Review Article

Wound Healing and the Use of Medicinal Plants

Aleksandra Shedoeva, David Leavesley, Zee Upton, and Chen Fan

1 Skin Research Institute of Singapore, Agency for Science, Technology and Research, A*STAR, 11 Mandalay Road, Singapore 308232
2 Institute of Medical Biology, A*STAR, Singapore

Correspondence should be addressed to Chen Fan; c3.fan@connect.qut.edu.au

Received 1 March 2019; Revised 3 May 2019; Accepted 1 September 2019; Published 22 September 2019

Academic Editor: Jae Youl Cho

Copyright © 2019 Aleksandra Shedoeva et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Cutaneous wound healing is the process by which skin repairs itself. It is generally accepted that cutaneous wound healing can be divided into 4 phases: haemostasis, inflammation, proliferation, and remodelling. In humans, keratinocytes re-form a functional epidermis (reepithelialization) as rapidly as possible, closing the wound and reestablishing tissue homeostasis. Dermal fibroblasts migrate into the wound bed and proliferate, creating “granulation tissue” rich in extracellular matrix proteins and supporting the growth of new blood vessels. Ultimately, this is remodelled over an extended period, returning the injured tissue to a state similar to that before injury. Dysregulation in any phase of the wound healing cascade delays healing and may result in various skin pathologies, including nonhealing, or chronic ulceration. Indigenous and traditional medicines make extensive use of natural products and derivatives of natural products and provide more than half of all medicines consumed today throughout the world. Recognising the important role traditional medicine continues to play, we have undertaken an extensive survey of literature reporting the use of medical plants and plant-based products for cutaneous wounds. We describe the active ingredients, bioactivities, clinical uses, formulations, methods of preparation, and clinical value of 36 medical plant species. Several species stand out, including Centella asiatica, Curcuma longa, and Paeonia suffruticosa, which are popular wound healing products used by several cultures and ethnic groups. The popularity and evidence of continued use clearly indicates that there still lessons to be learned from traditional practices. Hidden in the myriad of natural products and derivatives from natural products are undescribed reagents, unexplored combinations, and adjunct compounds that could have a place in the contemporary therapeutic inventory.

1. Introduction

Our skin is the key to our survival, sensing the environment, maintaining physicochemical and thermal homeostasis, acting as a reservoir of essential nutrients, providing passive and active defence, and responding to trauma and injury [1]. Maintaining these critical functions requires robust and effective mechanisms to protect it from trauma and insult and to repair and replace critical skin functions when damaged or lost. Humans have been treating their wounds for millennia [2]. Traditional wound management is limited by what is immediately at hand or can be acquired locally, such as water, soil, and plant and animal products, and is frequently complemented with ceremony and ritual as an added measure. For millions of people across Asia, Africa, the Middle East, and Latin America, traditional medicines derived from local plants, animals, and natural products are the mainstay of wound care; for some, it is the only source of wound care [3]. We discuss herein some of the evidence supporting the use of medicinal plants as effective and affordable treatments for cutaneous wounds.

2. Cutaneous Wound Healing

Maintaining homeostasis is critical for the survival of the organism; hence, skin needs and possesses a robust and effective repair mechanism. Cutaneous wound healing is the process by which skin repairs itself following injury caused by surgery, trauma, and burns [4]. The healing process is classically divided into 4 phases (Figure 1): coagulation
Healing of acute wounds follows an orderly sequence of overlapping, interacting physiological processes (Figure 1). This sequence can take over a few days in juveniles or over a few weeks in adults to occur. Most wounds heal without complication and reestablish homeostasis, skin barrier function, pliability, and physiological functions in less than 4 weeks. Clinical evidence indicates that shorter periods to wound closure are associated with reduced fibrosis and scarring. In contrast, full-thickness wounds and wounds that are slow to heal are associated with increased fibrosis, developing in some individuals into hypertrophic scars and keloids. Deep, full-thickness, and partial-thickness wounds that do not heal within 6 weeks appear to “stall” and fail to progress through the phases of healing described in Figure 1 (Figure 2). These hard-to-heal wounds are considered to be “chronic” wounds [17]. Hard-to-heal wounds become “chronic” for a number of reasons, including underlying conditions such as diabetes, vascular disease, hyperglycaemia, ischemia, and neuropathy. The underlying cause of the wound is often used to describe the wound: diabetic foot ulcers, venous leg ulcers, arterial leg ulcers, and pressure ulcers.

Nonhealing, chronic wounds clearly pose a risk to the health and well-being of the individual; patients often suffer from pain, impaired mobility, excessive exudates, wound malodour, and restricted social life [18], resulting in substantial disruption, morbidity, and indirect costs to social and healthcare systems [19]. As many as 1-2% of individuals in all populations worldwide will acquire a chronic wound during their life-time [20]. In the USA, chronic wounds are reported to affect 6.5 million people and cost over US $25 billion each year [21]. Alarming, the burden of chronic wounds is expected to intensify due to global increases in...(a.k.a. haemostosis), inflammation and proliferation (a.k.a. granulation), and remodelling (a.k.a. maturation) [5]. Upon injury, a fibrin clot rapidly forms to restore haemostasis [6, 7]. Platelets present in the blood trigger the clotting cascade and secrete several growth factors, initiating wound healing [8]. In the following inflammation phase, neutrophils migrate into the wound site engulfing foreign debris and killing bacteria by phagocytosis and releasing proteolytic enzymes [8, 9]. Coincidently, blood monocytes infiltrate the injury site and differentiate into macrophages, releasing proteases to debride the wound [8], and secrete a mixture of bioactive molecules, including transforming growth factor-beta 1 (TGF-β1), that stimulates the migration of fibroblasts and epithelial cells [10]. The proliferation phase usually starts about 3 days after wounding; it involves diverse activities including angiogenesis (by endothelial cells), granulation tissue formation (by fibroblasts), and reepithelialization (by keratinocytes) [11, 12]. In this stage, fibroblasts produce a large amount of extracellular matrix (ECM), mainly collagen, to form the granulation tissue which replaces the damaged tissue. Meanwhile, the keratinocytes migrate, proliferate, differentiate, and re-form a functional epidermis (reepithelialization), closing the lesion and protecting underlying tissues from further trauma [13]. As the wound matures, the characteristic disorganized ECM of granulation tissue is actively remodelled by the dermal fibroblast cell population [14], whose numbers are progressively reduced through apoptosis [15]. The outcome of wound healing is scar tissue (aka fibrosis) with sparsely distributed fibroblasts within a collagen-rich ECM. Compared to the original tissue, scar tissue, having distinct texture and reduced biomechanical and functional properties, is characteristically altered [16].

Figure 1: Wound healing cascade—humans. The wound healing process is an orderly sequence of overlapping, interacting processes commonly categorised into four distinct phases: coagulation, inflammation, proliferation/migration/reepithelialization/granulation, and remodelling/maturity. (1) Coagulation: a clot is formed, providing a temporary barrier to fluid loss and pathogen entry, restores haemostasis; acts as a reservoir of bioactive factors and antimicrobials; provides provisional ECM which supports immune cell infiltration and migration; and initiates tissue repair pathways. (2) Inflammation: damage-associated molecular patterns, free radicals, and reactive molecular species are signals to recruit immune cells; increased blood vessel leakiness; release of antimicrobial species; infiltrating immune cells secretes amplifying alarmin (also known as DAMPs) signals; and activation of keratinocytes and fibroblasts. (3) Proliferation/migration/reepithelialization/granulation: migration and proliferation of keratinocytes, fibroblasts, endothelia; resolution of inflammation; cells secrete amplifying alarmin (also known as DAMPs) signals; and activation of keratinocytes and fibroblasts. (3) Proliferation/angiogenesis: collagen/ECM synthesis; decreased vessel permeability; new capillary and lymphatic vessel angiogenesis; reepithelialization; and de novo formation of granulation tissue. (4) Remodelling/maturity: collagen/ECM turnover (synthesis and degradation); ECM reorganisation and realignment; ECM contraction; endothelia and fibroblast apoptosis; repigmentation.
vascular diseases, diabetes, obesity, metabolic syndrome, and the general aging of the population [21]. Although the mechanisms of wound healing are relatively well known, the pathogenesis of chronic wounds remain poorly defined [22]. It is generally accepted that chronic wounds result from some dysregulation of the normal wound healing process. For example, microbial biofilms, overexpression of inflammatory cytokines, high levels of proteases and reactive oxygen species (ROS), and reduced mitogenic activity stall wound healing in the inflammation phase, inhibiting progression to the proliferation and reepithelialization phases. In addition, overactive matrix metalloproteinases (MMPs) have been shown to contribute to delayed healing [23]. The result is a wound that remains open, does not heal, and becomes chronic [24].

Selecting an appropriate clinical strategy to manage cutaneous wounds is dictated by the aetiology underlying each wound. Consideration is given to (1) removing nonvital (necrotic) tissue, termed debridement; (2) inflammation or infection; (3) controlling moisture (too wet or too dry); and (4) state of the tissue surrounding the wound [25]. This approach has its roots in Greek and Roman medicine [26], where removing these “barriers to healing” was prescribed to allow the healing cascade to progress to completion. Debridement is considered to benefit wounds, restarting the healing process by returning it to an acute presentation. Debridement exposes healthy and well-perfused tissue, facilitating cell proliferation and migration [27]. In addition to removing dead and necrotic tissue, debridement effectively reduces, if not removes, proinflammatory factors, damage-associated molecular patterns (DAMPs), and pathogen-associated molecular patterns (PAMPs). Debridement also removes “extracellular traps” and microorganisms from the wound. Microorganisms in wounds have long been considered deleterious [28]; however, recent evidence suggests that not all microbes impede healing. Microbial pathogens such as Staphylococcus sp., Streptococcus sp., Propionibacterium sp., and Pseudomonas sp. are commonly equated with infection, while others including Malassezia sp., Candida sp., and Corynebacterium sp. can be isolated from non-infected wounds and may even contribute to wound healing [29]. The optimal frequency and when to perform debridement, however, remains unclear [27]. Dressings provide a physical barrier to re-infection from commensal and adventitious microorganisms, can deliver antimicrobial agents (e.g., honey and iodine), and, in some designs, absorb wound exudates, providing a measure of moisture control.

3. Traditional Medical Practices

Traditional medicine is often described by practitioners of “modern” (western) medicine using sceptical terms such as “alternative,” “nonconventional,” “indigenous,” and “complementary,” when in fact many of the techniques and practices of “modern” medicine are little different from traditional practices when it comes to wounds. Traditional approaches depend almost entirely upon natural resources, such as water, plants, animals, and minerals, and continue to be valued and widely practiced by a majority of the world’s population [3]. The practice of traditional Chinese medicine (TCM) is based on the Five-Phases theory and Yin-Yang theory, recorded in the ancient Chinese medical documents such as "Shen Nong Ben Cao Jing" and "Ben Cao Gang Mu." Many, but not all, TCM makes extensive use of plants, ensuring it is effective, affordable, and accessible [30]. Interestingly, of the new anticancer drugs developed between 1940 and 2002, approximately 54% were derived from natural products [31]. Another study has determined that of all current pharmaceutical products, about 73%, include ingredients derived from natural products [32]. The therapeutic activity of many traditional medicines are conferred by natural ingredients produced within the plant;
consequently, the efficiency of TCM preparations can vary widely and are determined by the genotype, environmental, and growing conditions encountered by each source plant [30, 33]. Urbanization and industrialization of pharmaceutical engineering have increased demand for "off the shelf" TCM products with consistent composition, quality, and clinical efficacy. Concomitantly, industrialization has also introduced rigorous product testing for evidence of biological activity and clinical efficacy.

4. Traditional Use of Medical Plants in Wound Healing

4.1. Aloe vera. Applied to wounds for over 5000 years by Egyptians, Romans, indigenous peoples of Africa, Asia, and the Americas, Aloe vera continues to be a first-line treatment for burns, ulcers, and surgical wounds [34]. Aloe vera contains many natural active compounds, including pyrocathecol, saponins, acemannan, anthraquinones, glycosides, oleic acid, phytol, as well as simple and complex water-soluble polysaccharides [35]. Acetone extracts from the leaves of Aloe vera exhibit stronger antimicrobial activity than alcohol and aqueous extracts. Gram-positive bacterial species appear to be more sensitive than Gram-negative species to Aloe vera [36]. Compounds with known antimicrobial activity are saponins, acemannan, and anthraquinone derivatives [37].

Acemannan, a major mucopolysaccharide (mesoglycan) from Aloe vera, is a potent stimulator of macrophage and T-cell activity and induces the transcription of proinflammatory mRNAs (including IL-1α, IL-1β, IL-6, TNF-α, PGE2, and nitrous oxide) [38]. Mesoglycan moieties bind and capture endogenous mitogen inhibitors and reactive oxygen species and promote phagocytosis. Coincidently, glycans stabilize secreted cytokines, growth factors, and other bioactives, prolonging their activity. Topically applied acemannan has been reported to significantly reduce the time to wound closure in a rat wound healing model, acting via cyclin D1 and AKT/mTOR signal pathways [39]. Aloe vera glycans are also reported to significantly improve de novo formation of granulation tissue by an unknown mechanism [40].

4.2. Arctium lappa. Arctium lappa, commonly known as burdock, is a widely cultivated perennial herb [41]. Arctium lappa is used in North America, Europe, and Asia to treat sore throat and skin pathologies such as boils, rashes, and acne [42, 43]. Scientific analyses demonstrate Arctium lappa has antioxidant [44], anti-inflammatory [45], antidiabetic [46], antimicrobial [47], antiviral [48], anticancer [49], and hepatoprotective [50] properties. The root extract of Arctium lappa has been shown to significantly improve dermal ECM metabolism, affecting glycosaminoglycan turnover and reducing visible wrinkles in human skin in vivo [51]. Arctium lappa is also reported to regulate cell adhesion and gene expression in canine dermal fibroblasts, affecting the Wnt/β-catenin signalling pathway, known to be a key regulator of wound healing [52]. In a pilot study of one commercial preparation including Arctium lappa, Burns and Wounds™ topical ointment (B&W), pain and healing of first- and second-degree burns in humans was demonstrated to be managed more effectively than the control treatment [53].

4.3. Astragalus propinquus and Rehmannia glutinosa. The root of Astragalus propinquus is a common TCM for the treatment of urinary retention and edema [54]. The root of Rehmannia glutinosa has been broadly used in hematology and diabetes-related diseases [55]. A formulation combining the root of Astragalus propinquus and Rehmannia glutinosa was initially reported to be clinically effective for the treatment of diabetic foot ulcers [56]. This outcome has subsequently been corroborated in diabetic rats [57]. Tam et al. reported that the root of Astragalus propinquus and Rehmannia glutinosa promote diabetic wound healing and postischemic neovascularization by improving angiogenesis and attenuating tissue oxidative stress in diabetic rats [58]. Zhang et al. demonstrated that the root of Astragalus propinquus and Rehmannia glutinosa activate the TGF-β1 signalling pathway and stimulate increased deposition of ECM in human skin fibroblasts [59].

4.4. Ampelopsis japonica. Growing throughout eastern Asia and eastern North America, the roots of Ampelopsis japonica are used as a traditional treatment for burns and ulcers, amongst other indications [60]. Multiple pharmacological activities have been documented for Ampelopsis japonica, including neuroprotective [61], antimicrobial, and anticancer [62] activities. Lee et al. demonstrated that ethanol extracts from dried roots of Ampelopsis japonica accelerated the healing of cutaneous scald injury in rats [63]. Tumour necrosis factor-alpha (TNF-α) and TGF-β1 were observed to be elevated 2 days after injury and declined as healing progressed. In contrast, interleukin-10 (IL-10) was found to be elevated after 14 days, coincident with wound closure [63]. When compared with wounds treated with Vaseline® (petroleum jelly) or silver sulfadiazine, topical treatment with ethanol Ampelopsis japonica improved reepithelialization, granulation tissue formation, vascularization, and collagen deposition [63].

4.5. Andrographis paniculata. Andrographis paniculata, also known as green chireta, is used in China, India, and south east Asian countries as a traditional treatment for fever, snake bite, dysentery, infections, wounds, and itchiness [64–67]. Extracts from Andrographis paniculata exhibit antioxidant [68], anti-inflammatory [69], antidiabetic [70], anticancer [66], antimicrobial [71], antiviral [72], antimalarial [73], hypotensive [74], immunostimulatory [66], and hepatoprotective [75] activities. In one study, wound closure in rats was observed to be significantly enhanced after treatment with a 10% aqueous leaf extract of Andrographis paniculata [76]. Animals treated with Andrographis paniculata exhibited reduced inflammation, reduced scarring, increased angiogenesis, and an increased number of collagen fibres in healed wounds [76]. Andrographolide, a bicyclic
diterpenoid isolated from the leaves of *Andrographis paniculata*, has been formally evaluated in clinical trials and shown to have positive effects on several autoimmune disorders [77].

4.6. *Angelica sinensis*. The dried root of *Angelica sinensis* is widely used in TCM prescriptions for the management of female maladies, inflammation, headaches, mild anemia, fatigue, and hypertension [78]. *Angelica sinensis* possesses pharmacological activities including anti-inflammatory [79], anti-cancer [80], antioxidant effects [81], and immune modulator [82]. Extracts from *Angelica sinensis* have been shown to activate an antiapoptotic pathway and enhance cell proliferation, collagen secretion, and cell mobility in human skin fibroblasts [83]. Extracts have also been shown to stimulate glycolysis and calcium fluxes, increasing cell viability during tissue repair [83]. The role of *Angelica sinensis* in angiogenesis remains unclear, with several studies reporting contradictory effects of *Angelica sinensis* on de novo blood vessel growth. An aqueous extract of *Angelica sinensis* was reported to promote blood vessel growth via activation of JNK1/2 and p38 phosphorylation, resulting in enhanced VEGF expression [84, 85]. In contrast, n-butyldenephthalide, a bioactive isolated from *Angelica sinensis*, inhibits cell cycle progression, induces apoptosis, and attenuates angiogenesis [86].

4.7. *Blumea balsamifera*. Endemic throughout the tropics and subtropics of Asia, *Blumea balsamifera* (also known as ngai camphor) is used widely as a traditional medicine. In the Philippines, *Blumea balsamifera* is known as sambong and is used as a diuretic. In Ayurveda, *Blumea balsamifera* is known as kakoranda and is used to treat fevers, coughs, aches, and rheumatism. Leaf extracts are directly applied to treat eczema, dermatitis, skin injury, bruises, beriberi, lumbago, menorrhagia, rheumatism, and skin injury [87]. Extracts from *Blumea balsamifera* demonstrate a variety of bioactivities: including antimalarial [88], antitumour [89], antifungal [90], and antiobesity [91] properties. Pang et al. reported that oils from *Blumea balsamifera* improve wound healing in mice by promoting angiogenesis, perfusion, collagen deposition, formation of organised granulation tissue, reepithelialization, and wound closure [92].

4.8. *Boswellia sacra*. Frankincense, a resinous extract from *Boswellia sacra*, is valued in Africa, India, and the Middle East for the treatment of trauma and inflammatory diseases such as rheumatoid arthritis [93, 94]. It has also been reported that the boswellic acid acetate extracted from frankincense induces apoptosis and differentiation in melanoma and fibrosarcoma cells [95]. It is a key component of ANBP, a TCM consisting of pulverised *Agrimonia eupatoria* (A), *Nelumbo nucifera* (N), *Boswellia sacra* (B), and pollen from *Typha angustifoliae* (P). ANBP stimulates Smad-dependent pathways in the TGF-β1 signalling cascade [96]. Using a rabbit ear model of hypertrophic scarring, Hou et al. demonstrated that ANBP moderates inflammation and accelerates the growth of organized granulation tissue and reepithelialization, events that reduce scar formation [96]. Intriguingly, ANBP was also noted to attenuate collagen biosynthesis and accelerate the maturation of the collagen extracellular matrix, contributing to reduced scarring and improved skin tissue repair. Recently, Hou et al. further demonstrated that ANBP reduced the time of wound closure in diabetic mice via direct effects on neovascularization [97].

4.9. *Caesalpinia sappan*. The heartwood of *Caesalpinia sappan* is well known for its qualities as a dye and has been used in TCM to improve blood circulation and reduce oedema and pain [98]. Homoisoflavonoids isolated from *Caesalpinia sappan* have been found to possess antiallergic [99] and anti-inflammatory [100] attributes and to inhibit viral neuraminidase activity [101]. Ethanol extracts of *Caesalpinia sappan* exhibit effective antibacterial activity against *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, Acinetobacter baumannii, *Escherichia coli*, and *Klebsiella pneumoniae* [102]. Unexpectedly, the ethanol root extract from *Caesalpinia sappan* also stimulates dermal fibroblast proliferation, migration, and collagen synthesis [103], in turn improving cutaneous wound healing.

