REVIEW PAPER

# A Comprehensive Review of Medicinal Plants and their bioactive as Sources of Wound Healing Agents: Mechanism of Action, Recent Developments and Future Perspectives

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***ABSTRACT***

Cutaneous wound healing is a complicated and highly regulated biological mechanism that restores the skin's functional and structural integrity after an injury. It represents a series of various phases: haemostasis, proliferation, inflammation and remodelling. Disruption of any of the mentioned phases can impair tissue repair, resulting in persistent, non-healing wounds that present serious economic and therapeutic difficulties. Although conventional wound-care therapies have improved patient outcomes, their effectiveness may be limited by factors such as antimicrobial resistance, adverse effects, high treatment costs, and delayed tissue regeneration. Consequently, there is increasing interest in plants with therapeutic benefits and their bioactive compounds as safer, cost-effective, and multifunctional alternatives for wound management. Medicinal herbs have long been used in traditional medicine systems globally, and growing scientific evidence supports their therapeutic potential in promoting wound healing. Flavonoids, phenolic acids, alkaloids, terpenoids, tannins, saponins, glycosides, and essential oils are examples of plant-derived bioactive chemicals that display a variety of pharmacological actions, including angiogenic, antibacterial, anti-inflammatory, antioxidant, and collagen-stimulating properties. These phytochemicals contribute to wound repair by key modulation of molecular pathways, including the upregulation of VEGF (vascular endothelial growth factor) and TGF-β (Transforming Growth Factor-β), thereby enhancing angiogenesis, fibroblast proliferation, extracellular matrix deposition, collagen synthesis, and re-epithelialization. In addition, many herbal compounds suppress pro-inflammatory mediators, including TNF-α (Tumour Necrosis Factor-α), IL-1β (interleukin-1β), and iNOS (inducible nitric oxide synthase), thereby reducing oxidative stress and creating a favourable environment for tissue regeneration.

This review summarises an overview of medicinal herbs with their bioactive constituents as promising wound-healing agents. It summarises the biological mechanisms underlying wound repair and highlights the therapeutic potential of plant-derived compounds. Furthermore, the review addresses current challenges, available preclinical and clinical evidence, and future research directions required for the successful translation of these natural products into evidence-based wound management. Collectively, the available literature suggests that medicinal plants represent a valuable source of multifunctional bioactive molecules with considerable potential for the development of safe, effective, and innovative wound-healing therapies.

**Key words:** Bioactive, herbal Hydrogels, phytochemicals, tissue regeneration, wound healing activity

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## 1. INTRODUCTION

Skin is the largest organ as well as an essential component of body functioning as the first line of protection against environmental threats [1]. By acting as a nutritional store, a defensive mechanism and a reaction to harm, this organ is essential to maintain homeostasis [2]. It responds to trauma and shields beneath structures like bones, internal organs, muscles, and ligaments. When a chemical, mechanical, or physical factor compromises the integrity of the skin, wounds result [3]. The body starts the wound healing process in reaction to injury in order to restore homeostasis and return to normal functionality [4]. Numerous cell types, including platelets, macrophages, fibroblasts, epithelial cells, endothelial cells, extracellular matrix components, cytokines, growth factors, and regulatory chemicals, are involved in the wound healing process [5]. Hemostasis, inflammation, proliferation and remodelling are the four continuous and coordinated stages of this process [6]. Chronic wounds fail to heal within the typical 7–10 days required for acute wounds because the healing process is prolonged, disorganised, and often interrupted by persistent inflammation and impaired tissue repair [7]. Underlying illnesses, persistent inflammation, infection, and oxidative stress brought on by age and medication use are all factors that contribute to wound chronicity [4,7].

The skin's anatomical structure and its underlying tissues are disrupted by a wound. Wounds can occur as a result of both accidental and intentional injuries. Accidental wounds are commonly caused by falls, animal bites, road traffic accidents, and other traumatic events, whereas intentional wounds are created during surgical procedures or other planned medical interventions [3]. Damage to the skin barrier increases the risk of infection and delays recovery by making it easier for bacteria and other materials to infiltrate [7]. Patients and healthcare systems around the world are significantly burdened by untreated or poorly healing wounds [8,9].

Chronic wounds are recognized as a severe health concern globally due to their prolonged healing time and substantial impact on patients' lives [10]. In wealthy nations, between 1% and 2% of people have persistent wounds at any given time; this percentage is expected to rise as a result of changing demographics and an increase in comorbidities [11]. DFUs (Diabetic foot ulcers), wounds associated with PAD (peripheral artery disease), VLUs (venous leg ulcers), PIs (pressure injuries), and AHHW (atypical hard-to-heal wounds) are the common classifications for chronic wounds, which can have a variety of causes [11,12].

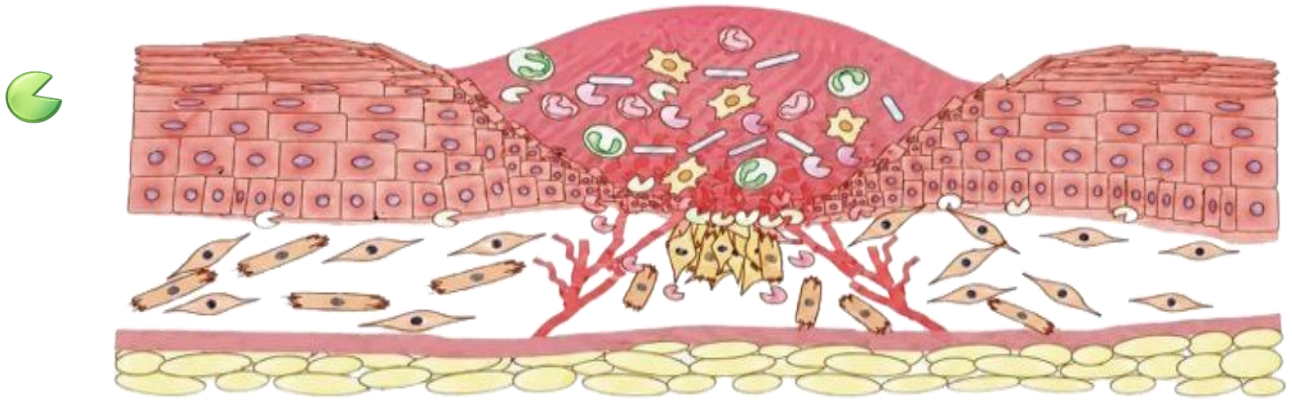
The epidemiological landscape of wounds in India represents a complex public health challenge, heavily influenced by regional socioeconomic disparities, shifting health literacy, and a steep rise in metabolic comorbidities. Because India lacks a centralized national wound registry, historical understanding has relied on localized, small-scale hospital audits or early regional surveys [13].

An early, seminal community-based epidemiological study established a baseline wound prevalence of 15.03 per 1,000 population [13]. More recent cross-sectional data indicate a lower but highly concentrated chronic wound prevalence of 1.89 per 1,000 population in selected districts [14]. This reduction is clinically attributed to an increased transition from unmonitored home remedies to supervised clinical care [14]. The burden of chronic non-healing wounds displays a marked geographic disparity. The prevalence in rural communities is significantly higher (approximately 2.64 per 1,000 population) than in urban areas (approximately 1.57 per 1,000 population) [14]. This variance is driven by occupational exposures (such as manual agricultural labour), lower health literacy, delayed medical consultation and restricted access to advanced wound care facilities [13,14]. The demographic distribution shows a distinctive gender bias, particularly in lower-extremity wounds. In several Indian cohorts, male patients comprise the vast majority, frequently reaching up to 80% of documented chronic wound cases [15]. The mean age of presentation consistently spans the most economically active years, typically between 30 and 59 years of age 16. The underlying causes of chronic, non-healing wounds in India differ significantly from those in Western nations. While vascular insufficiency (specifically venous stasis) is the primary cause in many developed countries, the Indian etiological profile is dominated by metabolic complications and neglected trauma 17].

## 2. WOUNDS CATEGORIZATION

### *2.1 Acute Wound*

Acute wounds include superficial mechanical injuries from burns or trauma, as well as clean penetrating wounds from knife cuts or surgical incisions. In a short duration of time, tissue damage from such wounds typically heals with little scarring [18]. The healing mechanism can be enhanced by providing appropriate wound care, such as the use of advanced dressings and therapeutic agents, which create a favourable environment for tissue repair and regeneration [3]. Pathogens that might worsen the wound and turn it into a persistent one must be avoided [7]. Typical wound site haemorrhage, redness, oedema, and pus production are all signs of an acute wound [5]. However, each patient may experience acute wound symptoms differently [6]. For example, a diabetic patient's wound healing mechanism is hampered by autonomic and sensory neuropathy, hypoxia, micro- and macro-circulatory dysfunction, hyperglycemia, and chronic inflammation [19]. Patients with venous or arterial illness, on the other hand, have wounds that heal far more slowly. It is very likely that inadequacy of the calf muscle pump and venous valve incompetence will cause recurrence. Venous stasis, hypertension, and tissue ischemia may result from these issues (Figure 1)[20]



| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | MMP-1 | | MMP-9 | | Macrophage | | Distinct Stroma Cell |
| | MMP-2 | | MMP-10 | | Neutrophil | | E. coli |
| | MMP-3 | | MMP-12 | | Monocyte | | S. aureus |
| | MMP-8 | | MMP-13 | | Fibroblast | | P. aerginosa |

**Figure 1. S**chematic representation of an acute wound

### *2.2 Chronic Wound*

Because the inflammatory, proliferative and remodelling phases overlap, Chronic wounds are those that do not heal through the normal healing process [7,12]. According to statistics, 30% of persistent wounds take a month to heal due to the location of the wounds or consequences from illnesses or infections [12]. Comparatively, the structure of chronic wounds (**Figure 2**) has more colonies of bacteria, which can result in various infections [21]. Additionally, with chronic wounds, there is no gradual healing and the inflammatory period is protracted. Neuropathy and poor circulation lead to unresolved inflammation, infection risk, and loss of protective sensation and are considered factors that contribute to this[19,12]. At this point, the physiological and inflammatory responses are still declining, which has a significant effect on collagen synthesis and basement membrane degradation [6,12]. Among other things, unchecked protease activity in chronic wounds causes defects in the epithelial layer, which encourages bacterial colonisation [23].In actuality, bacterial colonisation is a defining feature of persistent wounds and presents a remarkable challenge to wound healing[24]



| | | | | | | | |
|---|---|---|---|---|---|---|---|
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**Figure 2.** Schematic representation of an acute wound

## 3. WOUND HEALING PHASES

The biological mechanism of healing, which repairs damaged tissues' integrity and functionality, is tightly controlled. Haemostasis, inflammation, proliferation and remodelling (maturation) are the four separate but related phases that comprise a series of overlapping cellular and molecular activities. The coordinated action of platelets, fibroblasts, inflammatory cells, endothelial cells, keratinocytes, cytokines, and growth factors ensures successful tissue repair. Disruption of these phases may result in delayed recovery or chronic wound formation [4,25]. The timeline of several phases of wound healing is depicted in **Figure 3**.

