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The Therapeutic Wound Healing activities of Various Medicinal Plants

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Abstract**—** *The skin protects the internal organs from mechanical, chemical, and thermal injury and is thus the body's first line of defence. It has an advanced immune response that protects the body from harmful microbes. Healing a wound is a dynamic process supported by a plethora of cellular processes such as homoeostasis, inflammation, proliferation, and remodelling, all of which must work in tandem to restore the health of the injured tissue. Following cutaneous injury, germs may rapidly invade subcutaneous tissues, leading to painful chronic sores and even death. Wound therapy and infection prevention have both benefited greatly from the use of natural phytomedicines, which have been used extensively due to their potent pharmacological effects. Phytotherapy has been used effectively to heal cutaneous wounds, delay the emergence of infections, and limit the use of antibiotics that contribute to dangerously widespread antibiotic resistance since ancient times. Achiella millefolium, Aloe vera, Althaea officinalis, Calendula officinalis, Matricaria chamomilla, Curcuma longa, Eucalyptus, Jojoba, plantain, pine, green tea, pomegranate, and Inula are only a few of the many commonly used botanicals in the Northern Hemisphere for wound healing. This article discusses the most popular medicinal plants of the Northern Hemisphere used for wound healing, and it also offers suggestions for effective natural alternatives.*

Keywords**— wounds; wound healing; bioactive components; medicinal plants**

I. INTRODUCTION

Skin, a complex organ, covers the whole external surface of the body. It serves as a physical barrier between the inside of the body and the outside, minimising fluid and electrolyte loss, reducing exposure to harmful chemicals, and protecting against invading microorganisms [1]. Due to the many microbiological issues that wounds create, including local or apparent infection, poor healing, and the growth of multi-resistant bacteria [2], they end up costing millions of dollars annually in affluent countries. People at the extremes of the age span, namely babies and the elderly, are disproportionately affected by traumatic wounds [3]. Chronic lower limb wounds are an increasing strain on healthcare systems [4] due to an ageing population. Chronic wounds may cause the healing process to fail in a planned way [5], but acute wounds do not often disturb the long-term restoration of the anatomical and functional integrity of the skin. Throughout the homoeostasis, inflammation, proliferation, re-epithelialization, and remodelling phases of wound healing, several distinct cell types with specialised roles move in concert with one another (see Figure 1).

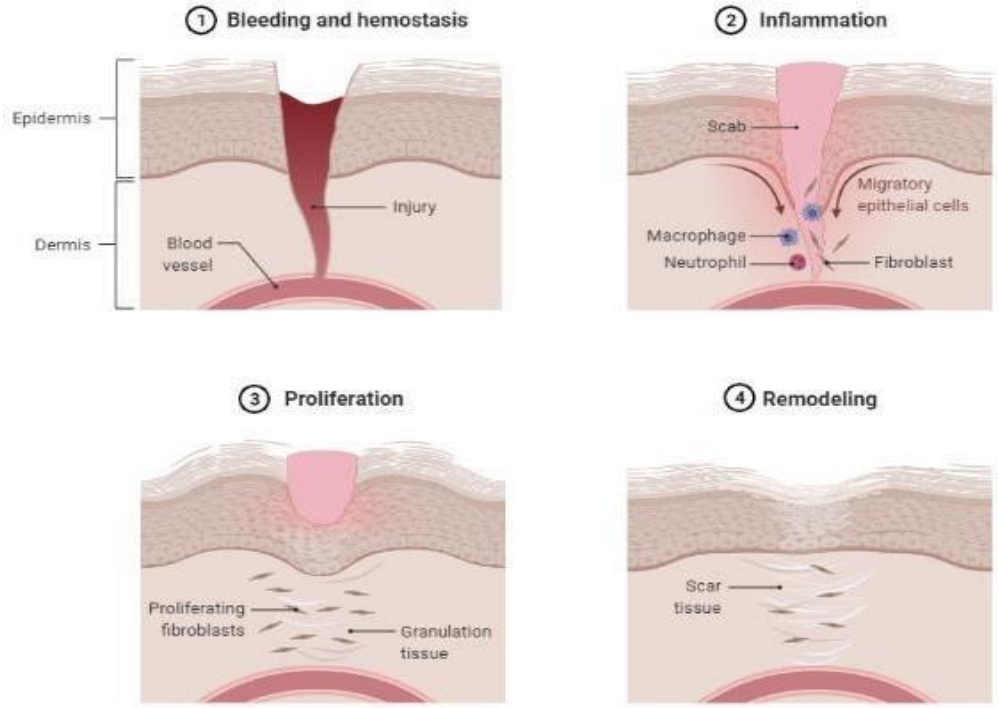


Fig.1. The four main phases of the wound healing process [6]. Adapted from https://app.biorender.com/biorender-templates2023/figures/all/t-5fa1b1622a60ac00a3d858ec-wound-healing (accessed on 15 December 2022).