4.10. *Calendula officinalis*. *Calendula officinalis*, commonly known as pot marigold, is a very widely distributed plant used for the treatment of a variety of skin conditions, such as wounds, burns, and dermatitis [104, 105]. A range of pharmacological activities are ascribed to *Calendula officinalis*, including anti-inflammatory, antioxidant, antibacterial, antiviral, antifungal, and anticaner activities [106]. However, the exact mechanisms involved in its activities on the wound healing remain unknown. Studies using cultures of human and murine fibroblasts demonstrated that extracts of *Calendula officinalis* stimulate fibroblast migration and proliferation in a PI3K-dependent manner [107, 108]. Extracts from the flower of *Calendula officinalis* stimulate granulation tissue formation by altering the expression of connective tissue growth factor (CTGF) and α-smooth muscle actin (α-SMA) in excisional wounds of BALB/c mice in vivo [109]. *Calendula officinalis* is also reported to enhance angiogenesis in vivo, demonstrated using the chicken chorioallantoic membrane (CAM) assay and a cutaneous wound healing model in rats [110].

4.11. *Camellia sinensis*. Green tea, an aqueous extract made from the leaves of *Camellia sinensis*, is revered throughout Asia for its reputed health benefits [111]. Centuries of anecdotal evidence has been experimentally validated by demonstrating that *Camellia sinensis* has antioxidant [112], anti-inflammatory [113], antimicrobial [114], anticancerogenic [115], antiaging [116], antiobesity [117, 118], cardioprotective [119], and neuroprotective [120] activities. Catechins, the polyphenolic compounds from *Camellia sinensis*, are primarily responsible for these pharmacological activities [121]. The major catechin, (-)-epigallocatechin-3-gallate (EGCG)
Evidence-Based Complementary and Alternative Medicine

[111], stimulates the proliferation and differentiation of keratinocytes [122]. Klass et al. found that EGCG suppresses TGF-β receptors by modifying TGF-β signalling, reducing MMP-1 and MMP-2 expression, and attenuating synthesis of collagen type 1 in human dermal fibroblasts. These properties suggest that EGCG is a potential antiscarring agent [123]. In addition, EGCG was demonstrated to induce keloid shrinkage [124] and inhibit growth and pathological features of keloids by suppressing STAT3 signalling [125]. Methanol extracts [124] and inhibit growth and pathological features of keloids, suggesting a potential antiscarring agent [123]. In vivo studies have demonstrated that Camellia sinensis significantly improves wound healing by increasing angiogenesis in rats [121, 126]. Extracts from Camellia sinensis are also reported to improve wound healing in a diabetic mouse model [127].

4.12. Carthamus tinctorius. Seeds from Carthamus tinctorius, or safflower, are a popular source for cooking oil in many countries. Less widely known, Carthamus tinctorius also has a long history as an ingredient in TCM formulations for the treatment of blood disorders. Recent experimentation has identified it as associated with a wide range of biological activities, including vasodilation, immune modulation, antioxidant and thromboprophylaxis, antioxidation, anti-inflammatory, anti-fatigue, anti-inflammation, antihypertensive, antimicrobial, antidiabetic, antilipidemic, anti-inflammatory, anti-inflammatory, and analgesic activities. Myrrh, the resinous exudate from Commiphora myrrha, has well-documented antioxidant [156], anti-inflammatory [157], antimicrobial [158], and analgesic [159] activities. Medicinal applications of myrrh include the treatment of gastrointestinal diseases, fractures, arthritis, obesity, parasitic infections, and as an anticoagulant [160–162]. Myrrh has been used topically to clean wounds, reduce oedema, and provide pain relief (analgesia) [163]. Myrrh is commonly used in combination with other ingredients. Galehdari et al. showed that the combination of myrrh, Adiantum capillus-veneris, Aloe vera, and Lawsonia inermis, significantly improved wound healing in diabetic mice [164]. The short-term application of myrrh effectively reduces pain and controls the recurrence of mouth ulcers in humans [165]. In common with several other herbal preparations described here, myrrh is found to modify the expression of TGF-β1 and VEGF in mouse dermal fibroblasts in vitro, suggesting a common mechanism of action [166].

4.13. Celosia argentea. Celosia argentea, also known as silver cock's comb, is used in traditional medicine to treat skin sores, eruptions, ulcers, mouth ulcers, and other skin diseases [137]. Leaf extracts of this plant possess antioxidant [138], hepatoprotective [139], anti-diabetic [140], and antimicrobial [141] activities. Priya et al. demonstrated that an alcohol extract of Celosia argentea accelerates burn wound closure in rats by increasing collagen and hexosamine content in granulation tissue wounds. In addition, the extract increased the proliferation and motility of primary rat dermal fibroblasts [137].

4.14. Centella asiatica. Centella asiatica, also known as Asiatic pennywort, has been used to promote wound healing for eons [142]. Extracts from the aerial parts of Centella asiatica are reported to improve the healing of chronic ulcers in Sprague-Dawley rats in terms of width, depth, and length [142]. Wounds associated with acute radiation dermatitis in rats were observed to heal earlier when treated with extracts from Centella asiatica compared to the no-treatment control group [143]. Asiaticoside isolated from Centella asiatica has been found to enhance collagen deposition and epithelialization in a punch wound model in the guinea pig [144]. Triterpenes isolated from Centella asiatica elevate collagen remodelling and glycosaminoglycan synthesis in a rat wound model [145]. Furthermore, oral administration of madecassoside from Centella asiatica was shown to facilitate collagen synthesis and angiogenesis in a mouse wound model [146].

4.15. Cinnamomum cassia. Cinnamomum cassia is a commonly used spice and flavouring agent, and the bark of Cinnamomum cassia is also used to increase blood circulation and as an analgesic [147]. Cinnamomum cassia is frequently formulated with other herbs; it is one of the seven botanical components of Shexiang Baoxin pill (SBP), a well-known TCM prescribed for chest pain and discomfort associated with coronary artery disease [148]. SBP is currently the subject of a randomized double-blinded clinical trial for the treatment of coronary artery disease not amenable to revascularization [149]. Attention is also focussed on SBP anti-inflammatory [150] and anticancer activities [151, 152], as well as its impact on hypertension, insulin resistance, and noninsulin-dependent diabetes mellitus [153]. In vitro and in vivo studies indicate that cinnamaldehyde, a bioactive component from Cinnamomum cassia, is a natural insecticide, is an antimicrobial, anti-diabetic, antilipidemic, anti-inflammatory, and neuroprotective agent [154], and activates PI3K/AKT and MAPK signalling pathways, increasing VEGF expression, and stimulating angiogenesis in human umbilical vein endothelial cells [147]. Cinnamaldehyde is also reported to improve wound healing in zebrafish [147].

4.16. Commiphora myrrha. Myrrh, the resinous exudate produced by Commiphora myrrha [155], has well-documented antioxidant [156], anti-inflammatory [157], antibacterial [158], and analgesic [159] activities. Medicinal applications of myrrh include the treatment of gastrointestinal diseases, fractures, arthritis, obesity, parasitic infections, and as an anticoagulant [160–162]. Myrrh has been used topically to clean wounds, reduce oedema, and provide pain relief (analgesia) [163]. Myrrh is commonly used in combination with other ingredients. Galehdari et al. showed that the combination of myrrh, Adiantum capillus-veneris, Aloe vera, and Lawsonia inermis, significantly improved wound healing in diabetic mice [164]. The short-term application of myrrh effectively reduces pain and controls the recurrence of mouth ulcers in humans [165]. In common with several other herbal preparations described here, myrrh is found to modify the expression of TGF-β1 and VEGF in mouse dermal fibroblasts in vitro, suggesting a common mechanism of action [166].
4.17. Curcuma longa. Curcumin, an active substance found in the root of Curcuma longa and a member of the ginger family, has long been used as a medicine and as food seasoning [167]. Practitioners of traditional Ayurveda medicine use curcumin to treat inflammation, respiratory disorders, liver disorders, and diabetes [168]. In traditional Chinese medicine, curcumin is a favoured treatment for abdominal pain. Having widespread use for centuries by diverse ethnic groups, curcumin is one of the most extensively studied nutraceuticals. This highly pleiotropic molecule has been demonstrated to interact with key cellular pathways at transcription, translation, and post-translational levels. Target pathways include proinflammatory cytokines, apoptosis, NF-κB, cyclooxygenase-2, 5-LOX, STAT3, C-reactive protein, prostaglandin E2, prostate-specific antigen, cell adhesion molecules, phosphorylase kinase, transforming growth factor-β, triacylglycerides, ET-1, creatinine, heme oxygenase-1, AST, and ALT [169]. The subject of more than 100 clinical trials, in vivo studies, have largely focused on curcumin as a treatment for epithelial cancers. Experimental findings from these in vivo studies and in vitro experiments indicate curcumin elicits most of its beneficial effects via altering the pericellular and extracellular matrix [168]. Perhaps, it is therefore not unexpected that curcumin enhances fibroblast proliferation, granulation tissue formation, and collagen deposition in cutaneous wound healing [170].

4.18. Daphne genkwa. Daphne genkwa, one of the 50 fundamental herbs used in TCM, grows in the Yellow and Yangtze Rivers regions in China. Daphne genkwa is used as an anticonvulsant, analgesic, diuretic, antitussive, expectorant, and mild sedative agent [171–174]. The principal bioactives isolated from Daphne genkwa are biflavonoids, coumarin, diterpenes, and triterpenes. These confer anti-inflammatory [175], antitumour [176, 177], immunoregulatory [178, 179], and antimelanogenesis [172] activities. Flavonoids extracted from the flowers of Daphne genkwa stimulate the ERK/MEK pathway regulating fibroblast proliferation and the expression of collagen (COL1A1 and COL3A1), resulting in improved wound healing [171].

4.19. Entada phaseoloides. Entada phaseoloides, also known as St. Thomas bean, is a liana in the pea family of climbing vines common throughout lowland tropical forests and coastal forests of Africa, Australia, Asia, and Western Pacific. The bark and seeds of Entada phaseoloides are rich in saponins and tannins and are used as analgesic, bacteriocide, haemostatic, and anticancer agents and as a topical treatment for skin lesions [180, 181]. Su et al. reported that extracts enriched with tannins from Entada phaseoloides reduced the time taken to heal infected wounds in rats. Analyses of the data concluded that the improved wound healing was due to the antibacterial, proproliferative, and promigration activity of the Entada phaseoloides extracts [182]. These data are yet to be validated in human patients.

4.20. Hibiscus rosa-sinensis. Hibiscus rosa-sinensis, or shoeblackplant, is an evergreen shrub native to tropical South Eastern Asia [183]. The flowers of Hibiscus rosa-sinensis are edible. Traditional texts describe preparations of the leaves and flowers promote hair growth and prevent greying [184]. Alcoholic extracts of Hibiscus rosa-sinensis flowers are claimed to provide women with control of their fertility [185]. Extracts from Hibiscus rosa-sinensis have also been found to have antibacterial [186] and wound healing properties [187]. They attenuate inflammation, enhance fibroblast proliferation, and collagen deposition, as well as upregulate VEGF and TGF-β1 expression in rat excisional wounds [188].

4.21. Ganoderma lucidum. Ganoderma lucidum, the lingzhi mushroom, is well known to the Chinese, Korean, and Japanese as “the mushroom of immortality” [189, 190]. Used in TCM to boost the patient’s immune system [191], Ganoderma lucidum stimulates a variety of pharmacobiological responses including immune modulation, inflammation modulation, anti-infective [192–194], antioxidant [195], cardioprotection [196], and antihyperlipidemia [197] activities. Clinical studies suggest that taking Ganoderma lucidum daily is beneficial and is reported to reduce the number of tumours in patients with colorectal adenomas; circulating viral particles in patients infected with hepatitis B; and symptoms of hypertension [189, 198–202]. Laboratory-based studies reveal that components from Ganoderma lucidum interact with and modulate key enzymes with known roles in lipid metabolism. However, clinical findings remain equivocal and suggest that Ganoderma lucidum is most effective when used as an adjunct with other therapies [203]. Polysaccharide extracts from the fruiting body of Ganoderma lucidum have been shown to improve wound healing in diabetic rats, potentially by stimulating fibroblast proliferation and migration [190], angiogenesis, and quenching oxidative stress [204]. Nevertheless, these responses may also represent indirect responses to Ganoderma lucidum via its established stimulation of humoral immunity.

4.22. Ligusticum striatum. The rhizome of Ligusticum striatum is another one of the 50 fundamental herbs used in TCM. It has a long history of use support cardiovascular and cerebrovascular well-being. It is commonly indicated for the treatment and prevention of ischemic disorders, menstrual disorders, and headache [205–207]. Thus far, about 174 chemical components have been isolated from Ligusticum striatum, among which phthalide lactones and alkaloids are the most numerous, pharmacologically active species [207]. It has been reported that essential oils from Ligusticum striatum inhibit dermal scarring in the rabbit ear scar model [208].

4.23. Lonicera japonica. Lonicera japonica, also known as honeysuckle, has a notable place in traditional medicine throughout its native range of Japan, Korea, and China,
where it has been used for thousands of years to treat infectious diseases [209]. In the 1980s, the Chinese State Ministry of Health performed extensive pharmacological and clinical analyses of *Lonicera japonica* and identified broad-spectrum antimicrobial, anti-inflammatory, antipyretic, antioxidant, anticancer, hepatoprotective, and anti-hyperlipidemic capabilities [210, 211]. More recently, Chen et al. demonstrated that the ethanol extracts of the flowering aerial parts of *Lonicera japonica* also support reepithelization, angiogenesis, granulation tissue formation, and contraction during cutaneous wound healing [212]. The plant may be consumed as a “health food,” providing some protection from gastric ulceration although, at high doses, it can cause some neurological pathologies [210].

4.24. *Paeonia suffruticosa*. *Paeonia suffruticosa*, also known as moutan peony, has been bred for millennia [213]; over 1000 distinct cultivars are now available. The root bark of *Paeonia suffruticosa* is the source for bioactive ingredients used for TCM preparations. Pharmacological investigation of *Paeonia suffruticosa* has demonstrated it has antioxidant [214], neuroprotective [215], antitumour [216], anti-inflammatory [217], and antidiabetic [218] properties. The dried root of *Paeonia suffruticosa* is commonly applied to cracked skin to assist healing and relieve pain [219]. When tested in *vitro* at low concentrations (≤10 μg/mL), *Paeonia suffruticosa* is found to stimulate the viability and proliferation of human primary dermal fibroblasts and HaCaT keratinocytes, suggesting its potential use as a wound healing therapy [220].

4.25. *Panax ginseng*. *Panax ginseng* is one of the most popular medicinal plants consumed in China, Japan, Korea, and Eastern Siberia to improve thinking, concentration, and memory. It is also claimed to support immunity and physical stamina and to reduce fatigue [221]. *Panax ginseng* is thus used to treat depression, anxiety, and chronic fatigue syndrome [222]. *Panax ginseng* has been demonstrated to induce vasodilatation [223], control blood lipids [224], reduce inflammation [225], and confer antioxidant [226], anticancer [227], antibacterial [228], antiallergic [229], antiaging [230], and immunomodulating [231] activities. *Panax ginseng* contains many bioactive substances, among which a class of saponins (termed ginsenosides by Asian researchers and panaxosides by Russian researchers) represent the most potent active constituents of *Panax ginseng* [232].

The root extracts of *Panax ginseng* have been shown to protect skin in C57BL mice from acute UVB irradiation [233] and significantly improve healing after laser burn injury and excisional wounding [221, 234, 235]. Studies demonstrate *Panax ginseng* extracts enhance keratinocyte migration [221, 236], as well as stimulate proliferation [237] and increase collagen synthesis in human dermal fibroblasts [238] in *vitro*. In addition, Choi demonstrated that the ginsenoside Rb2, isolated from *Panax ginseng*, induces the formation of the epidermis in raft culture via increased expression of epidermal growth factor and its receptor, fibronectin and its receptor, and keratin 5/14 and collagenase I [239], all of which have critical roles in wound healing.

4.26. *Panax notoginseng*. *Panax notoginseng*, not to be confused with *Panax ginseng* and other ginsengs, is used to stop bleeding, reduce oedema, reduce bruising, and reduce pain [240, 241]. Terpene saponins isolated from the leaves of *Panax notoginseng* possess substantial pharmacological activities, including antioxidative effects [242], anti-inflammatory effects [243], immunostimulation [244], neuroprotective effects [245], anticancer [246], and anti-diabetic activities [247]. Terpene saponins stimulate VEGF expression and angiogenesis, key factors in wound healing [240, 241]. Mechanism of action studies has found *Panax notoginseng* flower extracts block NF-kB signalling [248, 249], thus affecting the expression of inflammatory cytokines, including IL-6, known to contribute to keloid pathogenesis [250, 251].

Interestingly, saponins isolated from *Panax notoginseng* exhibit antihaemostatic (antiplatelet and anticoagulant) activity when assayed in *vitro* and in *vivo* in a rat model [252]. It was proposed that when administered orally, key bioactive constituents responsible for the haemostatic activity could be modified, which does not occur when administered topically. Of particular note, it is now evident that ginsenosides exhibit significant stereospecific differences in pharmacokinetic properties, including absorption, distribution, and metabolism [253]. These findings may account for some the confusing and contradictory experimental observations. For example, 20(R)-ginsenoside Rh2 inhibits osteoclastogenesis without cytotoxicity. In contrast, 20(S)-ginsenoside Rh2 is strongly cytotoxic for osteoclasts [254]. Such observation highlights the crucial importance of reagent preparation and the need for rigorous quality control.

4.27. *Polygonum cuspidatum*. The root of *Polygonum cuspidatum* is usually formulated with several other ingredients and is most commonly prescribed for treating coughs, hepatitis, jaundice, amenorrhea, leucorrhrea, arthralgia, burns, and snake bite [255]. A diversity of compounds have been isolated from *Polygonum cuspidatum*, dominated by resveratrol, polydatin, and anthraquinones and are presumed to be responsible for *Polygonum cuspidatum*‘s anti-inflammatory, estrogenic, antitumour, antiaging, neuroprotective, and cardio-proactive activities [256–258]. In one recent *in vivo* study examining wound healing in rats, extracts of *Polygonum cuspidatum* were found to increase TGF-β1 expression and to significantly improve wound healing in terms of reepithelization, granulation tissue formation, collagen synthesis, and angiogenesis [259]. Novel anthraquinones isolated from *Polygonum cuspidatum* have been verified to inhibit tyrosinase, the rate-limiting enzyme controlling the synthesis of melanin that gives colour to skin [260].

4.28. *Lithospermum erythrorhizon*. The dried root of *Lithospermum erythrorhizon* is indigenous to northeast China and has potent biological activities, including anti-inflammatory, antibacterial, antiangiogenic, and antitumour qualities [261]. Shikonin, a naphthoquinone, is extracted
Evidence-Based Complementary and Alternative Medicine

from the root of Lithospermum erythrorhizon and stimulates the activity of caspases, poly-(ADP-riboseyl) polymerase (PARP) and reactive oxygen species (ROS), triggering programmed cell death in cancer cell lines [262]. These characteristics prompted investigation of shikonin as a novel scar remediation therapy. These studies found that shikonin inhibits cell proliferation and collagen production in hypertrophic scar-derived human skin fibroblasts [263]. Arnebin-1, a related naphthoquinone extracted from Lithospermum erythrorhizon, has been reported to synergise with VEGF, resulting in significantly improved wound healing in a rat diabetic model [264].

4.29. Rheum officinale. Rheum officinale, also known as Chinese rhubarb, is one of the best known traditional herbal medicines with pharmacological activities. Extracts from the roots of Rheum officinale have strong antibacterial [265], antitumourative [266], anti-inflammatory [267], and haemostatic [268] effects, validating its widespread use for constipation, chronic liver and kidney diseases [265, 269], and skin lesions [270]. Using a rat excisional wound model, Tang et al. found healing was stimulated via TGF-β1-related pathways [270]. The nature of the active component responsible for this activity is not clear. Emodin [1,3,8-trihydroxy-6-methyl-anthaquinone], an anthraquinone derived from the roots of Rheum officinale, has been shown to act as a ligand for PPAR-γ and interact with HSP90 and androgen receptors, in part explaining its therapeutic benefit for chronic diseases [271]. Experimental evidence also indicates a direct association of emodin with NF-κB, AP-1, and STAT3, known regulators of proinflammatory cytokine and mitogenic kinase pathways [272, 273].

4.30. Rhodiola imbricata. Rhodiola imbricata, a perennial herb native to high altitudes (4000–5000 m) of the western Himalayas, is known to contain bioactive flavonoids, coumarine, and phenyl glycosides. These compounds are commonly found in botanical herbal medicines. Ethanolic extracts of rhizomes from Rhodiola imbricata stimulate a robust wound healing response when applied to excisional wounds in rats [274]. Others have reported related functions that may contribute to tissue repair, namely, immunomodulation [275], antioxidation [276], hepatoprotection [277], radioprotection [278], and anticancer [279] properties.