### *3.1 Hemostasis Phase*

The goal of the haemostatic phase, which starts right after damage, is to stop blood loss. Constriction of vessels and platelet activation are the results of blood vessel damage. PDGF (Platelet-derived growth factor), TGF-β (transforming growth factor-beta) and EGF (epidermal growth factor) are released by platelet activation and stick to exposed collagen [26,27]. Fibrin clot formation results from the activation of the coagulation cascade at the same time. In addition to halting bleeding, the fibrin clot acts as a transient extracellular matrix (ECM), enabling cell migration during later stages of recovery [25,27].

### *3.2 Inflammatory Phase*

Following an injury, the phase of inflammation often exists for about 24 hours to a few days. Neutrophils are the first immune cells that enter a wound site and use phagocytosis to eliminate bacteria and cell debris [4,28]. Macrophages then take over as the predominant inflammatory cells and are essential for promoting healing [25,28]. TNF-α (Tumour necrosis factor-alpha), IL-1(Interleukin-1), VEGF (Vascular endothelial growth factor) and TGF-β are among the cytokines and growth factors released by macrophages. These mediators promote angiogenesis, tissue regeneration, and fibroblast recruitment [25,29]. Prolonged or excessive inflammation can hinder healing and lead to the formation of chronic wounds [30].

### *3.3 Proliferative Phase*

After damage, the phase of proliferation usually lasts for about 3 to 21 days. Granulation tissue development, angiogenesis, collagen synthesis and re-epithelialization are the hallmarks of this stage [4,29]. Fibroblasts that travel into the wound bed create extracellular matrix components such as collagen type III[2]. Through angiogenesis, endothelial cells multiply and create new blood vessels, supplying oxygen and nutrients to repairing tissues [2,29]. To restore epidermal integrity, keratinocytes multiply and move over the wound area [2,25]. Various factors that support cellular proliferation and tissue regeneration include VEGF (Vascular Endothelial Growth Factor), FGF (fibroblast growth factor), PDGF (Platelet-derived growth factor) and EGF (epidermal growth factor) [26,29].

### *3.4 Remodelling (Maturation) Phase*

After an accident, the remodelling phase starts about three weeks later and could last for months or even years. Stronger Collagen (Type I) substantially replaces collagen type III during this phase [25,31]. Extracellular matrix turnover and tissue remodelling are controlled by MMPs (Matrix metalloproteinases) and their TIMP inhibitors [31,32]. Myofibroblasts, which aid in wound contraction, are differentiated from fibroblasts [31]. The Tensile strength of the healed tissue progressively increases, reaching approximately 70–80% approx. of normal skin strength [4,25]. Proper remodelling minimises scar formation and restores tissue function [3

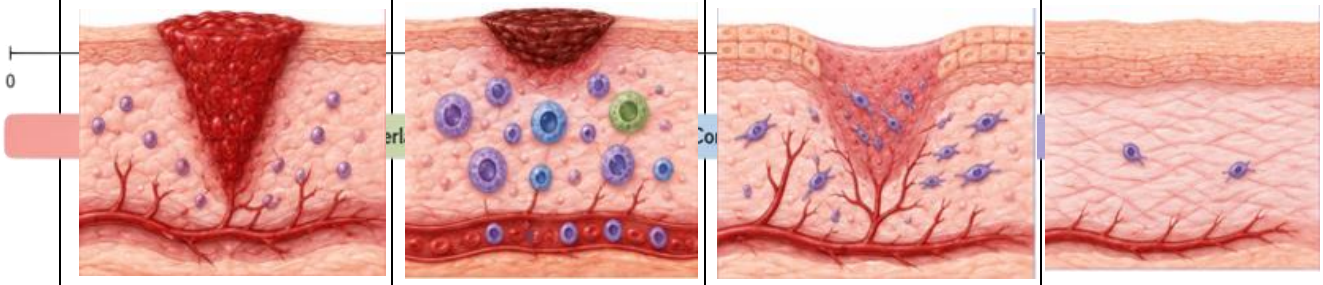
| | 1. HEMOSTASIS | 2. INFLAMMATION | 3. PROLIFERATION | 4.REMODELING / MATURATION |
|---|---|---|---|---|
| | (0-24 HOURS) | (1-4 Days) | (Day 3 – Day 21) | (3 Weeks –2Year) |
| **Phase** |  | | | |
| **Key Event** | • Vasoconstriction<br>• Platelet adhesion and aggregation<br>• Activation of coagulation cascade<br>• Fibrin clot formation<br>• Release of growth factors | • Infiltration of Neutrophil<br>• Macrophage recruitment<br>• Removal of debris and pathogens<br>• Release of cytokines and growth factors<br>• Initiation of granulation tissue | • Fibroblast proliferation and migration<br>• Angiogenesis (new blood vessel formation)<br>• Collagen (Type III) synthesis<br>• Granulation tissue formation<br>• Re- epithelialization | • Collagen III replaced by Collagen I<br>• Wound contraction<br>• Extracellular matrix remodeling<br>• Increased tensile strength<br>• Scar maturation |
| **Major Cells** | Platelets | Neutrophils, Macrophages, Mast cells, Lymphocytes | Fibroblasts, Endothelial cells, Keratinocytes | Fibroblasts (Myofibroblasts) |
| **Major Mediators** | PDGF, TGF- β, EGF, Thrombin, Fibrin | TNF- α, IL-1, IL-6, VEGF, TGF- β, PDGF | VEGF, FGF, PDGF, TGF- β, EGF, IL-10 | TGF- β, MMPs, TIMPs, PDGF |

**Figure 3.** Timeline of Wound Healing Phases

## 4.TRADITIONAL MEDICINE SYSTEMS AND THEIR ROLE IN WOUND HEALING

Traditional medicine systems are crucial for the treatment of wounds, and they are now key sources for the creation of contemporary treatments for wound healing. Herbal, mineral, and natural bioactive compositions with antibacterial, anti-inflammatory, antioxidant, angiogenic and tissue-regenerative capabilities are used in Ayurveda, Unani, Siddha, and Traditional Chinese Medicine (TCM). The therapeutic potential of these conventional methods in the treatment of acute and chronic wounds has been increasingly confirmed by recent scientific research [46,47]. A comparative overview of traditional wound management system provided in **Table 1**.

### 4.1 Ayurveda

Ayurveda describes wounds as *Vrana* and classifies them into *Agantuja Vrana* (traumatic wounds) and *Nija Vrana* (wounds arising from internal pathological conditions). Wound treatment is primarily based on two principles: *Vrana Shodhana* (cleansing and debridement) and *Vrana Ropana* (healing and tissue regeneration) [33,34]. Traditional formulations such as Jatyadi Taila, Jatyadi Ghrita, and Madhughrita are widely used because of their antimicrobial, Anti-inflammatory, and wound-healing activities [34,35]. Panchavalkala decoction is commonly employed for wound cleansing, while medicinal leech therapy improves local circulation and reduces venous congestion [33,36].

### *4.2 Siddha Medicine*

The Siddha system emphasises restoration of the balance among the three humours (*Vatham, Pitham*, and *Kapham*) [37]. Wound management commonly involves herbal and herbo-mineral preparations with potent antimicrobial and regenerative activities [37][38]. Traditional formulations such as Kuppaimeni (*Acalypha indica*) and Mathan Thailam are used in chronic ulcers, diabetic wounds, and burns [38]. These remedies

facilitate granulation tissue formation, wound contraction and removal of necrotic tissue while reducing microbial contamination [38,39].

### *4.3 Unani Medicine*

In Unani medicine, chronic wounds (*Quruh*) are believed to result from humoral imbalance and accumulation of morbid matter [40]. Treatment focuses on wound cleansing, infection control and restoration of tissue integrity [40,41]. Topical preparations known as Marham, including Marham-e-Ral and Marham-e-Dakhilyun, are traditionally used to reduce inflammation, control exudate, improve local circulation and support tissue regeneration [41].

### *4.4 Traditional Chinese Medicine*

Traditional Chinese Medicine (TCM) explains impaired wound healing through concepts such as blood stasis, Qi deficiency, and toxic heat accumulation [42]. The principle of *Sheng Ji* (generation of new tissue) focuses on restoring blood flow, eliminating damaged tissue and promoting granulation [42,43]. Angiogenic, antioxidant, and immunomodulatory properties have been shown by herbal remedies such as *Astragalus membranaceus* (Huang Qi) and *Angelica sinensis* (Dang Gui)[43,44]. Research shows that TCM formulations can promote angiogenesis, control inflammatory mediators, alleviate the vascular expression of vascular endothelial growth factor (VEGF)and speed up tissue regeneration [44,45].

### *4.5 Modern Relevance*

Traditional wound-healing therapies contain diverse phytochemicals such as flavonoids, tannins, terpenoids, alkaloids, polysaccharides and phenolic compounds. These bioactive constituents act through multiple mechanisms, including microbial inhibition, reduction of oxidative stress, modulation of inflammatory pathways, stimulation of collagen synthesis, and enhancement of angiogenesis [46]. Traditional formulations have gained renewed attention in wound care because they contain several bioactive compounds that work together to promote healing while remaining affordable and widely available. Their ability to target several aspects of the healing process, including inflammation, microbial infection, oxidative stress, and tissue regeneration, has encouraged researchers to incorporate them into modern wound care technologies. As a result, these formulations are now being investigated for use in advanced wound dressings, hydrogels, biomaterials, and regenerative medicine approaches to improve healing outcomes and support faster tissue repair [46,47].

