<td>Cleomaceae</td>
<td>Topical application of leaf paste directly on wounds</td>
<td>100</td>
</tr>
<tr>
<td>Combretum</td>
<td>Combretaceae</td>
<td>Wounds and cuts treated with the</td>
<td>101</td>
</tr>
<tr>
<td>flagrocarpus m</td>
<td>application of leaf juice.</td>
<td></td>
<td>102</td>
</tr>
<tr>
<td>Datura stramonium m L.</td>
<td>Solanaceae</td>
<td>Leaf latex applied to wounds</td>
<td>103</td>
</tr>
<tr>
<td>Daucus carota L.</td>
<td>Apiaceae</td>
<td>Root juice used topically on wounds</td>
<td>104</td>
</tr>
<tr>
<td>Dendrophth hoe falcata L.f.</td>
<td>Loranthacea e</td>
<td>Leaf and stem paste applied to heal wounds</td>
<td>105</td>
</tr>
<tr>
<td>Diotacanth us albiflorus</td>
<td>Acanthaceae</td>
<td>Leaf paste applied topically to heal wounds</td>
<td>106</td>
</tr>
<tr>
<td>Dodonaea viscosa Linn.</td>
<td>Sapindaceae</td>
<td>Leaf paste with albumin applied as plaster</td>
<td>107</td>
</tr>
<tr>
<td>Dumasia villosa DC.</td>
<td>Fabaceae</td>
<td>Whole plant parts used to wash wounds</td>
<td>108</td>
</tr>
<tr>
<td>Eupatorium odoratum L.</td>
<td>Asteraceae</td>
<td>Leaf applied to wounds and cuts</td>
<td>109</td>
</tr>
<tr>
<td>Euphorbia antiquorum L.</td>
<td>Euphorbiaceae</td>
<td>Stem latex applied on burn injury</td>
<td>110</td>
</tr>
<tr>
<td>Euphorbia pilosa</td>
<td>Euphorbiaceae</td>
<td>Plant latex applied locally</td>
<td>111</td>
</tr>
<tr>
<td>Ficus religiosa L.</td>
<td>Moraceae</td>
<td>Bark extract applied on wounds</td>
<td>112</td>
</tr>
<tr>
<td>Gelsemium elegans</td>
<td>Loganiaceae</td>
<td>Leaf juice applied to wounds and cuts</td>
<td>113</td>
</tr>
<tr>
<td>Ixora coccinia L.</td>
<td>Rubiaceae</td>
<td>Flower decoction applied to heal wounds</td>
<td>114</td>
</tr>
<tr>
<td>Jatropha gossypifol a L.</td>
<td>Euphorbiaceae</td>
<td>Plant resin used to heal wounds</td>
<td>115</td>
</tr>
<tr>
<td>Jatropha curcas L.</td>
<td>Euphorbiaceae</td>
<td>Bark exudate applied on wounds</td>
<td>116</td>
</tr>
<tr>
<td>Melastoma malabathric um</td>
<td>Melastomat aceae</td>
<td>Bark and juice paste applied to wounds</td>
<td>117</td>
</tr>
<tr>
<td>Mentha viridis L.</td>
<td>Lamiaceae</td>
<td>Leaf paste applied on wounds</td>
<td>118</td>
</tr>
<tr>
<td>Mikania micrantha HBK</td>
<td>Asteraceae</td>
<td>Leaf juice applied to wounds and cuts</td>
<td>119</td>
</tr>
</tbody>
</table>
CONCLUSION

Wound healing is a complex process that involves several interrelated phases, each crucial for the restoration of tissue integrity. At the outset, inflammation sets in, initiating the body's response to injury. This phase is marked by the influx of immune cells, which not only combat pathogens but also orchestrate subsequent healing events. As inflammation subsides, granulation tissue formation commences. This stage is characterized by the proliferation of endothelial cells, which sprout new blood vessels, ensuring adequate oxygen and nutrient supply to the healing site. Simultaneously, connective tissue cells contribute to the synthesis of extracellular matrices, including collagen, laying down the framework for tissue regeneration. Integral to these processes are proteoglycans and glycosaminoglycans (GAGs), essential components of the extracellular matrix. These molecules provide structural support and regulate cellular activities critical for wound repair. Moreover, their interactions with various binding proteins modulate biological functions vital for tissue regeneration.

Traditional remedies, often derived from medicinal plants, have long been recognized for their wound healing properties. Tribal communities, in particular, have relied on these natural remedies for generations, attesting to their efficacy. By compiling evidence of the therapeutic benefits of medicinal plants, this review underscores their importance in promoting wound healing. Ultimately, further research is required to unlock the full potential of medicinal plants in treating wounds, offering hope for improved healthcare outcomes.

Conflicts of Interest: The authors declare that there are no conflicts of interest.

Acknowledgement: NA

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