4.31. Salvia miltiorrhiza. The root of the perennial plant Salvia miltiorrhiza (also known as red sage) is highly valued in TCM and used to treat cerebrovascular and cardiovascular diseases, such as stroke, coronary heart disease, and hyperlipidemia [280–283]. To date, Salvia miltiorrhiza has been demonstrated to reduce ischemia and necrosis and to improve the survival of skin flaps after mastectomy [284, 285]. Salvianolic acids isolated from Salvia miltiorrhiza have potent antioxidative capabilities due to their polyphenolic structure [286]. Although hepatoprotective [287], neuroprotective [288], antimicrobial [289], anti-inflammatory [290], and anticancer [291] activities have been reported, the greatest clinical benefit of salvianolic acids appears to be cardiovascular protection, via the promotion of cardiac angiogenesis and inhibition of ischemia and hypoxia during myocardial injury [292]. Water-soluble extracts from Salvia miltiorrhiza, containing danshensu (DSU) and salvianolic acid B (SAB), have been shown to enhance the proliferation of fibroblasts and increase collagen synthesis [293]. Salvianolic acid B is also a potent antagonist of epithelial-to-mesenchymal transition, necessary for wound closure [294]. In contrast, cryptotanshinone, a lipid-soluble terpenoid isolated from Salvia miltiorrhiza, has been demonstrated to downregulate the expression of COL1A1, COL3A1, and α-SMA in hypertrophic scar-derived fibroblasts (HSF), as well as reduce HSF migration and HSF contraction, thus ameliorating fibrosis and scarring [295].

4.32. Sanguisorba officinalis. Sanguisorba officinalis, a member of the family Rosaceae and commonly known as great burnet, is widely distributed in the cooler northern districts of Asia, Europe, and North America [296]. Roots of this plant are a potent haemostatic [297], with antioxidant [298], immunomodulatory [298], anti-inflammatory [299], and antiallergy [300] properties. The traditional use of Sanguisorba officinalis is to control bleeding disorders. It is also applied to heal scalds, burns, allergic skin diseases, urticaria, eczema, and allergic dermatitis [299]. Aqueous extracts made from the root of Sanguisorba officinalis suppress mast cell degranulation, as well as inhibit activation of STAT-1, Jak-2, p38, and JNK pathways and release of inflammatory cytokines [301]. In mouse studies, the oral administration of polysaccharides isolated from Sanguisorba officinalis is claimed to stimulate wound contraction, reduce the time required for reepithelization (wound closure), increase collagen synthesis, and improve angiogenesis [296]. Administration of the polysaccharide extract also resulted in elevated IL-1β and VEGF in mice [296].

4.33. Sophora flavescens. Sophora flavescens is a species from a genus of over 50 plants distributed throughout Asia, Oceania, and the islands of the Pacific. The root of Sophora flavescens is used for conditions involving the heart, liver, intestinal tract, and skin. Experimental investigations indicate extracts from Sophora flavescens stimulate anti-cancer, antibacterial, antiviral, anti-inflammatory, and antipruritic responses and benefits wound healing [302]. One recent report claims it is a potent inhibitor of tyrosinase, the enzyme responsible for synthesizing melanin, thus has potential cosmetic applications as a skin whitener [303]. Other reports claim specific compounds present in Sophora flavescens benefit individuals with androgenetic alopecia [304]. Recently, Xu et al. demonstrated that a mixture of Sophora flavescens and other herbs significantly reduced perianal ulceration in a rat model, finding that the expression of prostaglandin E2 and IL-8 was concomitantly reduced in treated animals [302].
| Botanical name | Traditional name | Plant family | Active ingredients | Part used | Type of extract | Assessment methods | Bioactivities | Clinical use | Formulation | Commercial product |
|---------------|------------------|--------------|--------------------|-----------|----------------|-------------------|---------------|--------------|-------------|------------------|
| Aloe vera     | Lu Hui Asphodelaceae | Leaves | Acemannan [40] | Punch biopsy wounds in Sprague-Dawley rats [40] | Immunomodulatory [40] | Wound healing [34] | Gel [323] | Aloe vera gel |
| Arctium lappa | Niu Bang Zi Asteraceae | Whole root | Arctigenin [324] Arctin [42] Chlorogenic acid [42] Dihydractigenin [42] Insulin [42] Lappasol F [49] Tannin [42] Trachelogenin 4 | No extraction, whole leaves | Human burn wounds [53] | Anticancer [49] | Acne vulgaris [43] | Ointment [53] | Not available |
| Astragalus propinquus | Rehmannia glutinosa | Roots | Astragaloside IV [57] Calycosin [57] Catalpol [57] | Aqueous | Anti-inflammatory [57] | Diabetic foot ulcer [56] | Herbal drink [56] | Not available |
| Ampelopsis japonica | Bai Lian Vitaceae | Root tuber | Catechins [325] Epicatechin gallate [325] Resveratrol [325] | Ethanol | Cutaneous scald injury in rats [63] | Anticancer [62] | Wound plaster (Patent: CN105748741A) | Hydrating Moisturizer |
| Andrographis paniculata | Chuan Xin Lian Acanthaceae | Leaves | Andrographolide [64] Kalmeghin [64] | Aqueous | Excision model in albino Wistar rats [76] | Antimalarial [73] | Dysentery [65] | Paste (applied externally), juice (internally) [326] | Chuan Xin Lian Nei Zhi Di Wan (穿心莲内酯滴丸) |
| Angelica sinensis | Dang Gui Apiaceae | Whole plant | Ferulic acid [83] n-Butyldienephthalide [86] | Ethanol | Cell line antioxidant activity assay [83] | Anticancer [80] | Amenorrhea [78] | Ointment [327] | Blumea leaf oil |
| Blumea balsamifera | Ai Na Xiang Asteraceae | Leaves | L-Borneol [92] | Excision wound model in mice [92] | Antifungal [90] | Beriberi [87] | Oil | Blumea leaf oil |
| Botanical name          | Traditional name | Plant family     | Active ingredients | Part used        | Type of extract | Assessment methods                                                                 | Bioactivities                                                                 | Clinical use                                                                 | Formulation | Commercial product     |
|------------------------|------------------|------------------|--------------------|------------------|-----------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-----------------------------------------------------------------------------|-------------|------------------------|
| *Boswellia sacra*      | Ru Xiang         | Burseraceae      | Boswellic acids    | Resin            | Dry extract     | Rabbit ear hypertrophic scar model of full-thickness scar defect [96]               | Anticancer [329]                                                             | Improvement of blood circulation [93]                                      | Spray        | Frankincense oil       |
|                        |                  |                  |                    |                  |                 | *In vitro* antibacterial assay [102]                                                 | Anti-inflammatory [102]                                                      | Pain treatment [94]                                                         |                          |                        |
|                        |                  |                  |                    |                  |                 | Anti-allergen [99]                                                                  | Viral neuraminidase inhibitor [101]                                          | Rheumatoid arthritis [93]                                                  |                          |                        |
|                        |                  |                  |                    |                  |                 | Anti-fibrotic [97]                                                                  |                                                                                  |                                                                            |                          |                        |
|                        |                  |                  |                    |                  |                 |                                                                                  |                                                                                |                                                                            |                          |                        |
| *Caesalpinia sappan*   | Su Mu            | Fabaceae         |Brazilin            | Roots            | Ethanolic       | *In vitro* anti-inflammatory and wound healing assays [103]                         | Anti-inflammatory [100]                                                     | Improvement of blood circulation [98]                                      | Tablets       |                        |
|                        |                  |                  | Sappanchalcone     | Roots            | Ethanol         | *Viral* neutrophil [101]                                                            |                                                                                  | Pain treatment [98]                                                        |                          |                        |
|                        |                  |                  |                    |                  |                 |                                                                                  |                                                                                |                                                                            |                          |                        |
| *Calendula officinalis*| Jin Zhan Ju      | Asteraceae       | Esculetin [108]    | Flower           | Hexane and ethanol | *Scratch* assay [107]                                                             | Anti-inflammatory [107]                                                     | Burns [105]                                                                | Tablets       |                        |
|                        |                  |                  | Quercetin-3-O-    | Flower           | Hexane and ethanol | *Excision wound* model in BALB/c mice [109]                                        | Anti-fibrotic [107]                                                        | Oedema [98]                                                               |                          |                        |
|                        |                  |                  | glucoside [108]    | Flower           | Ethanol         | *Punch* wound model in rats [110]                                                   | Anti-inflammatory [106]                                                    |                                                                            |                          |                        |
|                        |                  |                  |                    |                  |                 |                                                                                      |                                                                                   |                                                                            |                          |                        |
| *Camellia sinensis*    | Cha Shu          | Theaceae         | Epcatechin-3-gallate | Leaves          | Methanol        | *In vitro and in vivo* keloid fibroblast models [125]                               | Anti-inflammatory [113]                                                     | Angina pectoris [332]                                                      | Oil          | Tea tree oil            |
|                        |                  |                  | Epicatechin [111]  | Leaves          | Methanol        | *Anti-fibrotic* model in NIH3T3 fibroblast proliferation assay [115]                | Anti-inflammatory [113]                                                     | Asthma [332]                                                              |                          |                        |
|                        |                  |                  | Epigallocatechin   | Leaves          | Methanol        | *Neuroprotective* model in Sprague-Dawley rats [121]                               | Anti-inflammatory [113]                                                     | Bacterial infections [332]                                                 |                          |                        |
|                        |                  |                  | [111]              |                |                 |                                                                                      |                                                                                   |                                                                            |                          |                        |
|                        |                  |                  | Epigallocatechin-3-gallate [111] | | |                                                                                      |                                                                                  |                                                                            |                          |                        |
|                        |                  |                  |                    |                  |                 |                                                                                      |                                                                                  |                                                                            |                          |                        |
| *Carthamus tinctorius* | Hong Hua         | Asteraceae       | Hydroxysafflor     | Seeds           | Re flux        | Antioxidant enzyme assay in azahalfish [333]                                        | Antioxidant [132]                                                          | Blood stasis [334, 335]                                                     | Oil          | Safflower oil (红花油) |
|                        |                  |                  | yellow A [130]     |                |               |                                                                                      |                                                                                  |                                                                            |                          |                        |
|                        |                  |                  |                    |                |               |                                                                                      |                                                                                  |                                                                            |                          |                        |
| *Celosia argentea*     | Qing Xiang       | Amaranthaceae    | Celosin I [139]    | Leaves          | Ethanol        | Rat burn wound model [137]                                                          | Antioxidant [137]                                                          | Skin sores [137]                                                          | Poultice of stems and leaves (topically) [336] | Not available |
|                        |                  |                  | Celosin II [139]   |                |               |                                                                                      |                                                                                  |                                                                            |                          |                        |
| Botanical name | Traditional name | Plant family | Active ingredients | Part used | Type of extract | Assessment methods | Bioactivities | Clinical use | Formulation | Commercial product |
|----------------|------------------|--------------|--------------------|-----------|-----------------|-------------------|---------------|-------------|-------------|-------------------|
| **Centella asiatica** | Ji Xue Cao | Apiaceae | Asiaticoside [144], Madecassoside [146] | Aerial parts | Hexane, ethyl acetate, methanol, and water | Incision and partial-thickness burn wound models in rats [142] | Anti-inflammatory [142], Antioxidant [142], Proangiogenic [142] | Wounds [142] | Oral form (tablets, drops) | Madecassol® [143], Centellase® Blastoeitimulina® [337], Collaven® [338] |
| **Cinnamomum cassia** | Rou Gui | Lauraceae | Cinnamaldehyde [147] | Bark, Whole plant | Volatile oil | *In vitro* and *in vivo* angiogenic activity assay [147], Excision wound model in rats [339], Excision wound model in diabetic rats [164], Human recurrent aphthous stomatitis [165], *In vitro* cell migration assay [166] | Analgesic [159], Antidiabetic [340], Anti-inflammatory [150], Antimicrobial [341], Antioxidant [342], Analgesia [147], Antioxidant [342] | Gastrointestinal diseases [161, 162], Wounds and pain [163, 165] | Oil | Cinnamon cassia oil |
| **Commiphora myrrha** | Mo Yao | Burseraceae | Furanoedesma-1,3-diene [165], Terpene [165] | Leaves and resin, Resin | Dry extract | *In vitro* and *in vivo* cell migration assay in diabetic rats [166] | Analgesic [159], Antibacterial [158], Anti-inflammatory [157], Antioxidant [156], Digestive diseases [347], Liver disorders [347], Menstrual difficulties [347], Pain disorders [347], Sprains [347], Wounds [347] | Capsules [348] | Kordel’s Theracurmin™, BCM-95®, Theracurmin™, CurcuVIVA™, CurcuMIND, Longvida RD, CAVACURMIN®, Biocurcumax™ [349] |
| **Curcuma longa** | Jiang Huang | Zingiberaceae | Curcuminoids [170] | Rhizomes | Nanosuspension | Antioxidant analysis [343], Antibacterial [344], Anti-inflammatory [345], Antioxidant [346] | Digestive diseases [347], Liver disorders [347], Menstrual difficulties [347], Pain disorders [347], Sprains [347], Wounds [347] | Capsules [348] | Kordel’s Theracurmin™, BCM-95®, Theracurmin™, CurcuVIVA™, CurcuMIND, Longvida RD, CAVACURMIN®, Biocurcumax™ [349] |
| **Daphne genkwa** | Yuan Hua | Thymelaceae | Daphnodorin B [177], Daphnodorin G [177], Daphnodorin G 3'-methylene [177], Daphnodorin H [177], Daphnodorin H 3'-methylene [177], Genkwanin [177], Genkwanol A [177], Yuanhucine [177], Yuenkanin [177] | Flower, Roots | Aqueous | Human wounds from anal fistula therapy [171], Anti-inflammatory [175], Antitumour [177], Immunoregulatory [178, 179], Melanogenesis inhibitory [172] | Coughs [174], Wounds [171] | Not available | Not available |
| Botanical name         | Traditional name  | Plant family | Active ingredients                      | Part used             | Type of extract | Assessment methods                                      | Bioactivities                                      | Clinical use                                      | Formulation               | Commercial product         |
|-----------------------|-------------------|--------------|----------------------------------------|-----------------------|-----------------|---------------------------------------------------------|---------------------------------------------------|-----------------------------------------------|---------------------------|----------------------------|
| **Entada phaseoloides** | Ke Teng           | Fabaceae     | Tannin [182]                           | Stem skin and seeds   | Ethanol         | Acetic acid-induced mouse writhing experiment [351]   | Antibacterial [180]                               | Aging [352]                     | Not available             | Not available             |
| **Hibiscus rosa-sinensis** | Zhu Jin           | Malvaceae    | Anthocyanins [353]                     | Flower                | Ethanol         | Excision, incision and dead space wound models in rats [187, 188] | Antioxidant [181]                                | Antitumour [353]                    | Powder                    | Lustrous Henna* Shampoo powder |
| **Ganoderma lucidum** | Ling Zhi          | Ganodermataceae | Ganoderma lucidum polysaccharide [204] | Fruiting body         | Aqueous         | Excision wound model in diabetic rats [190]           | Antihyperlipidemic [197]                         | Anti-inflammatory [192–194] | Cancer                     | Diabetes                  | Leukaemia [189]             | Uker [201]                 |
| **Ligusticum striatum** | Chuan Xiong       | Apiaceae     | Ferulic acid [206]                     | Rhizome               | Extracted by hydrodistillation | Hypertrophic scar rabbit model [208] | Anti-inflammatory [211]                           | Headache [206]                     | Ischaemic disorders [205] | Not available             | Chuanxiong chatiao Wan (川芎茶调丸) |
| **Lonicera japonica** | Jin Yin Hua       | Caprifoliaceae | Biflavonoids [209] Dicaffeoylquinic acid [209] Phenolic acids [209] Quercetin [209] | Flowering aerial parts | Ethanol         | Rat excision wound model [212]                       | Anti-inflammatory [211]                           | Antimicrobial [211]                  | Essential oils [210]     | Not available             |
| **Paeonia suffruticosa** | Mu Dan            | Paeoniaceae  | Saffrophanes A, B, C, and D [359] Glycolyoxypaeoniflorin [359] Glycoly-paeoniflorin [359] | Root bark             | Water, ethanol-water | In vitro cell viability and proliferation assays [220] | Infectious diseases [209]                        | Genital diseases [360]            | Ointment                   | Winvivo (Puji) ointment     |
| Botanical name       | Traditional name | Plant family | Active ingredients | Part used         | Type of extract | Assessment methods                                                                 | Bioactivities                                                                 | Clinical use                                                                 | Formulation                                                                 |
|---------------------|------------------|--------------|--------------------|-------------------|-----------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| *Panax ginseng*     | Ren Shen         | Araliaceae   | Ginsenosides Rb1, Rb2, R, and Rd [232] | Leaves, root, and whole plant | Ethanol, Dichloromethane, ethanol, butanol, and methanol | Laser burn and excision wounds models in mice [236] | Cell migration and wound healing assays [221, 237–239] | Antiaging [230] | Wound healing [221] | Not available | Ginseng Strong 200 mg | Ginsemax® | Ginseng Vita-Complex |
| *Panax notoginseng* | San Qi           | Araliaceae   | Notoginsenoside F1 [240] | Leaves, flower, roots, and rhizome | Steamed extraction, | In vitro anticoagulation and antioxidation test, in vivo hemostasis and anti-inflammation test [362] | Anticancer [246] | Trauma [240, 241] | Powder on wound | Spray on wound | San Qi Fen (三七粉) | Yunnan Baiyao (云南白药) |
| *Polygonum cuspidatum* | Hu Zhang         | Polygonaceae | Emodin [260]Polydatin [258] Resveratrol [256] | Roots | Ethanol | Full-thickness excision wounds in rats [259] | Antiangiogenic [261] | Capsules | Resveratrol supplement |
| *Lithospermum erythrorhizon* | Zi Cao           | Boraginaceae | Amethin-1 [264]Shikonin [363] | Roots | Frozen and ground | Apoptotic effects against murine primary peritoneal macrophages [364] | Anticancer [265] | Wounds [264] | Oil formulations, gel [365] | Burt’s bee Res-Q ointment (神奇紫草膏) |
| *Rheum officinale*  | Da Huang         | Polygonaceae | Emodin [270] | Roots | Ethanol | Rat excision wound model [270] | Antiangiogenic [267] | Pills | Dahuang Zhechong Wan (大黄蛰虫丸) |
| *Rhodiola rosea*    | Hong Jie         | Crassulaceae | Gallic acid [277] p-Tyrosol [277] Resveratrol [277] Rosin [277] | Rhizome | Ethanol | Rat excision wound model [274] | Antioxidative [276] | Not available | Not available |

Table 1: Continued.
| Botanical name       | Traditional name | Plant family | Active ingredients                  | Part used | Type of extract | Assessment methods                                                                 | Bioactivities                                                                 | Clinical use                                                                 | Formulation            | Commercial product          |
|----------------------|------------------|--------------|-------------------------------------|-----------|-----------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------|------------------------|-----------------------------|
| *Salvia miltiorrhiza* | Dan Shen         | Lamiaceae    | Cryptotanshinone [366] Danshensu [293] Salvianolic acid B [293] | Leaves    | Aqueous         | In vitro proliferative and angiogenic assays; second-degree burn wound model in rats [367]; Cell proliferation assay; in vitro assays for collagen and melanin synthesis [293] | Anticancer [291]; Anti-inflammatory [290]; Antimicrobial [289]; Antioxidant [286]; Antiplatelet aggregation [368]; Proangiogenic [367, 369, 370] | Blood stasis [371, 372]; Cardiovascular diseases [282] | Pills                 | Compound danshen dripping pills (复方丹参滴丸) |
| *Sanguisorba officinalis* | Di Yu            | Rosaceae     | Tannins [296] Triterpenoid glycosides [296] Triterpenoids [296] | Roots     | Ethanol         | Burn wound model in mice [296] | Antiallergy [300]; Anti-inflammatory [299]; Antioxidant [298]; Haemostatic [297]; Immunomodulatory [298] | Burns [299]; Chronic intestinal infections [373]; Haemorrhoids [373]; Menorrhagia [373]; Scalds [299]; Asthma [374]; Burns [374]; Dysentery [374]; Eczema [374]; Fever [374]; Hematochepia [374]; Inflammatory [374]; Jaundice [374]; Oliguria [374]; Vulvar swelling [374] | Oral administration | Sanguisorba officinalis Mother Tincture |
| *Sophora flavescens*  | Ku Shen          | Fabaceae     | Kushenol [374] Sophoradavananone B [374] | Roots     | Cellulose column | Human liver LO2 proliferation and viability assay [375] | Analgesic [376]; Antihelmintic [376]; Antipyretic [376]; Skin whitening [376]; Stomachic [376] | Burns; Dysentery; Eczema; Menorrhagia; Oliguria; Rheumatism; Skin infections | Gel                  | Kushen gel (苦参凝胶) | GATULINE® Spot-Light |
| *Stemona tuberosa*    | Bai Bu           | Stemonaceae  | Tubernostemonine N [306]            | Roots     | Methanol        | Mouse fibroblast NIH3T3 proliferation assay [309] | Antibacterial [307]; Anti-inflammatory [306]; Antioxidant [308]; Antitussive [305]; Neuroprotective [377] | Insect pests [307] | Not available               | Not available          |
| *Wedelia tribracteata*|                  | Asteraceae   | Kaurenoic acid [310] Luteolin [311] | Leaves    | Ethanol         | In vitro antimicrobial assay, cell proliferation, and viability assays [310] | Antimicrobial [310]; Antioxidant [311]; Antitumour [311] | Arthritic painful joints [310]; Rheumatism [310]; Stubborn wounds [310] | Not available | Not available               |
| *Zanthoxylum bungeanum*| Hua Jiao         | Rutaceae     | Azelcin [378] Hyperoside [378] Quercitrin [378] Rutin [378] | Seed oil  | Press extraction | Rat scald wound model [378] | Anaesthetic [314]; Antiasthma [318]; Anti-inflammatory [317]; Antioxidant [316]; Antitumour [315] | Skin wrinkles [321] | Cream                     | ZANTHALENE*             |
4.34. Stemona tuberosa. *Stemona tuberosa* is another of the 50 fundamental herbs used in TCM. It has strong insecticidal activity, the foundation property for its traditional use in treating impetigo, scabies, louse, lice, and ticks. It is also used as a mosquito repellent and preservative to protect stored cereals from insects [305]. In traditional medicine, it is used to treat coughs and lung infections. Alkaloid and stilbenoid isolated from the root of *Stemona tuberosa* are reported to have anti-inflammatory [306] and antibacterial [307] effects, while the dehydrotocopherol derivatives have been found to scavenge oxygen and free radicals [308]. Tocopherols isolated from the root of *Stemona tuberosa* increase cell proliferation in the mouse fibroblast NIH3T3 cells, suggesting the potential use of these compounds as wound healing agents [309].