**Table 1: Comparative overview of traditional wound management systems**

| Traditional System | Wound Concept | Major Therapeutic Approach | Common Formulations | Principal Wound-Healing Actions | References |
|---|---|---|---|---|---|
| Ayurveda | *Vrana* | Shodhana (cleansing) and Ropana (healing) | Jatyadi Taila, Jatyadi Ghrita, Madhughrita, Panchavalkala | Antimicrobial activity, wound cleansing, inflammation reduction, tissue regeneration | [33,36] |
| Siddha | *Vranam/ Kayangal* | Humoral balance and herbo-mineral therapy | Kuppaimeni, Mathan Thailam | Granulation promotion, wound contraction, desloughing action | [37,39] |
| Unani | *Quruh* | Removal of morbid matter and humoral correction | Marham-e-Ral, Marham-e-Dakhilyun | Infection control, oedema reduction, tissue repair | [40,41] |
| TCM | Blood stasis and Qi deficiency | Sheng Ji (new tissue generation) | Huang Qi, Dang Gui, Yunnan Baiyao | Angiogenesis, immunomodulation, enhanced tissue regeneration | [42,45] |

## 5. MEDICINAL PLANTS AND BIOACTIVES USED IN WOUND HEALING

Medicinal plants have attracted considerable attention in wound-care research as they exert therapeutic effects through multiple biological targets. In contrast to conventional single-compound drugs, plant-derived preparations contain complex mixtures of bioactive constituents, including polysaccharides, phenolic compounds, terpenoids and alkaloids. These phytochemicals may influence several phases of wound repair, such as hemostasis, inflammation, tissue proliferation and extracellular matrix remodeling, thereby contributing to enhanced healing outcomes [46,47]. The therapeutic exploitation of botanical agents in tissue repair represents a multi-targeted pharmacological approach. Unlike single-entity synthetic drugs, medicinal plants contain diverse matrices of secondary metabolites—including polysaccharides, polyphenols, terpenoids, and alkaloids—that act synergistically across the Hemostatic, Inflammatory, Proliferative, and Remodelling stages of wound healing [48,49]. The following section summarises thirty-three medicinal plant species reported for wound management, highlighting their major bioactive constituents and the molecular mechanisms associated with their wound-healing activities [50,51].

**Polysaccharide, Mucilage and Glycoside-Rich Barrier Restorers**

Botanical extracts characterised by high concentrations of high-molecular-weight

polysaccharides, mucilages as well as glycosides, serve an indispensable structural and regulatory role in the clinical management of severe cutaneous injuries [50]. Upon application to the compromised dermal layers, these highly hydrophilic plant polymers rapidly self-assemble to establish a robust, viscoelastic physical barrier directly over the exposed tissue bed [51]. This naturally derived hydrogel matrix effectively seals the lesion from external pathogens while critically optimising localised moisture retention, preventing the severe cellular dehydration that typically stalls epithelial migration [50]. Beyond their passive structural functions, these bioactive macromolecules actively interact with host immune receptors to regulate the early response at the wound interface [52]. Specifically, particular plant mucilages and glycosidic fractions stimulate the targeted activation and phagocytic activity of localised macrophages, aggressively accelerating the clearance of necrotic debris and invading microbes [51]. By successfully mitigating continuous Oxidative stress and restricting the excessive release of Pro-inflammatory Cytokines, these barrier restorers physically transition the wound from a destructive inflammatory state into a constructive regenerative phase [52]. Ultimately, the synergistic capacity of these botanical polymers to simultaneously provide a hydrated physical shield and actively direct local immune responses creates an optimal physiological microenvironment for rapid, uninterrupted tissue repair [50].

***Aloe vera (L.) Burm.f.*** **(Family: Asphodelaceae)**: It is a semi-tropical shrub also known as "Ghee Kunwar" (in Sanskrit). Aloe vera is valued in traditional medicine systems, including Ayurveda, Unani, Siddha, and Homoeopathy, for possessing a wide range of medicinal properties. For centuries, it has been used as a natural remedy to treat various health conditions, particularly skin disorders and wounds, making it an important medicinal plant in indigenous healthcare practices [48]. The active constituent is acemannan, a water-soluble acetylated polymannose found in the inner leaf parenchyma [55]. In wound healing, acemannan's direct binding to mannose receptors on local macrophages upregulates vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), hastening neovascularisation [54,55].

***Arctium lappa L. (*****Family: Asteraceae*****):*** *It serves as* a medicinal and edible plant which is widely distributed globally, especially in Asia, commonly known as Burdock; its roots contain high concentrations of inulin and mucilaginous polysaccharides. These polymers protect exposed nerve endings, reduce localised desiccation, and limit the production of pro-inflammatory nitric oxide within the wound bed [56], as well as showing efficacy in reducing oedema in carrageenan-induced inflammation (in a rat-paw model). Its extract demonstrated a significant reduction in the release of various inflammatory mediators by inhibiting degranulation and cysteinyl leukotriene release [57].

***Astragalus propinquus Schischkin*** **(Family: Fabaceae):** The chemical makeup of plants and their extracts varies; essential oils, flavonoids, polysaccharides and glycosides are the most often reported components [58]. *Astragalus propinquus Schischkin (A. propinquus Schischkin),* commonly found in northeast, north, and northwest China as well as Russia. It is recognised as huangqi in Chinese. It was widely thought to strengthen animals' antiviral, antioxidant, and immunological systems [59]. One of *A. propinquus's* primary physiologically active compounds was identified as polysaccharides [59]. According to related research, *A. propinquus Schischkin* polysaccharides can enhance the antioxidant capacity of lambs. 60 boost the cellular immunity of weaned pigs[62].and relieve the immunity of mice weakened by cyclophosphamide e[61]. Its primary active compound, astragaloside IV, stimulates the proliferation of epidermal keratinocytes and advances granulation tissue development by activating the p38 MAPK signalling pathway [59].

***Rehmannia glutinosa (Gaertn.) Libosch. ex Fisch. &C.A.Mey. (Family: Orobanchaceae):*** Around 6 species of the genus *Rehmannia Libosch.(*ex-Fisch. & C. A. Mey.) are native to China [59]. Among these, *R. glutinosa* (Gaertn.) Libosch. ex Fisch. & C. A. Mey. is cultivated in Korea & Japan and is a significant species in Traditional Chinese Medicine [60].*R.glutinosa* has been cultivated in China for over a millennium, and it is one of the well-known "Huai" medicines in Henan Province. The cultivar of *R. glutinosa* in its geo-authentic spread is unknown, although the entire chloroplast (cp) genome of six species in Rehmannia has been reported [61]. It was established that the *R. glutinosa* cultivar originated from the wild population [62]. The primary domestication characteristic of the *R. glutinosa* cultivar Wen 85-5 is its expanded tuberous root and dense, hypertrophic leaves. According to recent pharmacological research, the expanding tuberous root of a cultivar of *R. glutinosa* is actively responsible for therapeutic efficacy. It contains the iridoid glycoside catalpol. Catalpol reduces oxidative stress-induced cell apoptosis within the wound margin, preserving local capillary networks during acute injury [63].

***Ampelopsis japonica (Thunb.) Makino (Family: Vitaceae)*****:** A medicinal tuber that has a well-documented history in ethnopharmacology for facilitating the debridement of necrotic tissue in chronic lesions [52]. Pharmacological investigations indicate that its wound-healing efficacy is largely driven by bioactive polysaccharide fractions, which target the dysregulated proteolytic environment characteristic of stalled wounds [63]. In cases of delayed healing, the persistent overexpression of MMPs (matrix metalloproteinases) leads to the continuous, uncontrolled degradation of structural host proteins [32]. Extracts of *A. japonica* intervene in this pathological cycle by upregulating the localised expression of TIMPs (tissue inhibitors of metalloproteinases) at the site of injury [63]. This targeted biochemical modulation restores the critical

homeostatic balance between MMPs and TIMPs, effectively halting the excessive enzymatic destruction of the wound bed [52]. By mitigating this proteolytic damage, the botanical fractions preserve the structural integrity of the newly forming extracellular matrix (ECM)[63]. Consequently, this preservation provides a stable, intact collagen scaffold that is fundamentally required to support continuous fibroblast migration, tissue remodelling, and durable epidermal resurfacing [63].

***Ganoderma lucidum (Curtis)*** **(Family: Polyocracies):** *Ganoderma lucidum* have been found 400 secondary metabolites of different chemical groups, including polysaccharides, terpenes, steroids, phenols, nucleosides, peptidoglycans, proteins, and vitamins are found in the body of the fruit and contribute to its medicinal value[67].whereas β-glucans are abundant in the fruiting body of this macrofungus[68]By interacting with immune cells' Dectin-1 receptors, these polysaccharides improve macrophage phagocytic ability to remove pathogens from the wound bed while encouraging fibroblast migration[68].

It has been identified as a facultative parasite that affects up to 144 different types of forest and fruit trees [65,66]. Since ancient times, humans have been particularly concerned about fungi due to their pathogenic qualities, unique nutritional and pharmaceutical values, and role in maintaining ecological equilibrium [64]. Since ancient times, mushrooms have been known to have therapeutic qualities. In particular, the red mushroom, also known as Reishi

**Phenolic, Flavonoid, and Stilbene Antioxidant Modulators:**

Polyphenols are being recognised in numerous studies for a wide range of biological mechanisms, including anti-inflammatory, immunomodulatory, Antioxidant, Cardiovascular protective, and Anti-cancer effects [69]. Plants produce polyphenols in a variety of forms, including free aglycones and glycoside esters [69]. The polyphenol nutrients contain more than 8000 structural variations. Polyphenols, bioactive compounds found in fruits and vegetables, are responsible for their colour, flavour, and pharmacological effects. Based on their chemical structures, they are divided into two categories: Nonflavonoids include phenolic acids, stilbenoids, and phenolic amides, whereas flavonoids include flavones, flavonols, isoflavones, neoflavonoids, chalcones, anthocyanidins, and proanthocyanidins [69]. Most of these compounds are plant metabolites, consisting of several aromatic rings with hydroxyl moieties [69]. Reactive oxygen species (ROS)-induced prolonged oxidative stress keeps tissues in a chronic inflammatory state [70]. Dense networks of polyphenols found in the following plants scavenge free radicals and inhibit chronic inflammatory pathways [70].

***Calendula officinalis L. (*****Family:** ***Asteraceae), also*** known as "**Pot Marigold**", is a medicinal herb rich in flavonoids, triterpenoids, carotenoids, phenolic acids, and various essential oils. It contains high concentrations of flavonoids and ferulic esters [70]. These constituents suppress leukocyte infiltration and downregulate the pro-inflammatory transcription factor NF-κB, allowing the wound bed to transition efficiently from inflammation to proliferation [70]. These bioactive compounds accelerate wound repair through their powerful antioxidant, Anti-inflammatory, antimicrobial & wound-healing properties, making it a valuable medicinal agent in skin regeneration and wound management. [70,71,72].

***Camellia sinensis (L.) Kuntze (Family: Theaceae):*** Commonly known as **"Tea Plant"**, is a perennial evergreen shrub. This plant abundantly contains biologically active constituents, particularly Alkaloids (caffeine, theobromine, and theophylline), Catechins, Flavonoids, Phenolic acids, Amino acids and Volatile compounds. Among these, EGCG (Epigallocatechin-3-gallate) is considered the major bioactive catechin responsible for many of the plant's pharmacological effects [73], such as antioxidant, anti-inflammatory, antimicrobial, cardioprotective, neuroprotective, antidiabetic and wound-healing potential. It is particularly rich in epigallocatechin gallate (EGCG)[74]. EGCG serves as a powerful antioxidant that protects migrating keratinocytes from oxidative death and directly inhibits the overexpression of MMP-2 and MMP-9(Matrix Metalloproteinase 2 & 9), preventing excessive matrix degradation [75].

***Polygonum cuspidatum Siebold &Zucc.*** **(Family: Polygonaceae):** Japanese knotweed is recognised as the primary and richest herbal source of the stilbene phytoalexin, trans-3,5,4′-trihydroxystilbene (resveratrol). It is a powerful molecular modulator in the tissue repair process, especially through the SIRT1 signalling axis as well as the simultaneous inhibition of the classical NF-κB (Nuclear factor-kappa B) pathway [76]. During the early stage of wound healing (inflammatory), activation of SIRT1 by resveratrol induction actively inhibits the nuclear translocation of NF-κB, thus preventing the subsequent cascade of pro-inflammatory mediators. Therefore, the selective inhibition of these pathways leads to a significant decrease in the concentration of the main inflammatory cytokines, especially TNF-α (Tumour Necrosis Factor-α) and IL-6 (interleukin-6) in the inflammatory focus, and in the expression of iNOS (Inducible Nitric Oxide Synthase) in macrophages [77]. It also promotes the conversion of the wound microenvironment into a regenerative state by restricting the long-lasting oxidative stress and persistent inflammation that usually impair tissue recovery. This metabolic and immunological reprogramming limits localised tissue damage and significantly accelerates fibroblast proliferation and overall re-epithelialization rate, ultimately promoting faster and more structurally sound wound closure [78].

***Paeonia suffruticosa Andrews*** **(Family: Paeoniaceae)**: The epidermal cortex of *Paeonia suffruticosa* is considered a primary source of paeonol, an active phenolic compound well-known for managing local inflammation. When tissues are

injured, blood vessels naturally become highly permeable, causing swelling and plasma extravasation. Paeonol steps in to control this excessive fluid buildup. It works directly at the vascular level by suppressing the NF-κB pathway, which in turn blocks the expression of critical adhesion molecules (like ICAM-1 and VCAM-1) on endothelial walls [79]. Without these adhesion molecules acting as anchors, circulating inflammatory cells cannot easily latch onto the blood vessels to flood the injury site. By limiting this immune cell overload, paeonol drastically reduces tissue congestion and localised swelling [80]. Ultimately, keeping the microcirculation clear of excess fluid provides a much healthier, less congested environment for the tissue to repair itself efficiently.

***Hibiscus rosa-sinensis*** **(Family: Malvaceae):** The flowers of *Hibiscus rosa-sinensis* contain highly concentrated levels of anthocyanins and polyphenols, making them powerful natural antioxidants. When applied topically to an injury, these bioactive compounds quickly neutralise localised free radicals, preventing oxidative stress from damaging vulnerable new cells. 8. Beyond simple tissue protection, the extract actively drives the repair process by stimulating cellular proliferation. Specifically, it heavily upregulates the synthesis of hydroxyproline, a core amino acid absolutely essential for building strong, organised collagen fibres [82]. By boosting this structural collagen deposition deep within the wound bed, *Hibiscus* extracts significantly accelerate the overall wound contraction rate and shorten the epithelialization phase. This allows the injury to close much faster while maintaining high tensile strength in the newly repaired skin [81].

**Terpenoid, Steroid, and Saponin Proliferative Promoters**

Terpenoids, phytosteroids and triterpenoid saponins constitute a structurally diverse class of secondary plant metabolites critically essential for accelerating the highly metabolic stages of cutaneous repair [83]. These potent botanical compounds specifically target the proliferative and tissue remodelling stages of wound healing, actively transitioning the local microenvironment from an inflammatory state into a biologically constructive foundation [84]. Upon penetrating the compromised dermal layers, these specialised lipophilic phytochemicals directly stimulate the rapid biological division and targeted migration of host fibroblasts toward the expanding wound margin [83]. This concentrated fibroblastic activity subsequently induces the massive localised synthesis and extracellular deposition of essential structural proteins, most notably orchestrating the critical biochemical shift from immature Collagen type III to the highly resilient collagen type I[84]. Concurrently, specific triterpenoid saponin fractions aggressively advance the phenotypic distinction of local fibroblasts into highly functional, alpha-smooth muscle actin-expressing myofibroblasts within the newly formed granulation tissue [83]. The sustained mechanical action of these specialised contractile cells directly generates the continuous physical tension required to aggressively draw the indurated wound edges together [84]. Ultimately, this combined pharmacological mechanism of robust collagen matrix deposition and myofibroblast-mediated structural contraction ensures rapid, resilient macroscopic wound closure and comprehensive epidermal repair [83].

***Centella asiatica (L.) Urb*****. (Family: Apiaceae):** The plant is a well-documented dermatological agent rich in pentacyclic triterpenes, primarily asiaticoside, madecassoside and their respective aglycones [85,86]. During tissue repair, asiaticoside directly stimulates the intracellular transcription of COL1A1 and COL1A2 genes, significantly alleviating Type I synthesis of collagen and optimising the tensile strength of the maturing scar [86,87]. Beyond structural reinforcement, these phytocompounds synergistically regulate the TGF-β/Smad signalling pathway, actively balancing extracellular matrix (ECM) deposition to prevent pathological hypertrophic scarring [88,89]. Furthermore, madecassoside complements this remodelling by exerting potent anti-inflammatory and antioxidant activities, mitigating localised oxidative stress while promoting crucial angiogenesis [90]. Collectively, this targeted modulation of collagen dynamics, inflammatory suppression and microvascular network formation positions *C. asiatica* as a multidimensional therapeutic agent for effective wound closure and scar management [85]

***Panax ginseng C.A.Mey.*** **(Family: Araliaceae):** It is a highly valued therapeutic botanical characterised by a rich concentration of triterpenoid saponins known as ginsenosides [91]. During the proliferative phase of tissue repair, potent biomolecules actively stimulate migration of endothelial cells and capillary sprouting through PI3K (phosphatidylinositol 3-kinase)/Akt signalling pathway activation [91-92]. In addition to driving this essential angiogenesis, ginsenosides enhance the proliferation of dermal fibroblasts, thereby upregulating collagen synthesis and accelerating the architectural reconstitution of the extracellular matrix (ECM)[93]. Due to remarkable Anti-inflammatory and Antioxidant activities, they effectively mitigate localised oxidative stress and prevent prolonged, deleterious inflammation at the wound site[94]. By synergistically promoting robust neovascularisation while modulating the inflammatory microenvironment, *P. ginseng* facilitates an accelerated healing cascade and ensures optimal tissue regeneration [93].

***Curcuma longa L.*** **(Family: Zingiberaceae):** It is a medicinal plant distinguished by its primary bioactive constituent, the lipophilic polyphenol curcumin [95]. During the early phases of tissue repair, curcumin exerts profound effects (anti-inflammatory and antioxidant) by scavenging ROS (Reactive Oxygen Species) and significantly decreasing the expression of pro-inflammatory enzymes, including COX-2 and iNOS.95-96 As

healing progresses into the proliferative phase, this polyphenol actively accelerates structural tissue recovery by inducing the differentiation of dermal fibroblasts into active myofibroblasts, a critical mechanism that physically contracts the wound margins closer together[97]. Additionally, curcumin enhances the deposition and remodelling of the extracellular matrix (ECM) by modulating TGF-β1 signalling and upregulating essential collagen synthesis at the injury site [96,97]. Ultimately, this synchronised dampening of oxidative-inflammatory stress, coupled with robust cellular proliferation and myofibroblast-driven wound contraction, establishes C. longa as a highly effective botanical agent for accelerated tissue regeneration [98].

***Blumea balsamifera* (L.) DC. (Family: Asteraceae)** It is a distinguished medicinal herb characterised by its rich essential oil profile, which yields high concentrations of L-borneol, a highly lipid-soluble bicyclic monoterpene [99,100]. In advanced dermatological applications, L-borneol functions as a potent transdermal penetration enhancer, dynamically interacting with the stratum corneum to significantly increase skin permeability and improve the localised bioavailability of co-administered therapeutics [100]. Beyond facilitating optimal drug delivery, this monoterpene acts as a highly effective localised analgesic by actively modulating nociceptive neural pathways, notably through the targeted activation of TRP (Transient Receptor Potential) channels such as TRPM8 [101-102]. Basically, the extracts of *B. balsamifera* exert robust anti-inflammatory and antioxidant effects, critically downregulating excessive localised inflammation to foster a highly favourable microenvironment for tissue repair [99]. Ultimately, this synchronised dual functionality, enhancing structural permeability while simultaneously dampening sensory pain and inflammatory stress, establishes *B. balsamifera* as an exceptionally versatile botanical for integrated topical wound management regimens.