4.35. Wedelia trilobata. The plant *Wedelia trilobata*, which is also known as *Sphagneticola trilobata*, was originally native to the tropical Americas; however, as one of the world’s most invasive species, it is now ubiquitous throughout the tropics. Alcohol extracts made from the leaves of *Wedelia trilobata* have been used to treat rheumatism, stubborn wounds, and arthritic painful joints [310]. Luteolin, a flavonoid present in the leaves, has been demonstrated to contribute to the medicinal value of *Wedelia trilobata*, conferring neuroprotective, anticancer, antioxidant, and immunomodulatory activities [311]. Traditional healers use the leaves of *Wedelia trilobata* to treat skin wounds. Luteolin inhibits the expression of NF-κB-regulated proinflammatory cytokines, a characteristic feature of skin infection and psoriasis [312]. In a study designed to validate this traditional use, Balekar et al. fractionated ethanolic extracts from the leaves of *Wedelia trilobata* and assayed them in vitro [310]. Specific subfractions were found to support fibroblast viability, proliferation, and migration. Different subfractions were also found to be active against Staphylococcus aureus and Staphylococcus epidermidis [310].

4.36. Zanthoxylum bungeanum. *Zanthoxylum bungeanum* is a flowering plant belonging to the Rutaceae family, native to eastern provinces of China. It yields important food ingredients such as sichuan pepper [313]. Over 140 compounds have been isolated from *Zanthoxylum bungeanum*, including alkaloids, terpenoids, flavonoids, and free fatty acids, eliciting a wide variety of biological responses, including analgesic [314], antitumor [315], antioxidant [316], anti-inflammatory [317], antibacterial, antifungal, and antiasthma properties [318]. *Zanthoxylum bungeanum* are known in traditional Western folk medicine as “toothache trees,” useful for treating pruritus (itch) and chronic pain. The pericarp from the fruit berry is commonly used to formulate TCM oils, powders, tinctures, elixirs, and pills [319]. Extracts from *Zanthoxylum bungeanum* are also prescribed for skin infections, including acne, eczema, scalds, and wound healing [320]. One unique property of fruit husk extracts from *Zanthoxylum bungeanum* is as a lifting agent for skin wrinkles. When applied topically to skin, subcutaneous muscles are relaxed, reducing skin wrinkles, thus has attracted the attention of cosmetic manufacturers [321]. Another interesting property reportedly associated with essential oils of *Zanthoxylum bungeanum* is the capacity to enhance percutaneous drug delivery [322].

5. Conclusion

We have surveyed and presented an overview of evidence that explains why many medicinal plants are used as traditional treatments for cutaneous wounds and clinical skin disorders. Medicinal plants have been the first line of treatment for trauma, infection, disease, and injury from prehistory. Over millennia, humans have learned to identify and transform the botanical resources from the immediate environment, and with the development of trade, as food and medicine. A great many of these “ancient” and traditional medical plants have been validated to confer therapeutic benefits, albeit not always in controlled clinical trials. One unexpected outcome from validation studies is just how many medical plants synthesize equivalent or closely related compounds. Consequently, it is not surprising that many biological properties are also shared by unrelated species. Also shared are many of the same biological targets and pathways; many of these are also key events in the mammalian wound healing cascade. Many of the identified compounds target mitogenic pathways (e.g., AKT, P13K, SMAD, and cyclins), the proinflammatory NF-κB pathway (e.g., caspases, interleukins, TNF-α, and TGF-β1), angiogenesis pathway (e.g., VEGF), extracellular matrix synthesis (e.g., MMPs), and differentiation pathways (e.g., α-SMA).

The active ingredients, part of use, type of extract, assessment methods, bioactivities, clinical use, formulation, and commercial product of the medicinal plants are summarized in Table 1. While experimental evidence has been acquired for each documented plant from in vitro or in vivo analyses, not every mechanism of action has been verified. On the contrary, several compounds, including acemannan (from Aloe vera), hydroxysafflor yellow A (from Carthamus tinctorius), polysaccharide (from Ganoderma lucidum), phthalide lactones, and alkaloids (from Ligusticum striatum), saponins (from Panax ginseng), shikonin and armebin-1 (from Lithospermum erythrorhizon), salvianolic acids (from Salvia miltiorrhiza), polysaccharides (from Sanguisorba officinalis), and alkaloid and stilbenoid (from Stemona tuberosa) are well characterised and have been demonstrated to have properties that benefit wound healing. In particular, Centella asiatica, Curcuma longa, and Paeonia suffruticosa are popular medicinal products in several global markets.

We provide these data in the belief that we still have much to learn from traditional practices, some of which undoubtedly could deliver novel reagents and therapies for today’s therapeutic challenges. Notwithstanding, we recognise that modern medicine and drugs remain effectively inaccessible (and unaffordable) to the majority of the world’s population. For this reason alone, traditional medicine continues to be the first line of treatment, indeed, frequently the only line of treatment for many. With greater understanding of traditional practices comes appreciation and
benefit to more of the world’s peoples. We would like to see that this knowledge is not discarded by “modern medicine” but leveraged through investigation to benefit all.

Abbreviations

- **a.k.a.:** Also known as
- **AKT:** Protein kinase B
- **ALT:** Alanine aminotransferase
- **ANBP:** *Agrimonia eupatoria* (A), *Nelumbo nucifera* (N), *Boswellia sacra* (B), and pollen from *Typha angustifolia* (P)
- **AP-1:** Activator protein 1 (transcription factor)
- **α-SMA:** Alpha smooth muscle actin
- **AST:** Aspartate aminotransferase
- **COX-2:** Cyclooxygenase-2
- **CTGF:** Connective tissue growth factor
- **DAMPs:** Damage-associated molecular patterns
- **DSU:** Danshensu
- **ECM:** Extracellular matrix
- **EGCG:** (-)-Epigallocatechin-3-gallate
- **ERK:** Extracellular signal-regulated kinase
- **ET-1:** Endothelin 1
- **HSF:** Hypertrophic scar-derived fibroblasts
- **HSYA:** Hydroxysafflor yellow A
- **iNOS:** Inducible nitric oxide synthase
- **Jak-2:** Janus kinase 2
- **IL-1α:** Interleukin-1 alpha
- **IL-1β:** Interleukin-1 beta
- **IL-6:** Interleukin-6
- **IL-8:** Interleukin-8 (CXCL8)
- **IL-10:** Interleukin-10
- **iNOS:** Inducible nitric oxide synthase
- **JNK:** c-Jun N-terminal kinase
- **MAPK:** Mitogen-activated protein kinase
- **MEK:** Mitogen-activated protein kinase, MAPK/ERK kinase
- **MMP-1:** Matrix metalloproteinase-1 (interstitial collagenase)
- **MMP-2:** Matrix metalloproteinase-2 (gelatinase A)
- **MMP-3:** Matrix metalloproteinase-3 (stromelysin-1)
- **mRNA:** Messenger ribonucleic acid
- **mTO:** Mammalian target of rapamycin
- **NF-κB:** Nuclear factor-kappa B
- **PAMPs:** Pathogen-associated molecular patterns
- **PARP:** Poly-ADP-ribosyl polymerase
- **PGE2:** Prostaglandin E2
- **PI3K:** Phosphatidylinositol-4,5-bisphosphate 3-kinase
- **ROS:** Reactive oxygen species
- **SAB:** Salvianolic acid B
- **SBP:** Shexiang Baoxin Pill
- **SMAD:** Sapien homologue of mothers against decapentaplegic
- **STAT-1:** Signal transducer and activator of transcription 1
- **STAT3:** Signal transducer and activator of transcription 3
- **TCM:** Traditional Chinese medicine
- **TGF-β1:** Transforming growth factor-beta 1
- **TNF-α:** Tumour necrosis factor-alpha
- **TXA2:** Thromboxane A2
- **VEGF:** Vascular endothelial growth factor
- **WHO:** World Health Organisation
- **5-LOX:** Arachidonate 5-lipoxygenase.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

This work was supported by funding from Singapore’s Agency for Science, Technology and Research, “SPF 2013/004: Skin Biology Basic Research” and the “Wound Care Innovation for the Tropics” IAF-PP/2017 (HBMS) (H17/01/a0/009).

References

[1] R. Xu, G. Luo, H. Xia et al., “Novel bilayer wound dressing composed of silicone rubber with particular micropores enhanced wound re-epithelialization and contraction,” *Biomaterials*, vol. 40, pp. 1–11, 2015.
[2] J. H. Talbott, “A short history of medicine,” *JAMA*, vol. 180, no. 9, p. 794, 1962.
[3] WHO Traditional Medicine Strategy: 2014–2023, ISBN: 9789241506090, http://www.who.int/traditional-complementary-integrative-medicine/en/.
[4] A. Ghahariy and A. Ghaffari, “Role of keratinocyte-fibroblast cross-talk in development of hypertrophic scar,” *Wound Repair and Regeneration*, vol. 15, no. 1, pp. 46–53, 2007.
[5] S. A. Eming, P. Martin, and M. Tomic-Canic, “Wound repair and regeneration: mechanisms, signaling, and translation,” *Science Translational Medicine*, no. 265, Article ID 265sr6, 2014.
[6] A. K. Arya, K. Tripathi, and P. Das, “Promising role of ANGPTL4 gene in diabetic wound healing,” *The International Journal of Lower Extremity Wounds*, vol. 13, no. 1, pp. 58–63, 2014.
[7] E. M. Golebiewska and A. W. Poole, “Platelet secretion: from haemostasis to wound healing and beyond,” *Blood Reviews*, vol. 29, no. 3, pp. 153–162, 2015.
[8] S. Enoch and D. J. Leaper, “Basic science of wound healing,” *Surgery (Oxford)*, vol. 26, no. 2, pp. 31–37, 2008.
[9] P. Martin and S. J. Leibovich, “Inflammatory cells during wound repair: the good, the bad and the ugly,” *Trends in Cell Biology*, vol. 15, no. 11, pp. 599–607, 2005.
[10] B. M. Delavary, W. M. van der Veer, M. van Egmond, F. B. Niessen, and R. H. J. Beelen, “Macrophages in skin injury and repair,” *Immunobiology*, vol. 216, no. 7, pp. 753–762, 2011.
[11] A. Kasuya and Y. Tokura, “Attempts to accelerate wound healing,” *Journal of Dermatological Science*, vol. 76, no. 3, pp. 169–172, 2014.
[12] D. Fan, A. Takawale, J. Lee, and Z. Kassiri, “Cardiac fibroblasts, fibrosis and extracellular matrix remodeling in heart disease,” *Fibrogenesis & Tissue Repair*, vol. 5, no. 1, p. 15, 2012.
[13] N. Kioka, T. Ito, H. Yamashita et al., “Crucial role of vinexin for keratinocyte migration in vitro and epidermal wound healing in vivo,” *Experimental Cell Research*, vol. 316, no. 10, pp. 1728–1738, 2010.
[14] S. K. Sarkar, B. Marmer, G. Goldberg, and K. C. Neuman, “Single-molecule tracking of collagenase on native type I
collagen fibrils reveals degradation mechanism,” *Current Biology,* vol. 22, no. 12, pp. 1047–1056, 2012.

[15] Y. Akasaka, I. Ono, T. Kamiya et al., “The mechanisms underlying fibroblast apoptosis regulated by growth factors during wound healing,” *The Journal of Pathology,* vol. 221, no. 3, pp. 285–299, 2010.

[16] S. McDougall, J. Dillon, J. Sherratt, and P. Maini, “Fibroblast migration and collagen deposition during dermal wound healing: mathematical modelling and clinical implications,” *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences,* vol. 364, no. 1843, pp. 1385–1405, 2006.

[17] R. Sharma and J. John, “Role of stem cells in the management of chronic wounds,” *Indian Journal of Plastic Surgery,* vol. 45, no. 2, pp. 237–243, 2012.

[18] D. Deufert and R. Graml, “Disease-specific, health-related quality of life (HRQoL) of people with chronic wounds—a descriptive cross-sectional study using the wound-QoL,” *Wound Medicine,* vol. 16, pp. 29–33, 2017.

[19] R. G. Frykberg and J. Banks, “Challenges in the treatment of chronic wounds,” *Advances in Wound Care,* vol. 4, no. 9, pp. 560–582, 2015.

[20] I. Garcia-Orue, J. L. Pedraza, R. M. Hernandez, and M. Igarreta, “Nanotechnology-based delivery systems to release growth factors and other endogenous molecules for chronic wound healing,” *Journal of Drug Delivery Science and Technology,* vol. 42, pp. 2–17, 2017.

[21] A. Budovsky, L. Yarmolinsky, and S. Ben-Shabat, “Effect of medicinal plants on wound healing,” *Wound Repair and Regeneration,* vol. 23, no. 2, pp. 171–183, 2015.

[22] S. Schreml, R.-M. Szeimies, L. Prantl, M. Landthaler, and P. Babillas, “Wound healing in the 21st century,” *Journal of the American Academy of Dermatology,* vol. 63, no. 5, pp. 866–881, 2010.

[23] M. P. Caley, V. L. C. Martins, and E. A. O’Toole, “Metalloproteinases and wound healing,” *Advances in Wound Care,* vol. 4, no. 4, pp. 225–234, 2015.

[24] G. Han and R. Celley, “Chronic wound healing: a review of current management and treatments,” *Advances in Therapy,* vol. 34, no. 3, pp. 599–610, 2017.

[25] M. C. Robson and A. Barbul, “Guidelines for the best care of chronic wounds,” *Wound Repair and Regeneration,* vol. 14, no. 6, pp. 647–648, 2006.

[26] S. Bhattacharyya, “Wound healing through the ages,” *Indian Journal of Plastic Surgery,* vol. 45, no. 2, pp. 177–179, 2012.

[27] G. Han and R. Celley, “Chronic wound healing: a review of current management and treatments,” *Advances in Therapy,* vol. 34, no. 3, pp. 599–610, 2017.

[28] R. Edwards and K. G. Harding, “Bacteria and wound healing,” *Current Opinion in Infectious Diseases,* vol. 17, no. 2, pp. 91–96, 2004.

[29] L. Kalan, M. Zhou, M. Labbie, and B. Willing, “Measuring the microbiome of chronic wounds with use of a topical antimicrobials dressing—a feasibility study,” *PLoS One,* vol. 12, no. 11, Article ID e0187728, 2017.

[30] F. Han, Y. Li, X. Zhang, A. Song, H. Zhu, and R. Yin, “A pilot study of direct infusion analysis by FT-ICR MS for rapid differentiation and authentication of traditional Chinese herbal medicines,” *International Journal of Mass Spectrometry,* vol. 403, pp. 62–67, 2016.

[31] H. Yuan, Q. Ma, L. Ye, and G. Piao, “The traditional medicine and modern medicine from natural products,” *Molecules,* vol. 21, no. 5, 2016.

[32] P. Wangchuk, “Therapeutic applications of natural products in herbal medicines, biodiscovery programs, and biomedicine,” *Journal of Biologically Active Products from Nature,* vol. 8, no. 1, pp. 1–20, 2018.

[33] Y. Qi, S. Li, Z. Pi et al., “Chemical profiling of Wu-tou decoction by UPLC-Q-TOF-MS,” *Talanta,* vol. 118, pp. 21–29, 2014.

[34] I. García-Orue, G. Gainza, F. B. Gutierrez et al., “Novel nanofibrous dressings containing rhEGF and Aloe vera for wound healing applications,” *International Journal of Pharmaceutics,* vol. 523, no. 2, pp. 556–566, 2017.

[35] B. Salehi, S. Albayrak, H. Antalak et al., “Aloe genus plants: from farm to food applications and phytopharmacotherapy,” *International Journal of Molecular Sciences,* vol. 19, no. 9, pp. 2843, 2018.

[36] R. Lawrence, P. Tripathi, and E. Jeyakumar, “Isolation, purification and evaluation of antibacterial agents from Aloe vera,” *Brazilian Journal of Microbiology,* vol. 40, no. 4, pp. 906–915, 2009.

[37] D. Martinez-Romero, N. Alburerque, J. M. Valverde et al., “Postharvest sweet cherry quality and safety maintenance by Aloe vera treatment: a new edible coating,” *Postharvest Biology and Technology,* vol. 39, no. 1, pp. 93–100, 2006.

[38] P. Ali, Y.-F. Chen, and E. Sargsyan, “Chapter 12-bioactive molecules of herbal extracts with anti-inflammatory and wound healing properties,” in *Microbiology for Surgical Infections,* K. Kon and M. Rai, Eds., pp. 205–220, Academic Press, Amsterdam, Netherlands, 2014.

[39] W. Xing, W. Guo, C.-H. Zou et al., “Acekmann accelerates cell proliferation and skin wound healing through AKT/mTOR signaling pathway,” *Journal of Dermatological Science,* vol. 79, no. 2, pp. 101–105, 2015.

[40] S. Jettanachewchankit, S. Sasithanasate, P. Sangvanich, W. Banlurana, and P. Thunyakitspal, “Acekmann stimulates gingival fibroblast proliferation; expressions of keratinocyte growth factor-1, vascular endothelial growth factor, and type I collagen; and wound healing,” *Journal of Pharmacological Sciences,* vol. 109, no. 4, pp. 525–531, 2009.

[41] S.-C. Lin, C.-H. Lin, C.-C. Lin et al., “Hepatoprotective effects of *Arctium lappa* linne on liver injuries induced by chronic ethanol consumption and potentiated by carbon tetrachloride,” *Journal of Biomedical Science,* vol. 9, no. 5, pp. 401–409, 2002.

[42] Y.-S. Chan, L.-N. Cheng, J.-H. Wu et al., “A review of the pharmacological effects of *Arctium lappa* (burdock),” *Inflammopharmacology,* vol. 19, no. 5, pp. 245–254, 2011.

[43] A. Miglani and R. K. Manchanda, “Observational study of *Arctium lappa* in the treatment of acne vulgaris,” *Homeopathy,* vol. 103, no. 3, pp. 203–207, 2014.

[44] R. C. Fierascu, M. I. Georgiev, I. Fierascu et al., “Mitodepressive, antioxidant, antifungal and anti-inflammatory effects of wild-growing Romanian native *Arctium lappa* L. (Asteraceae) and *Veronica persica* Poiret (Plantaginaceae),” *Food and Chemical Toxicology,* vol. 111, pp. 44–52, 2018.

[45] A. B. de Almeida, M. Sánchez-Hidalgo, A. R. Martin et al., “Anti-inflammatory intestinal activity of *Arctium lappa* L. (Asteraceae) in TNBS colitis model,” *Journal of Ethnopharmacology,* vol. 146, no. 1, pp. 300–310, 2013.

[46] A. Ahangpour, H. Heidari, A. A. Oroojan, F. Mirzavandi, K. Nasr Esfehani, and Z. Dehghan Mohammadi, “Antidiabetic, hypolipidemic and hepatoprotective effects of *Arctium lappa* root’s hydro-alcoholic extract on nicotinamide-streptozotocin induced type 2 model of diabetes in male rats,” *Pharmacological Research,* vol. 100, pp. 1–8, 2015.
mice,” *Avicenna Journal of Phytomedicine*, vol. 7, no. 2, pp. 169–179, 2017.