***Celosia argentea* L. (Family: Amaranthaceae):** It is a traditional medicinal plant widely utilised as a topical leaf paste for treating superficial cutaneous injuries and burns [103]. Its dermatological efficacy is primarily attributed to a rich phytochemical profile, particularly its high concentration of biologically active triterpenoid saponins and peptides [104]. During the proliferation stage of wound healing, these saponins promote the formation of granulation tissue by accelerating the localised deposition of basic extracellular matrix (ECM) proteins [103]. Furthermore, extracts of *C. argentea strongly* stimulate the migration thereby dermal fibroblasts proliferation, as a result rapid epithelialisation and wound margin closure [103]. This regenerative capacity is augmented by intrinsic anti-inflammatory and free-radical scavenging activities, which protect the newly synthesised ECM architecture from oxidative degradation [105]. Consequently, the synchronised enhancement of cellular proliferation and modulation of oxidative stress establishes *C. argentea* as a highly potent botanical agent for comprehensive skin regeneration [103].

***Entada phaseoloides* (L.) Merr. (Family: Fabaceae)** Commonly known as the "**St. Thomas bean"**, it is a climbing liana whose bark and seeds are highly utilised in traditional dermatological treatments [106]. The bark is rich in triterpenoid saponins, which function as antiseptic washes for cutaneous injuries while exhibiting anti-inflammatory activity [107]. Upon topical application, these saponins facilitate the precipitation of surface proteins; this action seals minor capillary leaks and establishes a protective barrier over the exposed wound bed[108]. Furthermore, the extracts exert significant broad-spectrum antimicrobial and anti-inflammatory activities, clearing opportunistic pathogens like Staphylococcus aureus from open wound surfaces while mitigating localised tissue oedema [106,108]. By simultaneously ensuring wound sterility, dampening inflammatory stress, and providing initial structural hemostasis, the bioactive phytocompounds of *E. phaseoloides* establish an optimal, infection-free microenvironment essential for accelerated epidermal regeneration [108].

**Oleo-Gum Resins and Essential Fatty Acid Matrice:**

Oleo-gum resins harvested from protective plant barks function as bio-interactive natural bandages, sealing injured tissue layers while delivering lipophilic terpenes that control the local microbial bioburden [109].

***Boswellia sacra* Flueck. (Burseraceae):** *C*ommonly known as frankincense, is a resin-producing tree utilised in traditional medicine systems. The oleo-gum resin is rich in bioactive compounds, including essential oils, polysaccharides, and pentacyclic triterpenes known as boswellic acids, which drive its pharmacological activities [110,111]. Studies have shown that boswellic acids, particularly AKBA (Acetyl-11-keto-β-boswellic acid), exhibit potent anti-inflammatory action by selectively inhibiting 5-lipoxygenase (5-LOX) activity. This targeted inhibition suppresses pro-inflammatory mediators, resolving chronic inflammation in non-healing wounds and minimising abnormal hypertrophic scarring [112]. Additionally, frankincense possesses robust antioxidant properties that neutralise ROS and protect damaged tissues from oxidative stress, creating a favourable microenvironment for tissue regeneration [113]. The resin has also demonstrated wide-ranging antimicrobial activity against diverse pathogens, reducing wound infection risk[114]. Furthermore, *Boswellia*-derived compounds actively promote proliferation of fibroblasts, deposition of collagen, and formation of granulation tissue, thereby accelerating wound contraction and re-epithelialization [111,112]

***Commiphora myrrha* (Nees) Engl. (Family: Burseraceae):** Commonly known as myrrh, is traditionally used to treat wounds, ulcers, and skin infections due to its diverse pharmacological properties. The oleo-gum resin contains bioactive

constituents, including sesquiterpenes, terpenoids, steroids, and volatile oils, that drive its robust therapeutic potential [115]. Studies demonstrate that myrrh exhibits significant anti-inflammatory activity by suppressing pro-inflammatory mediators and cytokines, thereby limiting excessive inflammation that can impair wound repair [116]. Additionally, the resin possesses wide-ranging antimicrobial activity against several pathogens (bacterial and fungal), serving localised antisepsis to reduce wound site contamination [117]. The antioxidant properties of myrrh further support wound healing by scavenging ROS and protecting several components from oxidative damage [118]. Experimental investigations have also suggested that myrrh promotes proliferation of fibroblasts, synthesis of collagen, formation of granulation tissue, and contraction of the wound, ultimately facilitating efficient re-epithelialization and tissue remodelling [116,118].

**Chromone, Naphthoquinone and Anthraquinone Matrix Protectors:**

Chromones, naphthoquinones, and anthraquinones represent important classes of natural phytochemicals that facilitate wound healing primarily by preserving and remodeling the ECM (Extracellular matrix). These compounds help maintain tissue integrity by modulating oxidative stress, inflammation, and matrix-degrading enzymes involved in wound pathology. Chromone derivatives exhibit potent anti-biofilm properties, potent Anti-inflammatory effects, and Antioxidant properties, reducing the generation of ROS that destroys newly formed tissue.[119] Naphthoquinones, particularly shikonin and its derivatives isolated from *Lithospermum erythrorhizon*, stimulate fibroblast proliferation, collagen synthesis, angiogenesis, and granulation tissue formation, thereby promoting wound closure and subsequent tissue regeneration [120]. Concurrently, Anthraquinones such as emodin modulate d inflammatory signalling pathways, enhance cellular proliferation, and protect the extracellular matrix from excessive degradation during the healing process [121]. Furthermore, these phytochemicals downregulate and inhibit matrix metalloproteinases (MMPs), to ensure balanced matrix remodelling

***Lithospermum erythrorhizon Siebold &Zucc.* (Family: Boraginaceae):** It is also known as purple gromwell, is an East Asian traditional medicinal herb extensively utilized to treat burns, wounds, ulcers, and inflammatory skin conditions. The plant's roots are rich in lipophilic naphthoquinone pigments, predominantly shikonin and its derivatives, which serve as the primary drivers of its wound-healing efficacy [120]. Beyond displaying direct bactericidal effects against *Staphylococcus aureus* biofilms, shikonin acts as a potent anti-inflammatory agent by regulating pro-inflammatory cytokine release, thereby preventing chronic inflammation at the injury site [122]. Experimental studies demonstrated that shikonin stimulates fibroblast proliferation, collagen synthesis, and re-epithelialization while actively upregulating granulation tissue proliferation during intermediate healing stages [123]. Furthermore,its antioxidant properties mitigate oxidative stress to protect injured extracellular tissues and facilitate extracellular matrix remodelling. Consequently*, L. erythrorhizon* represents a promising botanical candidate for advanced skin regeneration [122].

***Rheum officinale Baill. (Polygonaceae*):** It is a prominent medicinal species within the Polygonaceae family and is characterised by an abundance of bioactive anthraquinones, among which emodin serves as the primary pharmacological constituent [124]. In the clinical management of highly exudative or weeping skin ulcers, emodin exerts a multi-targeted therapeutic effect initiated by robust antimicrobial activity. This anthraquinone restricts microbial proliferation by disrupting cell membrane integrity and inhibiting vital pathogenic protein synthesis [124]. Beyond its antibacterial properties, emodin actively regulates microvascular dynamics during the acute inflammatory phase of early wound repair. By suppressing localised pro-inflammatory signalling cascades, it effectively decreases capillary hyper-permeability and prevents excessive fluid extravasation into the surrounding tissues. This stabilisation of the endothelial barrier prevents ongoing inflammatory damage, effectively alleviating the localised oedema typical of weeping lesions [124]. Consequently, the concurrent capacity of *R. officinale* extracts to eliminate microbial bioburden, normalise vascular permeability, and physically condense edematous proteins establishes an optimal physiological microenvironment that accelerates epidermal regeneration [124].

***Sanguisorba officinalis L.* (Family: Rosaceae):** *Great Burnet* (*Sanguisorba officinalis*) is a well-known medicinal herb remarked for its high content of bioactive polyphenols, tannins, polysaccharides, and unique ziyu-glycosides. Traditionally, it has been used as an effective hemostatic agent to control both internal and external bleeding [125]. Its major active compounds, including ziyu-glycoside I and sanguiin H-6, promote hemostasis by inducing localised vasoconstriction and enhancing platelet activation and aggregation at the wound site. Together, these actions help reduce bleeding, accelerate clot formation, and support wound healing without causing significant local toxicity [125].

***Caesalpinia sappan L.* (Fabaceae*):*** It is a medicinal herb probably recognized in traditional pharmacognosy for its profound ability to activate blood circulation and resolve pathological blood stasis [126]. The therapeutic efficacy of its dried heartwood is primarily attributed to brazilin, a potent bioactive homoisoflavonoid that exerts extensive protective effects on the host microvasculature. In the context of wound healing within ischemic or otherwise compromised tissue environments, brazilin acts as a critical modulator of vascular dynamics and cellular survival [126]. Specifically, it actively inhibits abnormal vascular smooth muscle cell proliferation and mitigates localised oxidative

stress, preventing progressive microvascular occlusion. By ameliorating these structural deficits and preserving the endothelial barrier, brazilin significantly enhances regional microvascular blood flow directly adjacent to ischemic injuries [126]. Furthermore, the intrinsic vasorelaxant and anti-platelet aggregation properties of the compound ensure a continuous, unimpeded delivery of vital oxygen to the expanding margins of the wound. Ultimately, the multi-targeted pharmacological profile rejuvenates the hypoxic tissue microenvironment, accelerating metabolic repair and facilitating the rapid closure of ischemic lesions [126].

**Phenylpropanoid and Essential Oil Hemodynamic Regulators:**

Phenylpropanoids and volatile essential oil constituents represent potent secondary plant metabolites increasingly recognised for their multi-targetedcontribution in tissue regeneration [127]. Within the pathological wound microenvironment, volatile compounds such as eugenol and cinnamaldehyde act as hemodynamic modulators by directly altering vascular tone[128]. The topical application of these lipophilic agents induces rapid localised vasodilation, significantly enhancing local blood perfusion to deliver vital oxygen and nutrients to ischemic tissues [129]. Concurrently, their high tissue penetrability allows essential oils to bypass surface barriers and eradicate deep-seated, persistent microbial infections that typically disrupt the healing cascade [128]. By successfully clearing this deep pathogenic burden and mitigating localised oxidative stress, these phytochemicals establish a stabilised, sterile foundation necessary for complex cellular repair [129]. Consequently, the synergistic combination of active infection control and sustained microvascular oxygenation directly accelerates the biological proliferation of keratinocytes and fibroblasts at the expanding wound margins.[127] This highly coordinated pharmacological action guarantees rapid epithelial resurfacing and structurally resilient wound closure [128].