[J7] J. V. Pereira, D. C. B. Bergamo, J. O. Pereira, S. d. C. França, R. C. L. R. Pietro, and Y. T. C. Silva-Sousa, “Antimicrobial activity of *Arctium lappa* constituents against microorganisms commonly found in endodontic infections,” *Brazilian Dental Journal*, vol. 16, no. 3, pp. 192–196, 2005.

[J8] M. M. Dias, O. Zuza, L. R. Riani et al., “In vitro schistosomicidal and antiviral activities of *Arctium lappa* L. (Asteraceae) against Schistosoma mansoni and Herpes simplex virus-1,” *Biomedicine & Pharmacotherapy*, vol. 94, pp. 489–498, 2017.

[J9] Q. Sun, K. Liu, X. Shen et al., “Lappanol F, a novel anticancer agent isolated from plant *Arctium Lappa L.*,” *Molecular Cancer Therapeutics*, vol. 13, no. 1, pp. 49–59, 2014.

[J10] F. de Souza Predes, M. A. da Silva Diamante, M. A. Foglio et al., “Biodegradable nanofibers derived from *Arctium lappa* L. (Asteraceae) for repair of the skin,” *Brazilian Journal of Chemical Engineering*, vol. 30, no. 4, pp. 953–962, 2013.

[J11] P.-P. Liu, G.-S. Shan, F. Zhang, J.-N. Chen, and T.-Z. Jia, “Preparations of *Arctium lappa* fruit extract: an effective model of estrogenic skin aging,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J12] L. Sun, B. Stefanoff, and M. Gold, “Preparations of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.

[J13] A. Amish Burn Study, N. M. Kolacz, M. T. Jaroch et al., “Hepatoprotective effect of *Arctium lappa* root extract on cadmium toxicity in adult Wistar rats,” *Biological Trace Element Research*, vol. 160, no. 2, pp. 250–257, 2014.

[J14] A. Knott, K. Reuschlein, H. Mielke et al., “Natural *Arctium lappa* fruit extract improves the clinical signs of aging skin,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J15] E. Pomari, B. Stefanon, and M. Colitti, “Effect of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.

[J16] G. Amish Burn Study, N. M. Kolacz, M. T. Jaroch et al., “Hepatoprotective effect of *Arctium lappa* root extract on cadmium toxicity in adult Wistar rats,” *Biological Trace Element Research*, vol. 160, no. 2, pp. 250–257, 2014.

[J17] A. Knott, K. Reuschlein, H. Mielke et al., “Natural *Arctium lappa* fruit extract improves the clinical signs of aging skin,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J18] E. Pomari, B. Stefanon, and M. Colitti, “Effect of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.

[J19] A. Amish Burn Study, N. M. Kolacz, M. T. Jaroch et al., “Hepatoprotective effect of *Arctium lappa* root extract on cadmium toxicity in adult Wistar rats,” *Biological Trace Element Research*, vol. 160, no. 2, pp. 250–257, 2014.

[J20] A. Knott, K. Reuschlein, H. Mielke et al., “Natural *Arctium lappa* fruit extract improves the clinical signs of aging skin,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J21] E. Pomari, B. Stefanon, and M. Colitti, “Effect of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.

[J22] A. Amish Burn Study, N. M. Kolacz, M. T. Jaroch et al., “Hepatoprotective effect of *Arctium lappa* root extract on cadmium toxicity in adult Wistar rats,” *Biological Trace Element Research*, vol. 160, no. 2, pp. 250–257, 2014.

[J23] A. Knott, K. Reuschlein, H. Mielke et al., “Natural *Arctium lappa* fruit extract improves the clinical signs of aging skin,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J24] E. Pomari, B. Stefanon, and M. Colitti, “Effect of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.

[J25] A. Amish Burn Study, N. M. Kolacz, M. T. Jaroch et al., “Hepatoprotective effect of *Arctium lappa* root extract on cadmium toxicity in adult Wistar rats,” *Biological Trace Element Research*, vol. 160, no. 2, pp. 250–257, 2014.

[J26] A. Knott, K. Reuschlein, H. Mielke et al., “Natural *Arctium lappa* fruit extract improves the clinical signs of aging skin,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J27] E. Pomari, B. Stefanon, and M. Colitti, “Effect of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.

[J28] A. Amish Burn Study, N. M. Kolacz, M. T. Jaroch et al., “Hepatoprotective effect of *Arctium lappa* root extract on cadmium toxicity in adult Wistar rats,” *Biological Trace Element Research*, vol. 160, no. 2, pp. 250–257, 2014.

[J29] A. Knott, K. Reuschlein, H. Mielke et al., “Natural *Arctium lappa* fruit extract improves the clinical signs of aging skin,” *Journal of Cosmetic Dermatology*, vol. 7, no. 4, pp. 281–289, 2008.

[J30] E. Pomari, B. Stefanon, and M. Colitti, “Effect of *Arctium lappa* (burdock) extract on canine dermal fibroblasts,” *Veterinary Immunology and Immunopathology*, vol. 156, no. 3-4, pp. 159–166, 2013.
punicata and Swertia chirayita, Food and Chemical Toxicology, vol. 49, no. 12, pp. 3367–3373, 2011.

[76] E. H. Al-Bayaty, M. A. Abdulla, M. I. A. Hassan, and H. M. Ali, “Effect of Andrographis paniculata leaf extract on wound healing in rats,” Natural Product Research, vol. 26, no. 5, pp. 423–429, 2012.

[77] A. Shamsizadeh, A. Roohbakhsh, F. Ayyoubi, and A. Moghaddammandi, “Chapter 25-the role of natural products in the prevention and treatment of multiple sclerosis,” in Nutrition and Lifestyle in Neurological Autoimmune Diseases, R. R. Watson and W. D. S. Killgore, Eds., pp. 249–260, Academic Press, Cambridge, MA, USA, 2017.

[78] M. Jin, K. Zhao, Q. Huang, C. Xu, and P. Shang, “Isolation, structure and bioactivities of the polysaccharides from Angelica sinensis (Oliv.) Diels: a review,” Carbohydrate Polymers, vol. 89, no. 3, pp. 713–722, 2012.

[79] W.-q. Zhang, Y.-l. Hua, M. Zhang et al., “Metabolic analysis of the anti-inflammatory effects of volatile oils of Angelica sinensis on rat model of acute inflammation,” Biomedical Chromatography, vol. 29, no. 6, pp. 902–910, 2015.

[80] Y.-l. Cheng, W.-l. Chang, S.-C. Lee et al., “Acetone extract of Angelica sinensis inhibits proliferation of human cancer cells via inducing cell cycle arrest and apoptosis,” Life Sciences, vol. 75, no. 13, pp. 1579–1594, 2004.

[81] T. Lei, H. Li, Z. Fanget al., “Polysaccharides from Angelica sinensis alleviate neuronal cell injury caused by oxidative stress,” Neural Regeneration Research, vol. 9, no. 3, pp. 260–267, 2014.

[82] T. Yang, M. Jia, J. Meng, H. Wu, and Q. Mei, “Immunomodulatory activity of polysaccharide isolated from Angelica sinensis,” International Journal of Biological Macromolecules, vol. 39, no. 4–5, pp. 179–184, 2006.

[83] C. Y. Hsiao, C.-Y. Hung, T.-H. Tsai, and K.-F. Chak, “A Study of the wound healing mechanism of a traditional Chinese medicine, Angelica sinensis, using a proteomic approach,” Evidence-Based Complementary and Alternative Medicine, vol. 2012, Article ID 467531, 14 pages, 2012.

[84] J. Wang, Z. Yuan, H. Zhao et al., “Ferulic acid promotes endothelial cells proliferation through up-regulating cyclin D1 and VEGF,” Journal of Ethnopharmacology, vol. 137, no. 2, pp. 992–997, 2011.

[85] H.-W. Lam, H.-C. Lin, S.-C. Lao et al., “The angiogenic effects of Angelica sinensis extract on HUVEC in vitro and zebrafish in vivo,” Journal of Cellular Biochemistry, vol. 103, no. 1, pp. 195–211, 2008.

[86] J.-C. Yeh, T. Cindrova-Davies, M. Belleri et al., “The natural compound n-butylidenephthalide derived from the volatile oil of Radix Angelica sinensis inhibits angiogenesis in vitro and in vivo,” Angiogenesis, vol. 14, no. 2, pp. 187–197, 2011.

[87] M. Chen, J.-J. Lin, J.-J. Fu et al., “Blumeaenes A-J, sesqui-terpenoid esters from Blumea balsamifera with NO inhibitory activity,” Planta Medica, vol. 76, no. 9, pp. 897–902, 2010.

[88] A. Noor Rain, S. Khozirah, M. A. Mohd Ridzuan et al., “Antiplasmodial properties of some Malaysian medicinal plants,” Tropical Biomedicine, vol. 24, no. 1, pp. 29–35, 2007.

[89] J. Li, G.-Z. Zhao, H.-H. Chen et al., “Antitumour and antimicrobial activities of endophytic streptomyces from pharmaceutical plants in rainforest,” Letters in Applied Microbiology, vol. 47, no. 6, pp. 574–580, 2008.

[90] C. Y. Ragasa, A. L. Kristin, and J. A. Rideout, “Antifungal metabolites from Blumea balsamifera,” Natural Product Research, vol. 19, no. 3, pp. 231–237, 2005.

[91] H. Kubota, A. Kojima-Yuasa, R. Morii et al., “Anti-obesity effect of Blumea balsamifera extract in 3T3-L1 preadipocytes and adipocytes,” The American Journal of Chinese Medicine, vol. 37, no. 05, pp. 843–854, 2009.

[92] Y. Feng, D. Wang, X. Hu et al., “Effect of volatile oil from Blumea balsamifera (L.) DC. leaves on wound healing in mice,” Journal of Traditional Chinese Medicine, vol. 34, no. 6, pp. 716–724, 2014.

[93] M. Jahandideh, H. Hajimehdipoor, S. A. Mortazavi, A. Dehpour, and G. Hassanzadeh, “A wound healing formulation based on iranian traditional medicine and its HPTLC fingerprint,” Iranian Journal of Pharmaceutical Research, vol. 15, pp. 149–157, 2016.

[94] N. Banno, T. Akihisa, K. Yasukawa et al., “Anti-inflammatory activities of the triterpene acids from the resin of Boswellia carteri,” Journal of Ethnopharmacology, vol. 107, no. 2, pp. 249–253, 2006.

[95] W. Zhao, F. Enslentchad, H. Liu et al., “Boswellic acid acetate induces differentiation and apoptosis in highly metastatic melanoma and fibrosarcoma cells,” Cancer Detection and Prevention, vol. 27, no. 1, pp. 67–75, 2003.

[96] Q. Hou, W.-J. He, H.-J. Hao et al., “The four-herb Chinese medicine ANBP enhances wound healing and inhibits scar formation via bidirectional regulation of transformation growth factor pathway,” PLoS One, vol. 9, no. 12, Article ID e112274, 2014.

[97] Q. Hou, W.-J. He, L. Chen et al., “Effects of the four-herb compound ANBP on wound healing promotion in diabetic mice,” The International Journal of Lower Extremity Wounds, vol. 14, no. 4, pp. 335–342, 2015.

[98] H. Zhao, X. Wang, W. Li, K. Koike, and H. Bai, “A new minor homoisoflavonoid from Caesalpinia sappan,” Natural Product Research, vol. 28, no. 2, pp. 102–105, 2014.

[99] O. Yodsouane, S. Cheenpracha, C. Karalai, C. Ponglimanont, and S. Tewtrakul, “Anti-allergic activity of principles from Blumea balsamifera with NO inhibition,” Phytotherapy Research, vol. 23, no. 7, pp. 1028–1031, 2009.

[100] B. S. Min, T. D. Cuong, T. M. Hung, B. S. Shin, and M. H. Woo, “Compounds from the heartwood of Caesalpinia sappan and their anti-inflammatory activity,” Bioorganic & Medicinal Chemistry Letters, vol. 22, no. 24, pp. 7436–7439, 2012.

[101] H. J. Jeong, Y. M. Kim, J. H. Kim et al., “Homoisoflavonoids from Caesalpinia sappan displaying viral neuraminidases inhibition,” Biological and Pharmaceutical Bulletin, vol. 35, no. 5, pp. 786–790, 2012.

[102] P. Temrangsee, S. Kondo, and A. Itharat, “Antibacterial activity of extracts from five medicinal plants and their formula against bacteria that cause chronic wound infection,” Journal of the Medical Association of Thailand, vol. 94, no. 7, pp. S166–S171, 2011.

[103] S. Tewtrakul, P. Tungcharoen, T. Sudsai, C. Karalai, and O. Yodsouane, “Antiinflammatory and wound healing effects of Caesalpinia sappan L,” Phytotherapy Research, vol. 29, no. 6, pp. 850–856, 2015.

[104] C. Nicolaus, S. Junghans, A. Hartmann, R. Murillo, M. Ganzer, and I. Merfort, “In vitro studies to evaluate the wound healing properties of Calendula officinalis extracts,” Journal of Ethnopharmacology, vol. 196, pp. 94–103, 2017.

[105] M. J. Leach, “Calendula officinalis and wound healing: a systematic review,” Wounds, vol. 20, no. 8, pp. 236–243, 2008.
Evidence-Based Complementary and Alternative Medicine

[106] P.K. Chandran and R. Kuttan, “Effect of Calendula officinalis flower extract on acute phase proteins, antioxidant defense mechanism and granuloma formation during thermal burns,” Journal of Clinical Biochemistry and Nutrition, vol. 43, no. 2, pp. 58–64, 2008.

[107] M. Fronza, B. Heinzmann, M. Hamburger, S. Laufer, and I. Merfort, “Determination of the wound healing effect of Calendula extracts using the scratch assay with 3T3 fibroblasts,” Journal of Ethnopharmacology, vol. 126, no. 3, pp. 463–467, 2009.

[108] M. Dinda, U. Dasgupta, N. Singh, D. Bhattacharyya, and P. Karmakar, “PI3K-mediated proliferation of fibroblasts by Calendula officinalis tincture: implication in wound healing,” Phytotherapy Research, vol. 29, no. 4, pp. 607–616, 2015.

[109] M. Dinda, S. Mazumdar, S. Das et al., “The water fraction of Calendula officinalis hydroethanol extract stimulates in vitro wound proliferation and dermal fibroblasts in wound healing,” Phytotherapy Research, vol. 30, no. 10, pp. 1696–1707, 2016.

[110] L. M. Parente, R. d. S. Lino Júnior, L. M. Faustino Tresvenzol, M. C. Vinaud, J. R. de Paula, and N. M. Paulo, “Wound healing and anti-inflammatory effect in animal models of Calendula officinalis L. growing in Brazil,” Evidence-Based Complementary and Alternative Medicine, vol. 2012, Article ID 375671, 2012.

[111] C. S. Yang, G. Chen, and Q. Wu, “Recent scientific studies of a traditional Chinese medicine, tea, on prevention of chronic diseases,” Journal of Traditional and Complementary Medicine, vol. 4, no. 1, pp. 17–23, 2014.

[112] C. Espinosa, J. A. López-Jiménez, F. Pérez-Llamas et al., “Long-term intake of white tea prevents oxidative damage caused by adriamycin in kidney of rats,” Journal of the Science of Food and Agriculture, vol. 96, no. 9, pp. 3079–3087, 2016.

[113] B. T. Chen, W.-X. Li, R.-R. He et al., “Anti-inflammatory effects of a polyphenols-rich extract from tea (Camellia sinensis) flowers in acute and chronic mice models,” Oxidative Medicine and Cellular Longevity, vol. 2012, Article ID 537923, 7 pages, 2012.

[114] D. Anwar Ibrahim and R. Noman Albadani, “Evaluation of the potential nephroprotective and antimicrobial effect of Camellia sinensis leaves versus Hibiscus sabdariffa (in vivo and in vitro studies),” Advances in Pharmacological Sciences, vol. 2014, Article ID 389834, 5 pages, 2014.

[115] S. Er and M. Dikmen, “Camellia sinensis increased apoptosis on U2OS osteosarcoma cells and wound healing potential on NIH3T3 fibroblast cells,” Cytotechnology, vol. 69, no. 6, pp. 901–914, 2017.

[116] S. Jadoon, S. Karim, M. H. H. Bin Asad et al., “Anti-aging potential of phytoextract loaded-pharmaceutical creams for human skin cell longevity,” Oxidative Medicine and Cellular Longevity, vol. 2015, Article ID 709628, 17 pages, 2015.

[117] R.-r. He, L. Chen, B.-h. Lin, Y. Matsui, X.-s. Yao, and H. Kurihara, “Beneficial effects of oolong tea consumption on diet-induced overweight and obese subjects,” Chinese Journal of Integrative Medicine, vol. 15, no. 1, pp. 34–41, 2009.

[118] S. Hasani-Ranjbar, Z. Jouyandeh, and M. Abdollahi, “A systematic review of anti-obesity medicinal plants—an update,” Journal of Diabetes & Metabolic Disorders, vol. 12, no. 1, p. 28, 2013.

[119] G. Khan, S. E. Haque, T. Anwer, M. N. Ahsan, M. M. Safhi, and M. F. Alam, “Cardioprotective effect of green tea extract on doxorubicin-induced cardiotoxicity in rats,” Acta Poloniae Pharmaceutica, vol. 71, no. 5, pp. 861–868, 2014.

[120] Y. Levites, O. Weinreb, G. Maor, M. B. H. Youdim, and S. Mandel, “Green tea polyphenol (-)-epigallocatechin-3-gallate prevents N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced dopaminergic neurodegeneration,” Journal of Neurochemistry, vol. 78, no. 5, pp. 1073–1082, 2001.

[121] F. Hajighaaliipour, M. S. Kanthimathi, M. A. Abdulla, and J. Sanusi, “The effect of Camellia sinensis on wound healing potential in an animal model,” Evidence-Based Complementary and Alternative Medicine, vol. 2013, Article ID 386734, 7 pages, 2013.

[122] S. Hsu, W. B. Bollag, J. Lewis et al., “Green tea polyphenols induce differentiation and proliferation in epidermal keratinocytes,” Journal of Pharmacology and Experimental Therapeutics, vol. 306, no. 1, pp. 29–34, 2003.

[123] B. R. Klass, O. A. Branford, A. O. Grobblea, and K. J. Rolfe, “The effect of epigallocatechin-3-gallate, a constituent of green tea, on transforming growth factor-β1-stimulated wound contraction,” Wound Repair and Regeneration, vol. 18, no. 1, pp. 80–88, 2010.

[124] F. Syed, R. A. Bagabir, R. Paus, and A. Bayat, “Ex vivo evaluation of antimicrobial compounds in skin scarring: EGCG and silencing of PAI-1 independently inhibit growth and induce keloid shrinkage,” Laboratory Investigation, vol. 93, no. 8, pp. 946–960, 2013.

[125] G. Park, B. S. Yoon, J.-H. Moon et al., “Green tea polyphenol epigallocatechin-3-gallate suppresses collagen production and proliferation in keloid fibroblasts via inhibition of the STAT3-signaling pathway,” Journal of Investigative Dermatology, vol. 128, no. 10, pp. 2429–2441, 2008.

[126] S. Y. Asadi, P. Parsaei, M. Karimi et al., “Effect of green tea (Camellia sinensis) extract on healing process of surgical wounds in rat,” International Journal of Surgery, vol. 11, no. 4, pp. 332–337, 2013.

[127] H. Kim, T. Kawazoe, D.-W. Han et al., “Enhanced wound healing by an epigallocatechin gallate-incorporated collagen sponge in diabetic mice,” Wound Repair and Regeneration, vol. 16, no. 5, pp. 714–720, 2008.

[128] D. Yao, Z. Wang, L. Miao, and L. Wang, “Effects of extracts and isolated compounds from safflower on some index of promoting blood circulation and regulating menstruation,” Journal of Ethnopharmacology, vol. 191, pp. 264–272, 2016.

[129] J. S. Roh, Y. H. Han, J. H. Kim, and J. K. Hwang, “Inhibitory effects of active compounds isolated from safflower (Carthamus tinctorius L.) seeds for melanogenesis,” Biological & Pharmaceutical Bulletin, vol. 27, no. 12, pp. 1976–1978, 2004.

[130] S.-Q. Gao, C. Chang, X.-Q. Niu, L.-J. Li, Y. Zhang, and J.-Q. Gao, “Topical application of Hydroxysafflor yellow A accelerates the wound healing in streptozotocin induced T1DM rats,” European Journal of Pharmacology, vol. 823, pp. 72–78, 2018.

[131] X. Wei, H. Liu, X. Sun et al., “Hydroxysafflor yellow A protects rat brains against ischemia-reperfusion injury by antioxidant action,” Neuroscience Letters, vol. 386, no. 1, pp. 58–62, 2005.

[132] L. Song, Y. Zhu, M. Jin, and B. Zang, “Hydroxysafflor yellow A inhibits lipopolysaccharide-induced inflammatory signal transduction in human alveolar epithelial A549 cells,” Fitoterapia, vol. 84, pp. 107–114, 2013.

[133] N. Zhang, M. Xing, Y. Wang et al., “Hydroxysafflor yellow A improves learning and memory in a rat model of vascular dementia by increasing VEGF and NR1 in the hippocampus,” Neuroscience Bulletin, vol. 30, no. 3, pp. 417–424, 2014.
K. J. Zhang, J.-Z. Zhu, X.-Y. Bao, Q. Zheng, and Y. Wang, "Shexiang baoxin pills for coronary heart disease in animal models: preclinical evidence and promoting angiogenesis mechanism," *Frontiers in Pharmacology*, vol. 8, p. 404, 2017.

P.-p. Tian, J. Li, J. Gao, and Y. Li, "Efficacy and safety of the Shexiang Baoxin Pill for the treatment of coronary artery disease not amenable to revascularisation: study protocol for a randomised, placebo-controlled, double-blinded trial," *BMJ Open*, vol. 8, no. 2, 2018.

S. H. Lee, S. Y. Lee, D. J. Son et al., "Inhibitory effect of 2'-hydroxycinnamaldehyde on nitric oxide production through inhibition of NF-κB activation in RAW 264.7 cells," *Biochemical Pharmacology*, vol. 69, no. 5, pp. 791–799, 2005.

S. S. Hamzah, A. R. Lawal, F. M. Madaki, and O. L. Erukainure, "Methanolic extract of Centella asiatica var. crista leaves modulates glucose homeostasis and abates oxidative hepatic injury in diabetic rats," *Comparative Clinical Pathology*, vol. 27, no. 4, pp. 1065–1071, 2018.

H. Y. H. Kwon, W. K. Jeon, J.-S. Hwang et al., "Cinnamon extract suppresses tumor progression by modulating angiogenesis and the effector function of CD8+ T cells," *Cancer Letters*, vol. 278, no. 2, pp. 174–182, 2009.

Y.-J. Chen, Y.-S. Dai, B.-F. Chen et al., "4Z′he effect of tetrandrine and extracts of *Centella asiatica* in incision and burn wound Centella asiatica research," *Wound Repair and Regeneration*, vol. 12, no. 6, pp. 618–625, 2004.

M. Afzal, and A. H. Shah, "Gastric antiulcer and cytoprotective effects of *Commiphora molmol* leaf extract and pure compound isolated from *Commiphora molmol* var. mukul," *BMC Complementary and Alternative Medicine*, vol. 14, no. 4, pp. 265–269, 2014.

M. Shuaib, A. Ali, M. Ali, B. Panda, and M. Ahmad, "Antibacterial activity of resin rich plant extracts," *Journal of Pharmacy and Biomedical Sciences*, vol. 5, no. 4, pp. 265–269, 2013.

M. Shalaby and A. Hammouda, "Algesic, anti-inflammatory and antihyperlipidemic activities of *Commiphora molmol* extract (myrrh)," *Journal of Ethnopharmacology*, vol. 3, no. 2, pp. 56–62, 2014.

R. A. Abdul-Ghani, N. Loutify, and A. Hassan, "Myrrh and trematodes in Egypt: an overview of safety, efficacy and effectiveness profiles," *Parasitology International*, vol. 58, no. 3, pp. 210–214, 2009.

T. Shen, G.-H. Li, X.-N. Wang, and H.-X. Lou, "The genus *Commiphora*: a review of its traditional uses, phytochemistry and pharmacology," *Journal of Ethnopharmacology*, vol. 142, no. 2, pp. 319–330, 2012.
Evidence-Based Complementary and Alternative Medicine

[163] E. Y. H. Nomicos, “Myrrh,” Holistic Nursing Practice, vol. 21, no. 6, pp. 308–323, 2007.

[164] H. Galehdari, S. Negahdari, M. Kesmati, A. Rezaie, and G. Shariati, “Effect of the herbal mixture composed of Aloe Vera, Henna, Adiantum capillus-veneris, and Myrrh on wound healing in streptozotocin-induced diabetic rats,” BMC Complementary and Alternative Medicine, vol. 16, no. 1, p. 386, 2016.

[165] G. Mansour, S. Ouda, A. Shaker, and H. M. Abdallah, “Clinical efficacy of new aloe vera- and myrrh-based oral mucosadhesive gels in the management of minor recurrent aphthous stomatitis: a randomized, double-blind, vehicle-controlled study,” Journal of Oral Pathology & Medicine, vol. 43, no. 6, pp. 405–409, 2014.

[166] S. Negahdari, H. Galehdari, M. Kesmati, A. Rezaie, and G. Shariati, “Wound healing activity of extracts and formulations of Aloe vera, Henna, Adiantum capillus-veneris, and Myrrh on mouse dermal fibroblast cells,” International Journal of Preventive Medicine, vol. 8, p. 18, 2017.

[167] D. Abkhi, M. Ghadiri, W. Chrzanoski, and R. Rohanizadeh, “Curcumin as a wound healing agent,” Life Sciences, vol. 116, no. 1, pp. 1–7, 2014.

[168] M. C. Fadus, C. Lau, J. Bikhchandani, and H. T. Lynch, “Curcumin: an age-old anti-inflammatory and anti-neoplastic agent,” Journal of Traditional and Complementary Medicine, vol. 7, no. 3, pp. 339–346, 2017.

[169] S. C. Gupta, S. Patchva, and B. B. Aggarwal, “Therapeutic roles of curcumin: lessons learned from clinical trials,” The AAPS Journal, vol. 15, no. 1, pp. 195–218, 2013.

[170] B. Joe, M. Vijaykumar, and B. R. Lokesh, “Biological properties of curcumin-cellular and molecular mechanisms of action,” Critical Reviews in Food Science and Nutrition, vol. 44, no. 2, pp. 97–111, 2004.

[171] D. Yang, J. H. Xu, and R. J. Shi, “Root extractive from Daphne genkwa benefits in wound healing of anal fistula through up-regulation of collagen genes in human skin fibroblasts,” Bioscience Reports, vol. 37, no. 2, Article ID BSR20170182, 2017.

[172] K. K. Bang, C.-Y. Yun, C. Lee et al., “Melanogenesis inhibitory daphnane diterpenoids from the flower buds of Daphne genkwa,” Bioorganic & Medicinal Chemistry Letters, vol. 23, no. 11, pp. 3334–3337, 2013.

[173] Z.-J. Zhan, C.-Q. Fan, J. Ding, and J.-M. Yue, “Novel diterpenoids with potent inhibitory activity against endothelial cell HMEC and cytotoxic activities from a well-known TCM plant Daphne genkwa,” Bioorganic & Medicinal Chemistry, vol. 13, no. 3, pp. 645–655, 2005.

[174] W. J. Du, J. Ji, L. Wang et al., “Relationship between the UPLC-Q-TOF-MS fingerprinted constituents from Daphne genkwa and their anti-inflammatory, anti-oxidant activities,” Biomedical Chromatography, vol. 31, no. 12, Article ID e4012, 2017.

[175] M. Y. Lee, B.-Y. Park, O.-K. Kwon et al., “Anti-inflammatory activity of (-)-aposimon isolated from Daphne genkwa in RAW264.7 cells,” International Immunopharmacology, vol. 9, no. 7-8, pp. 878–885, 2009.

[176] J.-Y. Hong, H.-J. Chung, H.-J. Lee, H. J. Park, and S. K. Lee, “Growth inhibition of human lung cancer cells via down-regulation of epidermal growth factor receptor signaling by yuanhuadine, a daphnane diterpene from Daphne genkwa,” Journal of Natural Products, vol. 74, no. 10, pp. 2102–2108, 2011.

[177] W. Zheng, X. Gao, C. Chen, and R. Tan, “Total flavonoids of Daphne genkwa root significantly inhibit the growth and metastasis of Lewis lung carcinoma in C57BL6 mice,” International Immunopharmacology, vol. 7, no. 2, pp. 117–127, 2007.

[178] E. Uyangaa, J. Y. Choi, H. W. Ryu, S.-R. Oh, and S. K. Eo, “Anti-herpes activity of vinegar-processed Daphne genkwa flnos via enhancement of natural killer cell activity,” Immune Network, vol. 15, no. 2, pp. 91–99, 2015.

[179] S. Z. Huang, X. J. Zhang, X. Y. Li et al., “Daphnane-type diterpene esters with cytotoxic and anti-HIV-1 activities from Daphne acutiloba Rehd.,” Phytochemistry, vol. 75, pp. 99–107, 2012.

[180] P. Widsten, C. D. Cruz, G. C. Fletcher, M. A. Pajak, and T. K. McGhie, “Tannins and extracts of fruit byproducts: antibacterial activity against foodborne bacteria and antioxidant capacity,” Journal of Agricultural and Food Chemistry, vol. 62, no. 46, pp. 11146–11156, 2014.

[181] M. C. Figueroa-Espinoza, A. Zafimahova, P. G. M. Alvarado, E. Dubreucq, and C. Pocnet-Legrand, “Grape seed and apple tannins: emulsifying and antioxidant properties,” Food Chemistry, vol. 178, pp. 38–44, 2015.

[182] X. Su, X. Liu, S. Wang et al., “Wound-healing promoting effect of total tannins from Entada phaseoloides (L.) Merr. in rats,” Burns, vol. 43, no. 4, pp. 830–838, 2017.

[183] A. Bhaskar and V. Nithya, “Evaluation of the wound-healing activity of Hibiscus rosa-sinensis L (Malvaceae) in Wistar albino rats,” Indian Journal of Pharmaceutical Sciences, vol. 44, no. 6, pp. 694–698, 2012.

[184] N. Adhirajan, T. Ravi Kumar, N. Shanmugasundaram, and M. Babu, “In vivo and in vitro evaluation of hair growth potential of Hibiscus rosa-sinensis Linn.,” Journal of Ethnopharmacology, vol. 88, no. 2–3, pp. 235–239, 2003.

[185] V. M. Jadhav, S. S. Kamble, and V. J. Kadam, “Herbal medicine: Syzygium cumini: a review,” Journal of Pharmacy Research, vol. 2, no. 8, pp. 1212–1219, 2009.

[186] Z. A. Khan, S. A. Naqvi, A. Mukhtar et al., “Antioxidant and antibacterial activities of Hibiscus Rosa-sinensis Linn flower extracts,” Pakistan Journal of Pharmaceutical Sciences, vol. 27, no. 3, pp. 469–474, 2014.

[187] B. Shivananda Nayak, S. Sivachandra Raju, F. A. Orette, and A. V. Chalapathi Rao, “Effects of Hibiscus rosa sinensis L (Malvaceae) on wound healing activity: a preclinical study in a sprague dawley rat,” The International Journal of Lower Extremity Wounds, vol. 6, no. 2, pp. 76–81, 2007.

[188] H.-M. Shen, C. Chen, J.-Y. Jiang et al., “The N-butyl alcohol extract from Hibiscus rosa-sinensis L. flowers enhances healing potential on rat excisional wounds,” Journal of Ethnopharmacology, vol. 198, pp. 291–301, 2017.

[189] B. Sanodiya, G. Thakur, R. Baghel, G. Prasad, and P. Bisen, “Ganoderma lucidum: a potent pharmacological macro-fungus,” Current Pharmaceutical Biotechnology, vol. 10, no. 8, pp. 717–742, 2009.

[190] P. G. Cheng, C.-W. Phan, V. Sabaratnam, P. G. M. Alvarado, E. Dubreucq, and C. Pocnet-Legrand, “Anti-herpes activity of vinegar-processed Daphne genkwa flnos via enhancement of natural killer cell activity,” Immune Network, vol. 15, no. 2, pp. 91–99, 2015.

[191] B. Boh, “Ganoderma lucidum: a potential for biotechnological production of anti-cancer and immunomodulatory drugs,” Recent Patents on Anti-Cancer Drug Discovery, vol. 8, no. 3, pp. 255–287, 2013.

[192] M. N. Baig, A. A. Shahid, and M. Ali, “In vitro assessment of extracts of the lingzhi or reishi medicinal mushroom, Ganoderma lucidum (higher basidiomycetes) against...
different plant pathogenic fungi,” *International Journal of Medicinal Mushrooms*, vol. 17, no. 4, pp. 407–411, 2015.

[193] O. M. Oluba, A. O. Olusola, B. S. Fagbokun, and E. C. Onyeneke, “Antimalarial and hepatoprotective effects of crude ethanolic extract of lingzhi or reishi medicinal mushroom, *Ganoderma lucidum* (W.Curt.:Fr.) P.Karst. (higher Basidiomycetes), in *Plasmodium berghei*-infected mice,” *International Journal of Medicinal Mushrooms*, vol. 14, no. 5, pp. 459–466, 2012.

[194] W. Zhang, J. Tao, Y. Yang et al., “Antiviral effects of two *Ganoderma lucidum* triterpenoids against enterovirus 71 infection,” *Biochemical and Biophysical Research Communications*, vol. 449, no. 3, pp. 307–312, 2014.

[195] P. Rani, M. R. Lal, U. Maheshwari, and S. Krishnan, “Antioxidant potential of lingzhi or reishi medicinal mushroom, *Ganoderma lucidum* (Higher Basidiomycetes) cultivated on *Artocarpus heterophyllus* sawdust substrate in India,” *International Journal of Medicinal Mushrooms*, vol. 17, no. 12, pp. 1171–1177, 2015.

[196] Y. Z. Xie, F. Yang, W. Tan et al., “The anti-cancer components of *Ganoderma lucidum* possesses cardiovascular protective effect by regulating circular RNA expression,” *Oncosience*, vol. 3, no. 7–8, pp. 203–207, 2016.

[197] D. Pan, D. Zhan, and J. Wu et al., “Antidiabetic, anti-hyperlipidemic and antioxidant activities of a novel proteoglycan from *Ganoderma lucidum* fruiting bodies on db/db mice and the possible mechanism,” *PLoS One*, vol. 8, no. 7, Article ID e68332, 2013.

[198] T.-C. Hsieh and J. M. Wu, “Regulation of cell cycle transition and induction of apoptosis in HL-60 leukemia cells by the combination of Coriolus versicolor and *Ganoderma lucidum,*” *International Journal of Molecular Medicine*, vol. 32, no. 1, pp. 251–257, 2013.

[199] I. J. Suarez-Arroyo, R. Rosario-Acevedo, A. Aguilera-Perez et al., “Anti-tumor effects of *Ganoderma lucidum* (reishi) in inflammatory breast cancer in *In Vivo* and *In Vitro* models,” *PLoS One*, vol. 8, no. 2, Article ID e57431, 2013.

[200] F. Li, Y. Zhang, and Z. Zhong, “Antihyperglycemic effect of *Ganoderma lucidum* polysaccharides on streptozotocin-induced diabetic mice,” *International Journal of Molecular Sciences*, vol. 12, no. 9, pp. 6135–6145, 2011.

[201] Y. Gao, W. Tang, H. Gao, E. Chan, J. Lan, and S. Zhou, “*Ganoderma lucidum* polysaccharide fractions accelerate healing of acetic acid-induced ulcers in rats,” *Journal of Medicinal Food*, vol. 7, no. 4, pp. 417–421, 2004.

[202] Y. Gao, S. Zhou, J. Wen, M. Huang, and A. Xu, “Mechanism of the antioxidant effect of *Ganoderma lucidum* polysaccharides on indomethacin-induced lesions in the rat,” *Life Sciences*, vol. 72, no. 6, pp. 731–745, 2002.

[203] X. Jin, J. Ruiz Bequerie, D. M. Sze, and G. C. Chan, “*Ganoderma lucidum* (Reishi mushroom) for cancer treatment,” *Cochrane Database of Systematic Reviews*, no. 6, Article ID CD007731, 2012.

[204] L. Tie, H.-Q. Yang, Y. An et al., “*Ganoderma lucidum* polysaccharide accelerates refractory wound healing by inhibition of mitochondrial oxidative stress in type 1 diabetes,” *Cellular Physiology and Biochemistry*, vol. 29, no. 3-4, pp. 583–594, 2012.

[205] J. Gu, J. Chen, N. Yang et al., “Combination of *Ligusticum chuanxiong* and *Radix Paeoniae* ameliorate focal cerebral ischemic in MCAO rats via endoplasmic reticulum stress-dependent apoptotic signaling pathway,” *Journal of Ethnopharmacology*, vol. 187, pp. 313–324, 2016.

[206] X. Ran, L. Ma, C. Peng, H. Zhang, and L.-P. Qin, “*Ligusticum chuanxiong* Hopt: a review of chemistry and pharmacology,” *Pharmaceutical Biology*, vol. 49, no. 11, pp. 1180–1189, 2011.

[207] Z. Chen, C. Zhang, F. Gao et al., “A systematic review on the rhizome of *Ligusticum chuanxiong* Hopt. (Chuanxiong),” *Food and Chemical Toxicology*, vol. 119, pp. 309–325, 2018.

[208] J.-G. Wu, Y.-J. Wei, X. Ran, H. Zhang, H. Nian, and L.-P. Qin, “Inhibitory effects of essential oil from rhizomes of *Ligusticum chuanxiong* on hypertrophic scarring in the rabbit ear model,” *Pharmaceutical Biology*, vol. 49, no. 7, pp. 764–769, 2011.

[209] J. Fu, L. Yang, M. A. Khan, and Z. Mei, “Genetic characterization and authentication of *Lonicera japonica* Thunb. by using improved RAPD analysis,” *Molecular Biology Reports*, vol. 40, no. 10, pp. 5993–5999, 2013.

[210] X. Shang, H. Pan, M. Li, X. Miao, and H. Ding, “*Lonicera japonica* Thunb.: ethnopharmacology, phytochemistry and pharmacology of an important traditional Chinese medicine,” *Journal of Ethnopharmacology*, vol. 138, no. 1, pp. 1–21, 2011.

[211] Y. Li, W. Cai, X. Weng et al., “*Lonicerae Japonicae Flos* and *Lonicerae Flos*: a systematic pharmacology review,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2015, Article ID 905063, 16 pages, 2015.

[212] W. C. Chen, S.-S. Liu, T.-F. Tseng, S.-L. Lee, and I.-M. Liu, “Wound repair and anti-inflammatory potential of *Lonicera japonica* in excision wound-induced rats,” *BMC Complementary and Alternative Medicine*, vol. 12, p. 226, 2012.

[213] S. L. Zhou, X.-H. Zhou, Z.-Q. Zhou et al., “Multiple species of wild tree peonies gave rise to the ‘king of flowers’, *Paeonia suffruticosa Andrews,*” *Proceedings of the Royal Society B: Biological Sciences*, vol. 281, no. 1797, Article ID 20141687, 2014.

[214] S. Rho, H.-S. Chung, M. Kang et al., “Inhibition of production of reactive oxygen species and gene expression profile by treatment of ethanol extract of Moutan Cortex Radicis in oxidative stressed PC12 cells,” *Biological & Pharmaceutical Bulletin*, vol. 28, no. 4, pp. 661–666, 2005.

[215] H. G. Kim, G. Park, Y. Piao et al., “Effects of the root bark of *Paeonia suffruticosa* on mitochondria-mediated neuro-protection in an MPTP-induced model of Parkinson’s disease,” *Food and Chemical Toxicology*, vol. 65, pp. 293–300, 2014.

[216] G. Xing, Z. Zhang, J. Liu, H. Hu, and N. Sugira, “Antitumor effect of extracts from moutan cortex on DLD-1 human colon cancer cells in vitro,” *Molecular Medicine Reports*, vol. 3, no. 1, pp. 57–61, 2010.

[217] M. Wu and Z. Gu, “Screening of biosactive compounds from moutan cortex and their anti-inflammatory activities in rat synoviocytes,” *Evidence-Based Complementary and Alternative Medicine*, vol. 6, no. 1, p. 63, 2009.

[218] H. Hong, Q. M. Wang, Z. P. Zhao et al., “Studies on antidiabetic effects of cortex Moutan polysaccharide-2b in type 2 diabetes mellitus rats,” *Yao Xue Xue Bao*, vol. 38, no. 4, pp. 255–259, 2003.

[219] D. Y. He and S. M. Dai, “Anti-inflammatory and immuno-modulatory effects of *paeania lactiflora* pall., a traditional Chinese herbal medicine,” *Frontiers in Pharmacology*, vol. 2, p. 10, 2011.

[220] R. Wang, M. Lechtenberg, J. Sendker, F. Peteriet, A. Deters, and A. Hensel, “Wound-healing plants from TCM: in vitro investigations on selected TCM plants and their influence on human dermal fibroblasts and keratinocytes,” *Fitoterapia*, vol. 84, pp. 308–317, 2013.
Evidence-Based Complementary and Alternative Medicine

[221] W. K. Kim, S.-Y. Song, W. K. Oh et al., “Wound-healing effect of ginsenoside Rd from leaves of *Panax ginseng* via cyclic AMP-dependent protein kinase pathway,” *European Journal of Pharmacology*, vol. 702, no. 1–3, pp. 285–293, 2013.