***Cinnamomum cassia*** **(L.) J.Presl (Family: Lauraceae):** It produces an essential oil rich in the bioactive phenylpropanoid cinnamaldehyde [130]. When applied to ischemic or chronic wounds, cinnamaldehyde acts as a potentendothelium - independent vasodilator. directly relaxing vascular smooth muscle to expand local capillary networks [131]. This increased microvascular perfusion alleviates tissue ischemia by delivering oxygenated blood and recruiting crucial defence cells, for instance neutrophils and macrophages, at the site of injury. Beyond immediate hemodynamic improvements, cinnamaldehyde stimulates angiogenesis by PI3K/AKT (Phosphoinositide 3 kinase) and MAPK (Mitogen-activated protein kinase) signalling pathway activation, triggering a significant exocytosis of VEGF (Vascular Endothelial Growth Factor) [130]. This targeted molecular signalling encourages local endothelial cells to multiply and form functional vessels at the wound edges. At the same time, this highly lipid-soluble compound controls deep bacterial infections and curbs the release of tissue-damaging inflammatory cytokines [132]. By combining better blood perfusion, active vessel growth, and infection control, *C. cassia* creates a highly supportive environment for rapid epidermal resurfacing.

***Andrographis paniculata*** **(Burm.f.) Nees (Family: Acanthaceae):** Phytochemically characterised by andrographolide, a bioactive diterpenoid lactone [133]. When applied to severely infected wounds, andrographolide acts as an immunomodulator that helps clear local bacterial loads while protecting surrounding healthy tissue. Its primary pharmacological action centres on downregulating iNOS (Inducible Nitric Oxide Synthase) and suppressing major proinflammatory transcription factors like NF-κB[134]. During severe localised infections, the unregulated overproduction of iNOS causes a massive buildup of nitric oxide. This excess directly triggers oxidative stress, cell death, and continuous tissue breakdown at the edges of the wound. By blocking this specific enzyme cascade, andrographolide physically stops the cytokine storm typically caused by deep bacterial growth [135]. This targeted intervention allows the host's immune system to clear the infection without causing the collateral cell destruction usually seen in chronic inflammation. Through this balanced immune regulation, *A. paniculata* preserves the structural integrity of the local blood vessels and sets up a stable, non-toxic bed necessary for rapid re-epithelialization [134].

***Lonicera japonica Thunb.*** **(Family: Caprifoliaceae):** It is pharmacologically significant and is characterised by a rich profile of bioactive phenylpropanoids and flavonoids (predominantly chlorogenic acid and luteolin) [136]. In traditional medicine, this species is renowned for "clearing heat and removing toxins." In modern pharmacological terms, this directly correlates with the extract's ability to neutralise bacterial lipopolysaccharides (LPS) in infected wounds.[137] During the acute phase of a severe infection, these bioactive compounds suppress the excessive swarming of neutrophils by blocking key inflammatory signalling pathways, specifically the TLR4/NF-κB pathway [138]. By severely limiting the continuous release of ROS and cytotoxic cytokines from overactive immune cells, chlorogenic acid protects surrounding healthy skin structures from collateral damage. Furthermore, this targeted drop in oxidative stress quickly forces the wound microenvironment to transition from a destructive, hyper-inflammatory state into a constructive tissue-building phase. The application of *L. japonica* extracts effectively establishes the non-toxic, stabilised foundation required for functional epithelial resurfacing [137].

***Daphne genkwa*** **Siebold & Zucc. (Family: Thymelaeaceae):** It is utilised in traditional medicine for its targeted therapeutic effect against stubborn, crusted dermatological ulcerations [139]. The primary application involves dried flower buds (Flos Genkwa), which contain high concentrations

of bioactive coumarin derivatives and biflavonoids, mostly daphnoretin. Within the hostile microenvironment of a severely crusted ulcer, daphnoretin attenuates progressive tissue degradation by hindering the NF-κB inflammatory pathway and reducing the hyper-activation of local macrophages [140]. This profound anti-inflammatory action halts the progressive necrosis of the epidermal layers, allowing the extract to naturally facilitate the loosening and clearance of dead, crusted scales that trap infectious fluids. By completing this natural debridement of the wound bed, daphnoretin quickly transforms a stagnant, rotting lesion into a stable environment capable of supporting new cell growth [140]. Once the necrotic debris is cleared, the bioactive constituents stimulate the division of dermal fibroblasts and significantly upregulate the local production of critical structural proteins, specifically collagen types I and III. This dual mechanism of macro-cleaning the wound and triggering targeted collagen synthesis ensures the rapid closure of deep ulcerations [139].

**Coumarin and Phthalide Blood-Stasis Resolvers:**

In traditional global medical systems, the active resolution of pathological blood stasis and the subsequent restoration of localised microvascular networks are recognised as fundamental physiological prerequisites for effective tissue regeneration [141]. Among the diverse phytochemical classes employed to correct these microcirculatory deficits, low-molecular-weight secondary metabolites, specifically coumarins and phthalides, have emerged as highly potent and reliable hemodynamic regulators [142]. Upon systemic absorption or topical application to the compromised tissue bed, these lipophilic compounds rapidly dismantle localised vascular congestion by physically inhibiting platelet aggregation and actively relaxing vascular smooth muscle [142]. This targeted structural vasodilation strictly mitigates regional ischemia, ensuring that heavily occluded capillary networks are reopened to deliver a continuous, high-volume supply of oxygen and essential immune cells directly to the damaged endothelium [141]. Ultimately, by aggressively clearing thrombotic blockages and neutralising localised oxidative stress within the hostile wound microenvironment, coumarin and phthalide derivatives establish a highly vascularized, nutrient-rich physiological foundation that is directly essential for accelerating the biological cascades of functional epithelial repair [141].

***Angelica sinensis*** **(Oliv.) Diels (Family: Apiaceae):** In traditional global medical systems, *it* is highly regarded for its clinical efficacy in resolving pathological blood stasis and subsequently restoring localised microvascular network integrity recognised as fundamental physiological prerequisites for effective tissue regeneration [141]. Among the diverse classes of plant secondary metabolites investigated for correcting microvascular deficits, low-molecular-weight phytochemicals, specifically coumarins and phthalides, have emerged as highly potent and reliable hemodynamic regulators [142]. Upon systemic absorption or topical application to the compromised tissue bed, these lipophilic compounds rapidly dismantle localised vascular congestion by physically inhibiting platelet aggregation and actively relaxing vascular smooth muscle [142]. This precise targeted structural vasodilation strictly mitigates regional ischemia, ensuring that heavily occluded capillary networks are reopened to deliver a continuous, high-volume supply of oxygen and essential immune cells directly to the damaged endothelium [141]. Ultimately, by aggressively clearing thrombotic micro-obstructions and neutralising localised oxidative stress within the hostile wound microenvironment, coumarin and phthalide derivatives establish a highly vascularized, nutrient-rich physiological foundation that is directly essential for accelerating the biological cascades of functional epithelial repair [141].

***Carthamus tinctorius L.*** **(Family: Asteraceae):** Also known as Safflower is a prominent therapeutic species that is extensively utilised in clinical pharmacognosy for its capacity to resolve blood stasis and enhance local microvascular circulation [143]. The therapeutic efficacy of its florets is attributed to water-soluble quinochalcone glycosides, hydroxysafflower yellow A (HSYA)[144]. Within an ischemic or traumatised wound bed, HSYA functions as a targeted hemodynamic regulator by inhibiting abnormal platelet aggregation [144]. Thisanti-platelet activity prevents obstructive micro-thrombi formation within damaged capillaries, clearing vascular congestion and restoring blood perfusion [144]. By dismantling microscopic clots and mitigating endothelial inflammation, HSYA prevents the progressive ischemic necrosis of surrounding viable tissues [143]. The restoration of unobstructed microvascular flow ensures continuous, high-volume oxygen delivery and critical metabolic nutrients directly to the expanding wound margins [143]. Satisfying the high metabolic demands of cellular regeneration [143]. Consequently, the sustained vascular patency established by HSYA directly accelerates fibroblastic proliferation, cellular migration, tissue remodelling, and resilient wound closure 144].

***Panax notoginseng*** **(Burkill) F.H.Chen (Family: Araliaceae):** It represents a highly valued medicinal root within the Araliaceae family and is phytochemically characterised by its unique profile of steroidal saponins known as notoginsenosides[145]. In managing severe traumatic injuries, this botanical extract demonstrates a remarkable and highly sophisticated "two-way" hemodynamic regulatory capacity [146]. Upon acute vascular trauma, specific active fractions within the extract immediately stimulate platelet activation and accelerate the coagulation cascade to rapidly arrest severe localised blood loss[146]. This potent hemostatic action effectively secures the ruptured endothelial barrier during the critical initial phase of tissue repair[145]. However,

unlike conventional pro-coagulant agents that frequently induce ischemic necrosis via excessive clot formation, *it* prevents the development of long-term unphysiological blood stasis [146]. As the wound stabilises, specific notoginsenosides actively modulate the release of endothelial nitric oxide and inhibit secondary platelet hyper-aggregation, aggressively dismantling obstructive micro-thrombi [145]. This synchronised thrombolytic and vasorelaxant action resolves localised vascular congestion, restoring microvascular perfusion to ischemic tissue [145]. Preservation of these unobstructed capillary networks ensures a continuous delivery of oxygen and essential metabolic nutrients directly to the site of injury [146]. Ultimately, this uniquely balanced pharmacology creates an optimally perfused microenvironment that accelerates total wound closure [145].

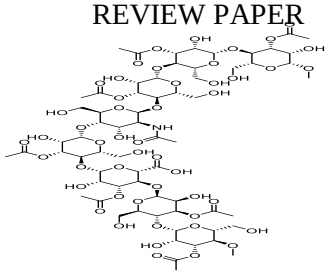
***Ligusticum striatum DC.*** **(Family: Apiaceae):** Historically known as Chuanxiong, it is renowned for its potent hemodynamic regulatory effects [147]. Its rhizome is rich in bioactive volatile phthalides, primarily Z-ligustilide and senkyunolide A, which act as key pharmacological agents [147]. Within chronic, non-healing lesions, these highly lipophilic compounds induceendothelium-independent vasorelaxation to dilate capillaries [148]. This action disperses obstructive micro-thrombi and resolves deep-seated blood stagnation that deprives the wound bed of oxygen [147]. By restoring microvascular perfusion, these phthalides ensure continuous nutrient and oxygen delivery to ischemic tissue [148]. Consequently, sustained vascular potency mitigates localised oxidative stress and prevents progressive tissue fibrosis at wound margins [147]. Furthermore, clearing congested inflammatory exudate softens indurated wound edges [148]. Ultimately, the robust capacity of *L. striatum* to resolve profound blood stasis establishes a vascularized, flexible physiological foundation that accelerates epithelial resurfacing and wound closure [147].

***Salvia miltiorrhiza Bunge*** **(Family: Lamiaceae):** Commonly known as Danshen, a critically important species that is phytochemically distinguished by a potent dual-action profile consisting of highly lipophilic tanshinones and water-soluble salvianolic acids [149]. During the remodelling and maturation phase of wound healing, this synergistic combination regulates extracellular matrix deposition [150]. Specifically, these bioactive constituents suppress dermal fibroblasts and downregulate the transforming growth factor-beta 1 (TGF-β1), a primary molecular driver of tissue fibrosis [150]. By controlling this fibrotic cascade, the extract prevents the disproportionate accumulation of rigid collagen type I fibres within the healing tissue [149]. This targeted structural regulation mitigates the formation of abnormal, hypertrophic keloidal scars that frequently complicate severe cutaneous injuries [150]. Concurrently, preserving organised elastin networks ensures that newly generated epidermal and dermal layers maintain optimal biomechanical flexibility [149]. Ultimately, the comprehensive cellular action of *S. miltiorrhiza* guarantees that the final physiological repair is both structurally resilient and highly elastic, yielding a functional tissue recovery without pathological induration [149].

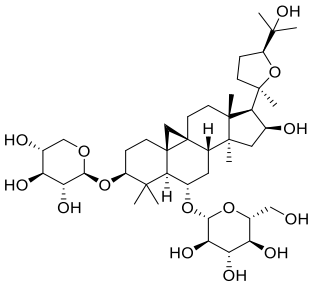
**Table 2: Comprehensive phytochemical & target matrix**

| Botanical Name | Dominant Phytochemical Core | Target Healing Phase | Primary Downstream Endpoint | References |
|---|---|---|---|---|
| *Aloe vera* | Acemannan | Proliferative | Upregulates VEGF and bFGF transcription | [48,54,55] |
| *Arctium lappa* | Inulin / Mucilage | Inflammatory | Reduces desiccation and suppresses local nitric oxide | [56,57] |
| *Astragalus propinquus* | Astragaloside IV | Proliferative | Stimulates keratinocyte migration via p38 MAPK | [58,62] |
| *Rehmanniaglutinosa* | Catalpol | Inflammatory | Scavenges local ROS; protects capillary cells | [59,63] |
| *Ampelopsis japonica* | Root Polysaccharides | Proliferative | Upregulates TIMPs to balance matrix degradation | [32,52,63] |
| *Ganoderma lucidum* | -Glucans | Inflammatory | Enhances macrophage phagocytosis via Dectin-1 | [46, 68] |
| *Calendula officinalis* | Faradiol Esters | Inflammatory | Blocks NF-B activation to reduce local oedema | [70,72] |
| *Camellia sinensis* | EGCG | Proliferative | Directly inhibits MMP-2 and MMP-9 overexpression [73-75] | [73,75] |
| *Polygonum cuspidatum* | Resveratrol | Inflammatory | Activates SIRT1 to reduce TNF-α and IL-6 | [76,78] |
| *Paeonia suffruticosa* | Paeonol | Inflammatory | Inhibits adhesion molecules on endothelial walls | [79,80] |
| *Hibiscus rosa-sinensis* | Anthocyanins | Proliferative | Increases local hydroxyproline for faster contraction | [82,81] |

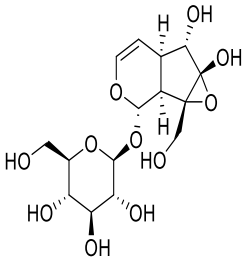
| | | | | |
|---|---|---|---|---|
| *Centella asiatica* | Asiaticoside | Proliferative | Activates COL1A1/COL1A2 for Type I collagen synthesis | [85,90] |
| *Panax ginseng* | Ginsenosides | Proliferative | Suppresses the angiogenesis pathway through the PI3K/Akt pathway | [91,94] |
| *Curcuma longa* | Curcumin | Inflammatory | Decreases COX-2 and drives myofibroblast differentiation | [95,98] |
| *Blumea balsamifera* | L-Borneol | Inflammatory | Modulates nociceptive pathways to relieve local pain | [99,102] |
| *Celosia argentea* | Leaf Saponins | Proliferative | Speeds up the deposition of basement matrix proteins | [103,105] |
| *Entada phaseoloides* | Bark Saponins | Inflammatory | Precipitates surface proteins to seal capillary leaks | [106,108] |
| *Boswellia sacra* | Boswellic Acids | Inflammatory | Inhibits 5-LOX to resolve non-healing indurations | [110,114] |
| *Commiphora myrrha* | Sesquiterpenes | Hemostasis | Stabilises structural cells within the early fibrin clot | [115,118] |
| *Lithospermum erythrorhizon* | Shikonin | Proliferative | Destroys *S. aureus* biofilms; drives tissue growth | [120,122,123] |
| *Rheum officinale* | Emodin | Inflammatory | Restricts bacterial protein synthesis and fluid weeping | [124] |
| *Sanguisorba officinalis* | Ziyu Glycosides | Hemostasis | Induces rapid platelet aggregation and vasoconstriction [1] | [125] |
| *Caesalpinia sappan* | Brazilin | Proliferative | Improves regional blood flow around ischemic injuries | [126] |
| *Cinnamomum cassia* | Cinnamaldehyde | Proliferative | Acts as a vasodilator to improve nutrient delivery | [130,132] |
| *Andrographis paniculata* | Andrographolide | Inflammatory | Suppresses iNOS to limit excess inflammatory damage | [133,135] |
| *Lonicera japonica* | Chlorogenic Acid | Inflammatory | Clears tissue endotoxins and stabilises neutrophils | [136,138] |
| *Daphne genkwa* | Daphnoretin | Inflammatory | Dissolves dead necrotic scales in stubborn ulcers [139-140] | [139,140] |
| *Angelica sinensis* | Ferulic Acid | Proliferative | Accelerates endothelial cell proliferation | [141, 142] |
| *Carthamus tinctorius* | HSYA | Proliferative | Reduces micro-thrombi inside damaged capillary beds | [143,144] |
| *Panax notoginseng* | Notoginsenosides | Hemostasis | Provides a two-way hemostatic balancing mechanism | [145,146] |
| *Ligusticum striatum* | Volatile Phthalides | Proliferative | Dilates capillaries to soften tough wound margins | [147,148] |
| *Salvia miltiorrhiza* | Tanshinones | Maturation | Restricts tissue fibrosis to prevent keloidal scars [149-150] | [149,150] |



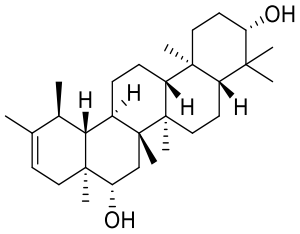
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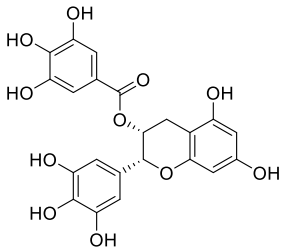
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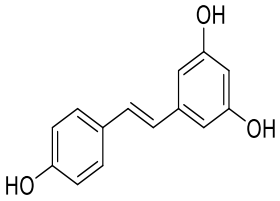
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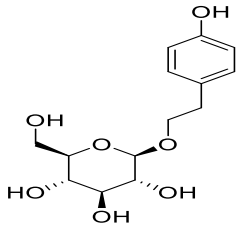
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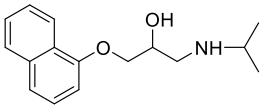
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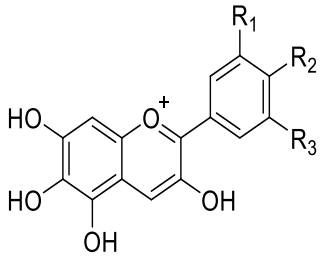
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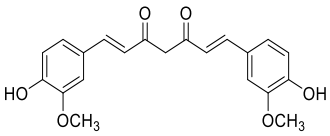
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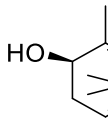
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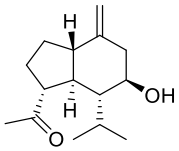
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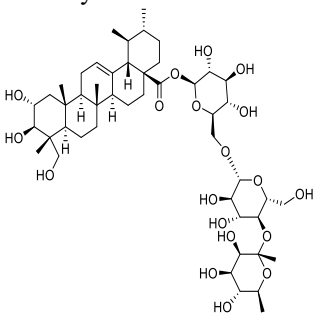
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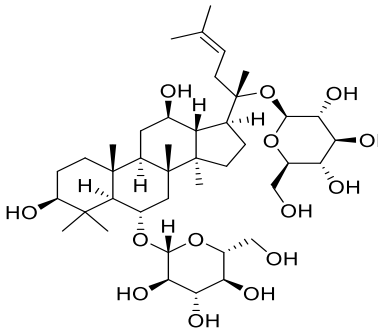
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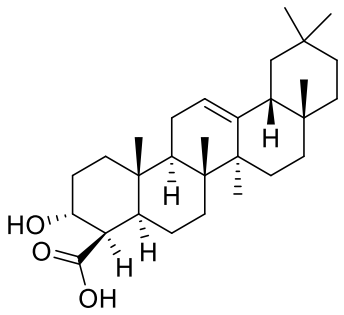
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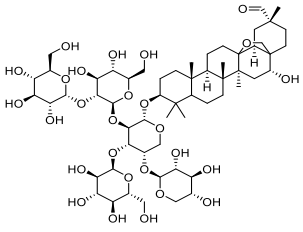
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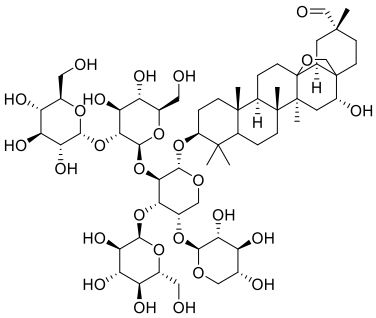
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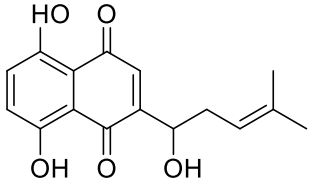
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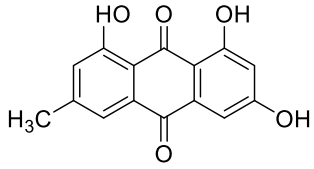
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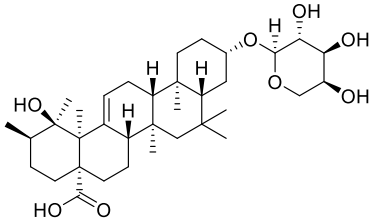
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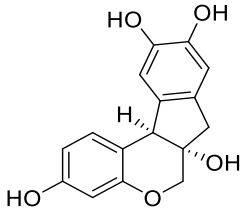
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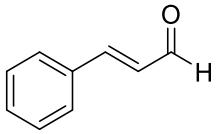
Emodin