[222] N. M. Arring, D. Millstine, L. A. Marks, and L. M. Nail, “Ginseng as a treatment for fatigue: a systematic review,” *The Journal of Alternative and Complementary Medicine*, vol. 24, no. 7, pp. 624–633, 2018.

[223] E. Jovanovski, V. Peeva, J. L. Sievenpiper et al., “Modulation of endothelial function by Korean red ginseng (*Panax ginseng* C.A. Meyer) and its components in healthy individuals: a randomized controlled trial,” *Cardiovascular Therapeutics*, vol. 32, no. 4, pp. 163–169, 2014.

[224] L.-S. Lee, C.-W. Cho, H.-D. Hong, Y.-C. Lee, U.-K. Choi, and Y.-C. Kim, “Hypolipidemic and antioxidant properties of phenolic compound-rich extracts from white ginseng (*Panax ginseng*) in cholesterol-fed rabbits,” *Molecules*, vol. 18, no. 10, pp. 12548–12560, 2013.

[225] Y. Yang, W. S. Yang, T. Yu et al., “ATF-2/CREB/IRF-3-targeted anti-inflammatory activity of Korean red ginseng water extract,” *Journal of Ethnopharmacology*, vol. 154, no. 1, pp. 218–228, 2014.

[226] L. Jiao, B. Li, M. Wang, Z. Liu, X. Zhang, and S. Liu, “Antioxidant activities of the oligosaccharides from the roots, flowers and leaves of *Panax ginseng* C.A. Meyer,” *Carbohydrate Polymers*, vol. 106, pp. 293–298, 2014.

[227] C. Li, Z.-N. Tian, J.-P. Cai et al., “*Panax ginseng* polysaccharide induces apoptosis by targeting Twist/AKR1C2/NF-1 pathway in human gastric cancer,” *Carbohydrate Polymers*, vol. 102, pp. 103–109, 2014.

[228] N. Fukuyama, M. Shibuuya, and Y. Orihara, “Antimicrobial polycyclolanes from *Panax ginseng* hairy root culture,” *Chemical and Pharmaceutical Bulletin*, vol. 60, no. 3, pp. 377–380, 2012.

[229] M. Sumiyoshi, M. Sakanaka, and Y. Kimura, “Effects of red ginseng extract on allergic reactions to food in Balb/c mice,” *Journal of Ethnopharmacology*, vol. 132, no. 1, pp. 206–212, 2010.

[230] E. Hwang, S.-Y. Park, C. S. Yin, H.-T. Kim, Y. M. Kim, and T. H. Yi, “Antiangiogenic effects of the mixture of *Panax ginseng* and *Crataegus pinnatifida* in human dermal fibroblasts and healthy human skin,” *Journal of Ginseng Research*, vol. 41, no. 1, pp. 69–77, 2017.

[231] J. Lee, H. Hwang, E.-J. Ko et al., “Immunomodulatory activity of red ginseng against influenza A virus infection,” *Nutrients*, vol. 6, no. 2, pp. 517–529, 2014.

[232] J.-G. Cho, M.-K. Lee, J.-W. Lee et al., “Physicochemical Characterization and NMR Assignments of Ginsenosides Rb1, Rb2, Rc, and Rd Isolated from *Panax ginseng*,” *Journal of Ginseng Research*, vol. 34, no. 2, pp. 113–121, 2010.

[233] Y. G. Kim, M. Sumiyoshi, K. Kawahira, M. Sakanaka, and Y. Kimura, “Effects of Red Ginseng extract on ultraviolet B-irradiated skin change in C57BL mice,” *Phytotherapy Research*, vol. 22, no. 11, pp. 1423–1427, 2008.

[234] Y. Kimura, M. Sumiyoshi, K. Kawahira, and M. Sakanaka, “Effects of ginseng saponins isolated from Red Ginseng roots on burn wound healing in mice,” *British Journal of Pharmacology*, vol. 148, no. 6, pp. 860–870, 2006.

[235] N. Morisaki, S. Watanabe, M. Tezuka et al., “Mechanism of angiogenic effects of saponin from ginseng Radix rubra in human umbilical vein endothelial cells,” *British Journal of Pharmacology*, vol. 115, no. 7, pp. 1188–1193, 1995.

[236] Y.-S. Kim, I.-H. Cho, M.-J. Jeong et al., “Therapeutic effect of total ginseng saponin on skin wound healing,” *Journal of Ginseng Research*, vol. 35, no. 3, pp. 360–367, 2011.

[237] X. Chen, M. Wang, X. Xu et al., “*Panax ginseng* total protein promotes proliferation and secretion of collagen in NIH/3T3 cells by activating extracellular signal-related kinase pathway,” *Journal of Ginseng Research*, vol. 41, no. 3, pp. 411–418, 2017.

[238] J. Lee, E. Jung, J. Lee et al., “*Panax ginseng* induces human type I collagen synthesis through activation of Smad signaling,” *Journal of Ethnopharmacology*, vol. 109, no. 1, pp. 29–34, 2007.

[239] S. Choi, “Epidermis proliferative effect of the *Panax ginseng* Ginsenoside Rb2,” *Archives of Pharmacal Research*, vol. 25, no. 1, pp. 71–76, 2002.

[240] K. Shen, L. Ji, C. Gong et al., “*Notoginsenoside F1t* promotes angiogenesis via HIF-1α mediated VEGF secretion and the regulation of PI3K/AKT and Raf/MEK/ERK signaling pathways,” *Biochemical Pharmacology*, vol. 84, no. 6, pp. 784–792, 2012.

[241] S.-J. Hong, J.-B. Wan, Y. Zhang et al., “Angiogenic effect of saponin extract from *Panax notoginseng* on HUVECs in vitro and zebrafish in vivo,” *Phytotherapy Research*, vol. 23, no. 5, pp. 677–686, 2009.

[242] N. Zhou, Y. Tang, R. F. Keep, X. Ma, and J. Xiang, “Antioxidative effects of *Panax notoginseng* saponins in brain cells,” *Phytotherapy Research*, vol. 21, no. 10, pp. 1189–1195, 2014.

[243] X.-P. Huang, H. Ding, J.-D. Lu, Y.-H. Tang, B.-X. Deng, and C.-Q. Deng, “Effects of the combination of the main active components of *Astragalus* and *Panax notoginseng* on inflammation and apoptosis of nerve cell after cerebral ischemia-reperfusion,” *The American Journal of Chinese Medicine*, vol. 43, no. 7, pp. 1419–1438, 2015.

[244] H. X. Sun, Y.-P. Ye, H.-J. Pan, and Y.-J. Pan, “Adjuvant effect of *Panax notoginseng* saponins on the immune responses to ovalbumin in mice,” *Vaccine*, vol. 22, no. 29-30, pp. 3882–3889, 2004.

[245] X.-S. Zeng, X.-S. Zhou, F.-C. Luo et al., “Comparative analysis of the neuroprotective effects of ginsenosides Rg1 and Rb1 extracted from *Panax notoginseng* against cerebral ischemia,” *Canadian Journal of Physiology and Pharmacology*, vol. 92, no. 2, pp. 102–108, 2014.

[246] Q. Yang, P. Wang, J. Cui, W. Wang, Y. Chen, and T. Zhang, “*Panax notoginseng* saponins attenuate lung cancer growth in part through modulating the level of Met/miR-222 axis,” *Journal of Ethnopharmacology*, vol. 193, pp. 255–265, 2016.

[247] R. Uzayisenga, P. A. Ayeka, and Y. Wang, “Anti-diabetic potential of *Panax notoginseng* saponins (PNS): a review,” *Phytotherapy Research*, vol. 28, no. 4, pp. 510–516, 2014.

[248] X.-d. Peng, L.-l. Dai, C.-q. Huang, C.-m. He, B. Yang, and L.-j. Chen, “Relationship between anti-fibrotic effect of *Panax notoginseng* saponin and serum cytokines in rat hepatic fibrosis,” *Biochemical and Biophysical Research Communications*, vol. 388, no. 1, pp. 31–34, 2009.

[249] H.-W. Jung, U.-K. Seo, J.-H. Kim, K.-H. Leem, and Y.-K. Park, “Flower extract of *Panax notoginseng* attenuates lipopolysaccharide-induced inflammatory response via blocking of NF-κB signaling pathway in murine macrophages,” *Journal of Ethnopharmacology*, vol. 122, no. 2, pp. 313–319, 2009.

[250] S. Makino, N. Mitsutake, M. Nakashima et al., “DHMEQ, a novel NF-kappaB inhibitor, suppresses growth and type I collagen accumulation in keloid fibroblasts,” *Journal of Dermatological Science*, vol. 51, no. 3, pp. 171–180, 2008.
Evidence-Based Complementary and Alternative Medicine

[251] M. Ghazizadeh, “Essential role of IL-6 signaling pathway in keloid pathogenesis,” *Journal of Nippon Medical School*, vol. 74, no. 1, pp. 11–22, 2007.

[252] A.-J. Lau, D.-F. Toh, T.-K. Chuah, Y.-K. Pang, S.-O. Woo, and H.-L. Koh, “Antiplatelet and anticoagulant effects of *Panax notoginseng*: comparison of raw and steamed *Panax notoginseng* with *Panax ginseng* and *Panax quinquefolium*,” *Journal of Ethnopharmacology*, vol. 125, no. 3, pp. 380–386, 2009.

[253] M. Peng, X. Yi, T. Zhang, Y. Ding, and J. Le, “Stereoisomers of saponins in *Panax notoginseng* (Sanqi): a review,” *Frontiers in Pharmacology*, vol. 9, p. 188, 2018.

[254] Y. Jiao, Y. Wu, and D. Du, “Polydatin inhibits cell proliferation, invasion and migration, and induces cell apoptosis in different *Polygonum cuspidatum* extracts in phospholipid-based microemulsions,” *Journal of Agricultural and Food Chemistry*, vol. 59, no. 17, pp. 9135–9141, 2011.

[255] W.-Y. Li, S.-W. Chan, D.-J. Guo et al., “Water extract of *Rheum officinale* Baill. induces apoptosis in human lung adenocarcinoma A549 and human breast cancer MCF-7 cell lines,” *Journal of Ethnopharmacology*, vol. 124, no. 2, pp. 251–256, 2009.

[256] A. Subramaniam, M. K. Shamanugam, T. H. Ong et al., “Emodin inhibits growth and induces apoptosis in an orthotopic hepatocellular carcinoma model by blocking activation of STAT3,” *British Journal of Pharmacology*, vol. 170, no. 4, pp. 807–821, 2013.

[257] X. Chu, M. Wei, X. Yang et al., “Effects of an anthraquinone derivative from *Rheum officinale* Baill. emodin, on airway responses in a murine model of asthma,” *Food and Chemical Toxicology*, vol. 50, no. 7, pp. 2368–2375, 2012.

[258] A. Subramaniam, M. K. Shamanugam, T. H. Ong et al., “Emodin inhibits growth and induces apoptosis in an orthotopic hepatocellular carcinoma model by blocking activation of STAT3,” *British Journal of Pharmacology*, vol. 170, no. 4, pp. 807–821, 2013.

[259] X. Chu, M. Wei, X. Yang et al., “Effects of an anthraquinone derivative from *Rheum officinale* Baill. emodin, on airway responses in a murine model of asthma,” *Cochrane Database of Systematic Reviews*, no. 7, Article ID CD008000, 2012.

[260] T. Long, Y. Yin, J. Yang, and G. Shan, “Emodin, an anthraquinone derivative from *Rheum officinale* Baill. enhances cutaneous wound healing in rats,” *European Journal of Pharmacology*, vol. 567, no. 3, pp. 177–185, 2007.

[261] B. Sung, “Chapter 3-regulation of inflammation-mediated chronic diseases by botanicals,” in *Advances in Botanical Research*, L.-F. Shyur and A. S. Y. Lau, Eds., pp. 57–132, Academic Press, Cambridge, MA, USA, 2012.

[262] A. Kumar, S. Dhawan, and B. B. Aggarwal, “Emodin (3-methyl-1,6,8-trihydroxyanthraquinone) inhibits TNF-induced NF-κB activation, IκB degradation, and expression of cell surface adhesion proteins in human vascular endothelial cells,” *Oncogene*, vol. 17, no. 7, pp. 913–918, 1998.

[263] A. Gupta, N. Upadhyay, K. Pal, R. Kumar, and R. Sawhney, “Effects of Rhodiola imbricata on dermal wound healing,” *Planta Medica*, vol. 73, no. 8, pp. 774–777, 2007.

[264] K. P. Mishra, L. Ganju, and S. B. Singh, “Anti-cellular and immunomodulatory potential of aqueous extract of Rhodiola integriforme,” *Immunopharmacology and Immunotoxicology*, vol. 34, no. 3, pp. 513–518, 2012.

[265] V. Gupta, S. S. Lahiri, S. Sultana, R. K. Tulsawani, and R. Kumar, “Anti-oxidative effect of Rhodiola imbricata root extract in rats during cold, hypoxia and restraint (C-H-R) exposure and post-stress recovery,” *Food and Chemical Toxicology*, vol. 48, no. 4, pp. 1019–1025, 2010.

[266] R. Senthilkumar, R. Chandran, and T. Parimelazhagan, “Hepatoprotective effect of Rhodiola imbricata rhizome against paracetamol-induced liver toxicity in rats,” *Saudi Journal of Biological Sciences*, vol. 21, no. 5, pp. 409–416, 2014.

[267] H. C. Goel, M. Bala, J. Prasad, S. Singh, P. K. Agrawala, and R. C. Swahney, “Radioprotection by Rhodiola imbricata in mice against whole-body lethal irradiation,” *Journal of Medicinal Food*, vol. 9, no. 2, pp. 154–160, 2006.

[268] R. Senthilkumar, T. Parimelazhagan, O. P. Chaurasia, and R. B. Srivastava, “Free radical scavenging property and antiproliferative activity of Rhodiola imbricata Edgew extracts in HT-29 human colon cancer cells,” *Asian Pacific Journal of Tropical Medicine*, vol. 6, no. 1, pp. 11–19, 2013.

[269] C.-Y. Su, J.-L. Ming, K. Rahman, T. Han, and L.-P. Qin, “Salvia miltiorrhiza: traditional medicinal uses, chemistry, and pharmacology,” *Chinese Journal of Natural Medicines*, vol. 13, no. 3, pp. 163–182, 2015.

[270] J. Zhang, Y. Li, X. Chen, Y. Pan, S. Zhang, and Y. Wang, “Systems pharmacology dissection of multi-scale mechanisms of action for herbal medicines in stroke treatment and
Evidence-Based Complementary and Alternative Medicine

prevention,” PLoS One, vol. 9, no. 8, Article ID e102506, 2014.

[282] J. Luo, W. Song, G. Yang, H. Xu, and K. Chen, “Compound Danshen (Salvia miltiorrhiza) dripping pill for coronary heart disease: an overview of systematic reviews,” The American Journal of Chinese Medicine, vol. 43, no. 1, pp. 25–43, 2015.

[283] L. Zhou, Z. Zuo, and M. S. S. Chow, “Danshen: an overview of its chemistry, pharmacology, pharmacokinetics, and clinical use,” The Journal of Clinical Pharmacology, vol. 45, no. 12, pp. 1345–1359, 2005.

[284] J. Chen, Q. Lv, M. Yu, X. Zhang, and J. Gou, “Randomized clinical trial of Chinese herbal medications to reduce wound complications after mastectomy for breast carcinoma,” British Journal of Surgery, vol. 97, no. 12, pp. 1798–1804, 2010.

[285] L. Zhou, Z. Zuo, and M. S. S. Chow, “Danshen: an overview of its chemistry, pharmacology, pharmacokinetics, and clinical use,” The Journal of Clinical Pharmacology, vol. 45, no. 12, pp. 1345–1359, 2005.

[286] Y. Tang, M. Wang, X. Le et al., “Antioxidant and cardioprotective effects of Danshensu (3-(3, 4-dihydroxyphenyl)-2-hydroxy-α-indanone) from Salvia miltiorrhiza on isoproterenol-induced myocardial hypertrophy in rats,” Phytomedicine, vol. 18, no. 12, pp. 1024–1030, 2011.

[287] M.-K. Tsai, Y.-L. Lin, and Y.-T. Huang, “Effects of salvianolic acids on oxidative stress and hepatic fibrosis in rats,” Toxicology and Applied Pharmacology, vol. 242, no. 2, pp. 155–164, 2010.

[288] T. Chen, W. Liu, X. Chao et al., “Salvianolic acid B attenuates brain damage and inflammation after traumatic brain injury in mice,” Brain Research Bulletin, vol. 84, no. 2, pp. 163–168, 2011.

[289] D. H. Shin, Y. J. Cha, G. J. Joe et al., “Whitening effect of Sapphra flavescens extract, and identification of the two active compounds in the extract that stimulate proliferation of human hair keratinocytes,” BMC Complementary and Alternative Medicine, vol. 16, p. 347, 2016.

[290] H. Gao, W. Sun, J. Zhao et al., “Tanshinones and diethyl-α-dehydrotocopherols from Salvia miltiorrhiza as a new chemical character of Sanguisorba officinalis,” Phytochemistry, vol. 65, no. 19, pp. 2719–2729, 2004.

[291] X. D. Su, R. H. Guo, H. X. Li et al., “Anti-inflammatory and immunomodulatory activities of polysaccharides from Sanguisorba officinalis L.,” Bioorganic & Medicinal Chemistry Letters, vol. 28, no. 12, pp. 2210–2216, 2018.

[292] H. Zhang, J.-M. Yoo, W.-K. Cho, and J. Y. Ma, “Antioxidant and immunomodulatory activities of polysaccharides from the roots of Sanguisorba officinalis,” International Journal of Biological Macromolecules, vol. 51, no. 5, pp. 1057–1062, 2012.

[293] J.-H. Yang, Y.-H. Hwang, M.-J. Gu, W.-K. Cho, and J. Y. Ma, “Ethanol extracts of Sanguisorba officinalis L. suppress TNF-α/IFN-γ-induced pro-inflammatory chemokine production in HaCaT cells,” Phytotherapy, vol. 22, no. 14, pp. 1262–1268, 2015.

[294] K.-H. Jung, Y.-S. Kil, J. Jung et al., “Tuberosostemonine N, an anti-inflammatory agent derived from Tuberostemon tuberosa Bunge (Danshen),” Phytochemistry, vol. 9, no. 8, Article ID e102506, 2016.

[295] Y.-S. Chen, S.-M. Lee, Y.-J. Lin, S.-H. Chiang, and C.-C. Lin, “Effects of danshensu and salvianolic acid B from Salvia miltiorrhiza bunge (Lamiaceae) on cell proliferation and collagen and melanin production,” Molecules, vol. 19, no. 2, pp. 2029–2041, 2014.

[296] Y.-Y. Tao, J.-L. Yuan, L. Shen, and C.-H. Liu, “Salvianolic acid B prevents epithelial-to-mesenchymal transition through the TGF-beta1 signal transduction pathway in vivo and in vitro,” BMC Cell Biology, vol. 11, no. 1, p. 31, 2010.

[297] Y. Li, S. Shi, J. Gao et al., “Cryptotanshinone downregulates the profibrotic activities of hypertrophic scar fibroblasts and accelerates wound healing: a potential therapy for the reduction of skin scarring,” Biomedicine & Pharmacotherapy, vol. 80, pp. 80–86, 2016.

[298] L. Zhou, Z. Zuo, and M. S. S. Chow, “Danshen: an overview of its chemistry, pharmacology, pharmacokinetics, and clinical use,” The Journal of Clinical Pharmacology, vol. 45, no. 12, pp. 1345–1359, 2005.

[299] W. Sun, Z.-L. Zhang, X. Liu et al., “Terpene glycosides from the roots of Sanguisorba officinalis L. and their hemostatic activities,” Molecules, vol. 17, no. 7, pp. 7629–7636, 2012.

[300] H. Zhang, S. R. Koyyalamudi, S. C. Jeong et al., “Antioxidant and immunomodulatory activities of polysaccharides from the roots of Sanguisorba officinalis,” International Journal of Biological Macromolecules, vol. 51, no. 5, pp. 1057–1062, 2012.

[301] M.-K. Tsai, Y.-L. Lin, and Y.-T. Huang, “Effects of salvianolic acids on oxidative stress and hepatic fibrosis in rats,” Toxicology and Applied Pharmacology, vol. 242, no. 2, pp. 155–164, 2010.

[302] X. D. Su, R. H. Guo, H. X. Li et al., “Anti-inflammatory and immunomodulatory activities of polysaccharides from Sanguisorba officinalis L.,” Bioorganic & Medicinal Chemistry Letters, vol. 28, no. 12, pp. 2210–2216, 2018.

[303] J. H. Yang, J.-M. Yoo, W.-K. Cho, and J. Y. Ma, “Anti-inflammatory effects of sanguisorbae radix water extract on the suppression of mast cell degranulation and STAT-1/Jak-2 activation in BMMCs and HaCaT keratinocytes,” BMC Complementary and Alternative Medicine, vol. 16, p. 347, 2016.