Ziyu Glycosides



Brazilin



Cinnamaldehyde

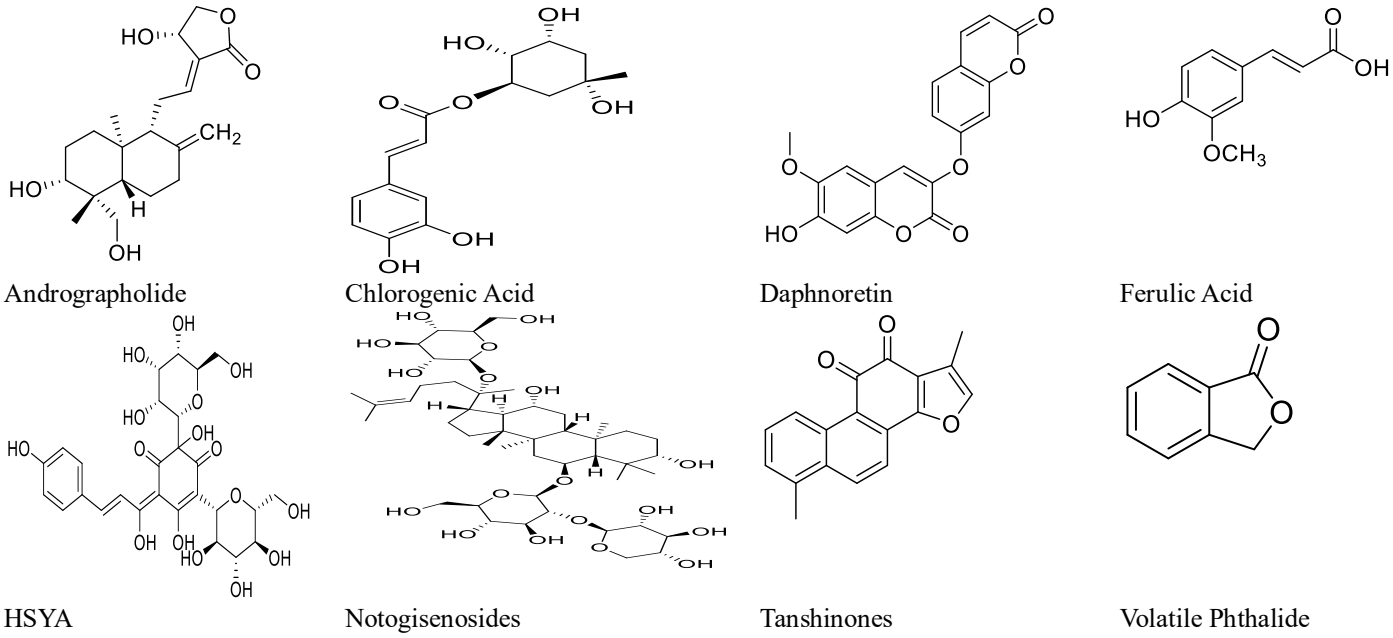



**Fig 4**. Structure of major bio active constitute use in wound Healing

**Modern Herbal Formulations in Wound Healing**

The creation of contemporary herbal formulations that integrate conventional medicinal plant bioactive with cutting-edge drug-delivery technologies such hydrogels, nanofibers, nanoparticles, films, scaffolds and biopolymeric dressings has been the main focus of recent developments in wound care. While preserving a moist wound environment and promoting tissue regeneration, these formulations enhance the stability, bioavailability, controlled release, and therapeutic efficacy of herbal substances in table. 3[151,152].

**Herbal Hydrogels**

Herbal hydrogels are three-dimensional polymeric networks capable of retaining large amounts of water and maintaining optimal wound moisture. Bioactive agents such as *Aloe vera*, curcumin, *Centella asiatica*, neem and honey are incorporated into hydrogel matrices to provide antimicrobial, antioxidantand anti-inflammatory effects. These formulations promote fibroblast proliferation, collagen deposition, angiogenesisand accelerated wound closure [151].

**Herbal Nanofiber**

Electrospun nanofibers loaded with herbal extracts are amongst the most promising modern wound-healing technologies. Nanofibrous dressings mimic the ECM (Extracellular matrix), providing high porosity, oxygen permeability and controlled release of phytoconstituents. Herbal compounds such as curcumin, neem, chamomile, *Nigella sativa*, and *Aloe vera* have been successfully incorporated into nanofibers to enhance epithelialization, reduce microbial infection, and accelerate tissue regeneration [152].

**Herbal Nanoparticle Formulations**

Nanotechnology-based herbal formulations alleviate the solubility and bioavailability of poorly absorbed phytoconstituents. Nano formulations containing curcumin, quercetin, resveratrol and essential oils exhibit enhanced Antimicrobial, Antioxidant, and Anti-inflammatory activities [153]. These nanoparticles facilitate targeted delivery, sustained drug release, and improved penetration into wound tissues, resulting in faster healing and reduced scar formation [153].

**Herbal Films and Biopolymeric**

Plant-derived bioactive compounds are increasingly incorporated into biodegradable films and biopolymeric wound dressings composed of chitosan, alginate, collagen, gelatin, cellulose, and hyaluronic acid. These dressings provide mechanical protection, moisture retention, infection control, and support for cellular proliferation. The incorporation of herbal extracts further enhances wound contraction, collagen synthesis, and re-epithelialization [154].

**Polyherbal Formulations**

Multiple medicinal plant extracts are combined in polyherbal preparations to produce synergistic therapeutic benefits [155]. Modern polyherbal preparations demonstrate significant antimicrobial, antioxidant, angiogenic, and collagen-stimulating activities [155]. Such formulations target multiple phases of wound healing simultaneously and have shown promising outcomes in both acute and chronic wounds [155].

**Table 3.** Comparative overview of modern herbal formulations

| Formulation Type | Common Herbal Bioactive | Major Advantages | Wound-Healing Effects | References |
|---|---|---|---|---|
| Hydrogels | *Aloe vera*, Curcumin, Honey | High moisture retention, biocompatibility | Enhanced angiogenesis and tissue regeneration | [151] |
| Nanofibers | Neem, Curcumin, Chamomile, *Nigella sativa* | ECM-like structure, controlled drug release | Accelerated epithelialization and collagen deposition | [152] |
| Nanoparticles | Curcumin, Quercetin, Resveratrol | Improved bioavailability and penetration | Reduced inflammation and faster wound closure | [153] |
| Biopolymeric Films | *Aloe vera*, *Centella asiatica*, Herbal extracts | Mechanical protection and sustained release | Improved re-epithelialization and infection control | [154] |
| Polyherbal Formulations | Mixed medicinal plant extracts | Synergistic pharmacological effects | Enhanced antimicrobial and regenerative activity | [155] |

## CONCLUSION AND FUTURE PERSPECTIVES

Hemostasis, inflammation, proliferation and tissue remodelling are part of the intricate and well-coordinated biological process of wound healing. Chronic wounds like diabetic foot ulcers, venous leg ulcers, and pressure ulcers frequently show impaired healing because of persistent inflammation, infection, biofilm formation, tissue hypoxia, and systemic metabolic disorders, whereas acute wounds typically go through these stages in an orderly fashion. Globally, these issues continue to place a heavy financial and healthcare burden. Herb-based treatments are being used for wound care in medical systems used by tribals. Numerous phytoconstituents generated from these systems have been shown by growing scientific evidence to have important antibacterial, antioxidant, anti-inflammatory, angiogenic and tissue-regenerative qualities. Growth factor signalling, extracellular matrix remodelling, collagen synthesis, angiogenesis and inflammatory regulation are among the important molecular pathways involved in wound repair that bioactive substances like acemannan, curcumin, epigallocatechin gallate,asiaticoside, and astragaloside IV have been demonstrated to modulate. The clinical application of herbal wound-healing medicines is constrained by a number of issues, notwithstanding their therapeutic potential. Numerous phytochemicals have limited penetration into wound tissues, low bioavailability, quick breakdown, and poor aqueous solubility. Furthermore, standardisation, quality control and regulatory approval of herbal formulations are challenging due to variations in plant sources, extraction techniques, and phytochemical content.

Future studies should concentrate on combining herbal bioactives with cutting-edge tissue engineering and medication delivery technology. Opportunities to enhance the stability, bioavailability and controlled release of phytoconstituents at the wound site are presented by innovative techniques such as hydrogel-based systems, electrospun nanofibers, nanoparticles, bioactive scaffolds and smart wound dressings. These multipurpose platforms may reduce systemic side effects while increasing therapeutic efficacy.

The safety, effectiveness and repeatability of herbal wound care products must also be established by carefully planned preclinical research, multicenter randomised clinical trials, and standardised manufacturing procedures. The development of next-generation wound therapies is anticipated to be fueled by the intersection of contemporary pharmacology, biomaterials science, nanotechnology, and traditional medical understanding. In the end, these interdisciplinary methods may improve patients' quality of life as well as outcomes by offering practical, economical, and long-lasting solutions for the treatment of both acute and chronic wounds.

## AUTHORS' CONTRIBUTIONS

The authors confirm their contribution to the paper as follows. PM and MY were responsible for the review study conception and design. PM conducted the review data collection. PM drafted the review manuscript. All authors reviewed and approved the final version of the manuscript.

## LIST OF ABBREVIATIONS

## CONSENT FOR PUBLICATION

Not applicable.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

## USE OF AI TOOLS DECLARATION

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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