[304] X. Xu, X. Li, L. Zhang et al., “Enhancement of wound healing by the traditional Chinese medicine herbal mixture Sapphra flavescens in a rat model of perianal ulceration,” In Vivo, vol. 31, no. 4, pp. 543–549, 2017.

[305] H. Gao, W. Sun, J. Zhao et al., “Tanshinones and diethylblechnics with anti-inflammatory and anti-cancer activities from Salvia miltiorrhiza Bunge (Danshen),” Scientific Reports, vol. 6, Article ID 33720, 2016.

[306] H. Gao, W. Sun, J. Zhao et al., “Tanshinones and diethylblechnics with anti-inflammatory and anti-cancer activities from Salvia miltiorrhiza Bunge (Danshen),” Scientific Reports, vol. 6, Article ID 33720, 2016.

[307] H. Gao, W. Sun, J. Zhao et al., “Tanshinones and diethylblechnics with anti-inflammatory and anti-cancer activities from Salvia miltiorrhiza Bunge (Danshen),” Scientific Reports, vol. 6, Article ID 33720, 2016.

[308] H. Gao, W. Sun, J. Zhao et al., “Tanshinones and diethylblechnics with anti-inflammatory and anti-cancer activities from Salvia miltiorrhiza Bunge (Danshen),” Scientific Reports, vol. 6, Article ID 33720, 2016.

[309] H. Gao, W. Sun, J. Zhao et al., “Tanshinones and diethylblechnics with anti-inflammatory and anti-cancer activities from Salvia miltiorrhiza Bunge (Danshen),” Scientific Reports, vol. 6, Article ID 33720, 2016.
Evidence-Based Complementary and Alternative Medicine

[310] N. Balekar, T. Nakpheng, N. G. Katkam, and T. Srichana, “Wound healing activity of ent-kaur-9(11),16-dien-19-oic acid isolated from Wedelia trilobata (L.) leaves,” Phytotherapy Research, vol. 19, no. 13, pp. 1178–1184, 2012.

[311] M. Govindappa, “Antimicrobial, antioxidant and in vivo anti-inflammatory activity of ethanolic extract and active phytochemical screening of Wedelia trilobata (L.) Hitchc.” Journal of Medicinal Plants Research, vol. 5, no. 24, pp. 5718–5729, 2011.

[312] Z. Weng, A. B. Patel, M. Vasiadi, A. Z’herianou, and M. Govindappa, “Antimicrobial, antioxidant and in vivo anti-inflammatory enhancer,” PLoS One, vol. 9, no. 2, Article ID e90739, 2014.

[313] C. Artaria, G. Maramaldi, A. Bonfigli, L. Rigano, and D. M. Bautista, Y. M. Sigal, A. D. Milstein et al., “Pungent derivatives of Zanthoxylum bungeanum Maxim.: a pharma-cochemical study,” Journal of Separation Science, vol. 39, no. 14, pp. 2728–2735, 2016.

[314] Y. Lan, Q. Wu, Y.-q. Mao et al., “Cytotoxicity and enhanced activity of essential oil from Zanthoxylum bungeanum Maxim. as a natural transdermal penetration enhancer,” Journal of Zhejiang University Science B, vol. 15, no. 2, pp. 153–164, 2014.

[315] Z. Zhang, J. Liu, P. Shen et al., “Zanthoxylum bungeanum percipar extract prevents dextran sulfate sodium-induced experimental colitis in mice via the regulation of TLR4 and TLR4-related signaling pathways,” International Immunopharmacology, vol. 41, pp. 127–135, 2016.

[316] W. Tang, Q. Xie, J. Guan, S. Jin, and Y. Zhao, “Phytochemical profiles and biological activity evaluation of Zanthoxylum bungeanum Maxim seed against asthma in murine models,” Journal of Ethnopharmacology, vol. 152, no. 3, pp. 444–450, 2014.

[317] M. Bautista, Y. M. Sigal, A. D. Milstein et al., “Pungent agents from Szechuan peppers excite sensory neurons by inhibiting two-pore potassium channels,” Nature Neuroscience, vol. 11, no. 7, pp. 772–779, 2008.

[318] M. Zhang, J. Wang, L. Zhu et al., “Zanthoxylum bungeanum Maxim. (Rutaceae): a systematic review of its traditional uses, botany, phytochemistry, pharmacology, pharmacokinetics, and toxicology,” International Journal of Molecular Sciences, vol. 18, no. 10, 2017.

[319] C. Artaria, G. Maramaldi, A. Bonfigli, L. Rigano, and G. Appendino, “Lifting properties of the alkalamide fraction from the fruit husks of Zanthoxylum bungeanum,” International Journal of Cosmetic Science, vol. 33, no. 4, pp. 328–333, 2011.

[320] Y. Lan, H. Li, Y.-y. Chen et al., “Essential oil from Zanthoxylum bungeanum Maxim. and its main components used as transdermal penetration enhancers: a comparative study,” Journal of Zhejiang University Science B, vol. 15, no. 11, pp. 940–952, 2014.

[321] Z. Molazem, F. Mohseni, M. Younesi, and S. Keshavarzi, “Aloe vera gel and cesarean wound healing: a randomized controlled clinical trial,” Global Journal of Health Science, vol. 7, no. 1, pp. 203–209, 2014.

[322] Q. Gao, M. Yang, and Z. Zuo, “Overview of the anti-inflammatory effects, pharmacokinetic properties and clinical efficacies of arctigenin and arctin from Arctium lappa L.” Acta Pharmacologica Sinica, vol. 39, no. 5, pp. 787–801, 2018.

[323] M.-R. Choi, D.-K. Choi, K.-D. Kim et al., “Amelopsia japonica makino extract inhibits the inflammatory reaction induced by pathogen-associated molecular patterns in epidermal keratinocytes,” Annals of Dermatology, vol. 28, no. 3, pp. 352–359, 2016.

[324] A. Okhuarobo, J. Ehiogie Falodun, O. Erharuyi, V. Imieje, A. Falodun, and P. Langer, “Harnessing the medicinal properties of Andrographis paniculata for diseases and beyond: a review of its phytochemistry and pharmacology,” Asian Pacific Journal of Tropical Disease, vol. 4, no. 3, pp. 213–222, 2014.

[325] K.-F. Huang, Y.-C. Hsu, C.-N. Lin, J.-I. Tseng, Y.-W. Chen, and J.-J. Wang, “Shiunko promotes epithelization of wounded skin,” The American Journal of Chinese Medicine, vol. 32, no. 03, pp. 389–396, 2004.

[326] H. Zhao, J. Deneau, G. O. L. Che et al., “Angelica sinensis isolate SBD4: composition, gene expression profiling, mechanism of action and effect on wounds, in rats and humans,” European Journal of Dermatology, vol. 22, no. 1, pp. 58–67, 2012.

[327] M. G. Dozmorov, Q. Yang, W. Wu et al., “Differential effects of selective frankincense (Ru Xiang) essential oil versus non-selective sandalwood (Tan Xiang) essential oil on cultured bladder cancer cells: a microarray and bioinformatics study,” Chinese Medicine, vol. 9, no. 1, p. 18, 2014.

[328] M. Buzzi, F. d. Freitas, and M. d. B. Winter, “Cicatrização de úlceras por pressão com extrato Plenusdermax de Calendula officinalis L.,” Revista Brasileira de Enfermagem, vol. 69, no. 2, pp. 250–257, 2016.

[329] A. F. M. d. Carvalho, M. C. F. Feitosa, N. P. M. d. F. Coelho et al., “Low-level laser therapy and Calendula officinalis in repairing diabetic foot ulcers,” Revista da Escola de Enfermagem da USP, vol. 50, no. 4, pp. 628–634, 2016.

[330] M. Akram, A. Hamid, A. Khalil et al., “Review on medicinal uses, pharmacological, phytochemistry and immunomodulatory activity of plants,” International Journal of Immunopathology and Pharmacology, vol. 27, no. 3, pp. 313–319, 2014.

[331] Q. Xia, Z. Ma, X. Mei et al., “Assay for the developmental toxicity of safflower (Carthamus tinctorius L.) to zebrafish embryos/larvae,” Journal of Traditional Chinese Medical Sciences, vol. 4, no. 1, pp. 71–81, 2017.

[332] G. Zhao, Y. Gai, W.-J. Chu, G.-W. Qin, and L.-H. Guo, “A novel compound N1,N5-(Z)-N10-(E)-tri-p-coumaroylspermidine isolated from Carthamus tinctorius L. and acting by serotonin transporter inhibition,” European Neuropsychopharmacology, vol. 19, no. 10, pp. 749–758, 2009.

[333] X. Zhou, L. Tang, Y. Xu, G. Zhou, and Z. Wang, “Towards a better understanding of medicinal uses of Carthamus tinctorius L. in traditional Chinese medicine: a phytochemical and pharmacological review,” Journal of Ethnopharmacology, vol. 151, no. 1, pp. 27–43, 2014.

[334] C. L. Kanu, I. O. Imosemi, and A. O. Malomo, “A review of the multifaceted usefulness of Celosia argentea Linn.,” European Journal of Pharmaceutical and Medical Research, vol. 4, no. 10, pp. 72–79, 2017.
Evidence-Based Complementary and Alternative Medicine

[337] W. Bylka, P. Zajdtek-Awizen, E. Studzinska-Sroka, and M. Brzezinska, “Centella asiatica in cosmetology,” Advances in Dermatology and Allergology, vol. 1, no. 1, pp. 46–49, 2013.

[338] B. Brinkhaus, M. Lindner, D. Schuppan, and E. G. Hahn, “Chemical, pharmacological and clinical profile of the East Asian medical plant Centella asiatica,” Phytomedicine, vol. 7, no. 5, pp. 427–448, 2000.

[339] M. Farahpour and M. Habibi, “Evaluation of the wound healing activity of an ethanolic extract of Ceylon cinnamon in mice,” Veterinarí Medicína, vol. 57, no. 1, pp. 53–57, 2012.

[340] A. Khan, M. Safdar, M. M. Ali Khan, K. N. Khattak, and R. A. Anderson, “Cinnamon improves glucose and lipids of people with type 2 diabetes,” Diabetes Care, vol. 26, no. 12, pp. 3215–3218, 2003.

[341] L. S. M. Ooi, Y. Li, S.-L. Kam, H. Wang, E. Y. L. Wong, and V. E. C. Ooi, “Antimicrobial activities of cinnamon oil and cinnamaldehyde from the Chinese medicinal herb Cinnamomum cassia Blume,” The American Journal of Chinese Medicine, vol. 34, no. 3, pp. 511–522, 2006.

[342] C.-H. Yang, R.-X. Li, and L.-Y. Chuang, “Antioxidant activity of various parts of Cinnamomum cassia extracted with different extraction methods,” Molecules, vol. 17, no. 6, pp. 7294–7304, 2012.

[343] D. d. M. Carvalho, K. P. Takeuchi, R. M. Geraldine, C. J. d. Moura, and M. C. L. Torres, “Production, solubility and antioxidant activity of curcumin nanosuspension,” Food Science and Technology, vol. 35, no. 1, pp. 115–119, 2015.

[344] S. H. Mun, D.-K. Joung, Y.-S. Kim et al., “Synergistic antibacterial effect of curcumin against methicillin-resistant Staphylococcus aureus,” Phytomedicine, vol. 20, no. 8-9, pp. 714–718, 2013.

[345] G. Liang, S. Yang, H. Zhou et al., “Synthesis, crystal structure and anti-inflammatory properties of curcumin analogues,” European Journal of Medicinal Chemistry, vol. 44, no. 2, pp. 915–919, 2009.

[346] B. Meng, J. Li, and H. Cao, “Antioxidant and antiinflammatory activities of curcumin on diabetes mellitus and its complications,” Current Pharmaceutical Design, vol. 19, no. 11, pp. 2101–2113, 2013.

[347] R. L. Thangapazham, S. Sharad, and R. K. Maheshwari, “Skin regenerative potentials of curcumin,” Biofactors, vol. 39, no. 1, pp. 141–149, 2013.

[348] J. L. Ryan, C. E. Hecker, M. Ling et al., “Curcumin for radiation dermatitis: a randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients,” Radiation Research, vol. 180, no. 1, pp. 34–43, 2013.

[349] C. Mohanty and S. K. Sahoo, “Curcumin and its topical formulations for wound healing applications,” Drug Discovery Today, vol. 22, no. 10, pp. 1582–1592, 2017.

[350] R. Zhang, Y. Wang, J. Li, H. Jin, S. Song, and C. Huang, “The Chinese herb isolate yuanyuanhun (YHL-14) induces G2/M arrest in human cancer cells by up-regulating p21 protein expression through an p53 protein-independent cascade,” Journal of Biological Chemistry, vol. 289, no. 10, pp. 6394–6403, 2014.

[351] Y. H. Zhao, Y. F. Lin, and Y. Zhao, “The analgesic activity study on Entada phaseoloides total saponin,” Journal of Medicine & Pharmacy of Chinese Minorities, vol. 2, pp. 53–55, 2011.

[352] Y. Dong, H. Shi, H. Yang, Y. Peng, M. Wang, and X. Li, “Antioxidant phenolic compounds from the stems of Entada phaseoloides,” Chemistry & Biodiversity, vol. 9, no. 1, pp. 68–79, 2012.

[353] Y.-C. Chang, K.-X. Huang, A.-C. Huang, Y.-C. Ho, and C.-J. Wang, “Hibiscus anthocyanins-rich extract inhibited LDL oxidation and oxLDL-mediated macrophages apoptosis,” Food and Chemical Toxicology, vol. 44, no. 7, pp. 1015–1023, 2006.

[354] H.-U. Son, S. Lee, J.-C. Heo, and S.-H. Lee, “The solid-state fermentation of Artemisia capillaris leaves with Ganoderma lucidum enhances the anti-inflammatory effects in a model of atopic dermatitis,” International Journal of Molecular Medicine, vol. 39, no. 5, pp. 1233–1241, 2017.

[355] Y. Xiao, Y.-C. Wang, L.-L. Li et al., “Lactones from Ligusticum chuanxiong Hort. reduces atherosclerotic lesions in apoE-deficient mice via inhibiting over expression of NF-kB-dependent adhesion molecules,” Fitoterapia, vol. 95, pp. 240–246, 2014.

[356] J.-L. Liu, S.-L. Zheng, Q.-J. Fan et al., “Optimisation of high-pressure ultrasonically-assisted extraction and antioxidant capacity of polysaccharides from the rhizome of Ligusticum chuanxiong,” International Journal of Biological Macromolecules, vol. 76, pp. 80–85, 2015.

[357] Y.-L. Lin, G.-J. Wang, C.-L. Huang et al., “Ligusticum chuanxiong as a potential neuroprotectant for preventing serum deprivation-induced apoptosis in rat pheochromocytoma cells: functional roles of mitogen-activated protein kinases,” Journal of Ethnopharmacology, vol. 122, no. 3, pp. 417–423, 2009.

[358] M.-J. Liang, L.-C. He, and G.-D. Yang, “Screening, analysis and in vitro vasodilatation of effective components from Ligusticum Chuanxiong,” Life Sciences, vol. 78, no. 2, pp. 128–133, 2005.

[359] H. Matsuda, T. Ohita, A. Kawaguchi, and M. Yoshikawa, “Bioactive constituents of Chinese natural medicines. VI. Moutan cortex. (2): structures and radical scavenging effects of suffruticosides A, B, C, D, and E and galloyl-oxy-paeoniflorin,” Chemical and Pharmaceutical Bulletin, vol. 49, no. 1, pp. 69–72, 2001.

[360] L. Sun, L. Liu, S. Zong et al., “Traditional Chinese medicine Guizhi Fuling capsule used for therapy of dysmenorrhea via attenuating uterus contraction,” Journal of Ethnopharmacology, vol. 191, pp. 273–279, 2016.

[361] H. Dan, L. Zhang, X. Qin et al., “Moutan cortex extract exerts protective effects in a rat model of cardiac ischemia/reperfusion,” Canadian Journal of Physiology and Pharmacology, vol. 94, no. 3, pp. 245–250, 2016.

[362] Y. Xiong, L. Chen, J. Man, Y. Hu, and X. Cui, “Chemical and bioactive comparison of Panax notoginseng root and rhizome in raw and steamed forms,” Journal of Ginseng Research, vol. 43, no. 3, pp. 385–393, 2019.

[363] S. Y. Jang, J. K. Lee, E. H. Jang, S. Y. Jeong, and J.-H. Kim, “Shikonin blocks migration and invasion of human breast cancer cells through inhibition of matrix metalloproteinase-9 activation,” Oncology Reports, vol. 31, no. 6, pp. 2827–2833, 2014.

[364] H. Azuma, J. Li, R. Youda et al., “Improved isolation procedure for shikonin from the root of the Chinese medicinal plant Lithospermum erythrorhizon and its solubilization with cyclodextrins,” Journal of Applied Research on Medicinal and Aromatic Plants, vol. 3, no. 2, pp. 58–63, 2016.

[365] J. Chen, Y. He, T. Gao, L. Zhang, and Y. Zhao, “Preparation and properties of compound Arnebiae Radix microemulsion gel,” African Journal of Traditional, Complementary and Alternative medicines, vol. 14, no. 3, pp. 274–279, 2017.

[366] Y. Zhang, P. Jiang, M. Ye, S.-H. Kim, C. Jiang, and J. Lü, “Tanshinones: sources, pharmacokinetics and anti-cancer...
activities,” International Journal of Molecular Sciences, vol. 13, no. 10, pp. 13621–13666, 2012.

[367] Y. Tan, K. Wang, N. Wang, G. Li, and D. Liu, “Ectopic expression of human acidic fibroblast growth factor 1 in the medicinal plant, Salvia miltiorrhiza, accelerates the healing of burn wounds,” BMC Biotechnology, vol. 14, no. 1, p. 74, 2014.

[368] J.-Q. Liu, T.-F. Lee, M. Miedzyblocki, G. C. F. Chan, D. L. Bigam, and P.-Y. Cheung, “Effects of tanshinone IIA, a major component of Salvia miltiorrhiza, on platelet aggregation in healthy newborn piglets,” Journal of Ethnopharmacology, vol. 137, no. 1, pp. 44–49, 2011.

[369] I.-S. Lay, J.-H. Chiu, M.-S. Shiao, W.-Y. Lui, and C.-W. Wu, “Crude extract of Salvia miltiorrhiza and salvianolic acid B enhance in vitro angiogenesis in murine SVR endothelial cell line,” Planta Medica, vol. 69, no. 1, pp. 26–32, 2003.

[370] Z. R. Zhang, J.-H. Li, S. Li et al., “In vivo angiogenesis screening and mechanism of action of novel tanshinone derivatives produced by one-pot combinatorial modification of natural tanshinone mixture from Salvia miltiorrhiza,” PLoS One, vol. 9, no. 7, Article ID e100416, 2014.

[371] P. Ma, J. Liu, C. Zhang, and Z. Liang, “Regulation of water-soluble phenolic acid biosynthesis in Salvia miltiorrhiza Bunge,” Applied Biochemistry and Biotechnology, vol. 170, no. 6, pp. 1253–1262, 2013.

[372] X. Dang, J.-j. Miao, A.-q. Chen et al., “The antithrombotic effect of RSNK in blood-stasis model rats,” Journal of Ethnopharmacology, vol. 173, pp. 266–272, 2015.

[373] T. Yu, Y. J. Lee, H. M. Yang et al., “Inhibitory effect of Sanguisorba officinalis ethanol extract on NO and PGE2 production is mediated by suppression of NF-κB and AP-1 activation signaling cascade,” Journal of Ethnopharmacology, vol. 134, no. 1, pp. 11–17, 2011.

[374] X. He, J. Fang, L. Huang, J. Wang, and X. Huang, “Sophora flavescens Ait.: Traditional usage, phytochemistry and pharmacology of an important traditional Chinese medicine,” Journal of Ethnopharmacology, vol. 172, pp. 10–29, 2015.

[375] H. Yang, Z. Zhou, L. He et al., “Hepatoprotective and inhibiting HBV effects of polysaccharides from roots of Sophora flavescens,” International Journal of Biological Macromolecules, vol. 108, pp. 744–752, 2018.

[376] Y. B. Ryu, I. M. Westwood, N. S. Kang et al., “Kurarinol, tyrosinase inhibitor isolated from the root of Sophora flavescens,” Phytotherapy, vol. 15, no. 8, pp. 612–618, 2008.

[377] K. Y. Lee, S. H. Sung, and Y. C. Kim, “Neuroprotective bibenzyl glycosides of Stemona tuberosa roots,” Journal of Natural Products, vol. 69, no. 4, pp. 679–681, 2006.

[378] X. Q. Li, X.-Q. Li, R. Kang, J.-C. Huo, Y.-H. Xie, and S.-W. Wang, “Wound-healing activity of Zanthoxylum bungeanum maxim seed oil on experimentally burned rats,” Pharmacognosy Magazine, vol. 13, no. 51, pp. 363–371, 2017.