Platelets are activated upon contact with the vascular sub-endothelial matrix, homoeostasis, and coagulation [7,8], causing injured blood vessels to quickly contract after injury and a blood clot to form to arrest exsanguination caused by vascular damage. Numerous cytokines and growth factors, including as insulin-like, platelet-derived, transforming, and epidermal growth factors, are found in abundance in platelets. The wound healing cascade [9] begins with the activation and attraction of neutrophils, which in turn attracts macrophages, endothelial cells, and fibroblasts as repair agents. Following the coagulation phase comes the inflammatory phase, which begins with the early inflammatory reaction and lasts until the early post-coagulation phase. During this time, neutrophils gather at the wound site to begin their work as cleansers. Within 24 to 36 hours of damage, bacteria and platelet products emit various chemo-attractive compounds that bring neutrophils to the wound region to eliminate the germs by phagocytosis and so avoid infection. After 48-72 hours, wound macrophages take over phagocytosis. Neutrophils are destroyed by apoptosis after all contaminating bacteria have been removed. Macrophages outlive neutrophils and serve as crucial regulatory cells, storing and releasing a wide variety of growth factors for fibroblasts, endothelial cells, and tissue repair. When neutrophils and macrophages clean up after themselves, they release growth factors, cytokines, proteases, reactive oxygen species, and coagulation factors [10]. Keratinocytes and fibroblasts are essential for the formation of granulation tissue, which seals the wound and provides a structural platform for cell adhesion, migration, growth, and differentiation throughout the wound repair process [11]. Fibroblasts, which produce mature collagen fibrils, are the major cell type engaged in remodelling the wound ECM [12]. Foreign bodies introduce the risk of infection, ischemia, edoema, or increased pressure, all of which slow the wound-healing process [13]. Therefore, correct diagnosis and treatment are critical to promote wound healing and avoid further complications [14].

Keeping the wound bed clean is an essential part of the healing process. The production of biofilms may be delayed and the bioburden reduced if wounds are properly washed. Even while antiseptics are used to clean wounds to prevent infection, it is unclear whether these solutions, like irrigation liquids, really help wounds heal more quickly. The most common and inevitable

obstacle to wound healing is an inappropriate healing technique [16], which may result in considerable injury, including skin loss and the onset of an infection, particularly in the case of chronic wounds.

Herbal medicines (HM) have been used for decades to treat medical diseases and improve wellbeing through its bioactive constituents [17]. HM fall under the category of complementary and alternative therapies (CAM). Over time, people have learned which types of plants are best for treating particular conditions. Applying botanicals topically to heal wounds and other dermatological issues is common practise in many herbal medicinal systems, including traditional Chinese medicine, Ayurveda, Unani, Russian herbalism, and others (Table 1). The pharmacological effects of plants are a direct result of the biological roles played by their secondary metabolites [18].

Table 1. Dermatological problems treated by various traditional herbal medicines.

Medical System	Dermatological Conditions	Reference
Chinese	Diabetic foot ulcers	[19]
Ayurveda	Psoriaisis	[20]
Unani	Pityriasis versicolor	[21]
Russian	Vitiligo, psoriasis	[22]

Improvements in antimicrobial use policies/regulations, infection control, sanitation, and alternatives to antimicrobials are all important measures, thus many countries and international organisations have incorporated a one-health approach in their action plans to deal with antibiotic resistance [23]. Persistent antibiotic resistance is associated with a higher risk of treatment failure and subsequent infections. Consequently, they are mostly responsible for the increasing death rates that drive up healthcare costs. The dangers of antibiotic resistance have been known for a long time, and standard microbiological tests make it easy to identify it. For whatever reason, certain bacteria are able to withstand antibiotic treatment, while being very susceptible to them. Treatment failure may occur because antibi- otic persistence, unlike antibiotic resistance, is difficult to evaluate and is commonly ignored [24]. In response to rising health care costs, an ageing population, growing awareness of infection hazards (including biofilms) that are difficult to treat, and the persistent threat of diabetes and obesity around the world, the National Institutes of Health have added a category for wounds to their Research Portfolio Online Reporting Tool. In addition, by 2024, the wound care industry is expected to generate between $15 and $22 billion yearly [25]. There has to be stricter enforcement of measures that slow the rise of antibiotic-resistant germs and stop their spread. That's why several dermatological conditions, including atopic dermatitis, acne vulgaris, and psoriasis, have been treated with plant-based drugs throughout the years [26, 27].

There is a certain order in which a medicine must go through discovery, development, and regulatory approval [28]. Screening and evaluating extracts against different pharmacological targets is a major issue for many labs across the globe who are looking to capitalise on the vast natural chemical diversity [29]. The purpose of this article is to provide an overview of the most important botanical and herbal therapies for wounds, together with a discussion of their mechanisms of action. This study aims to identify the most successful natural alternatives in the wound care industry and make them available to dermatologists and scientists.

Plant Species and Their Potential Therapeutic Interests

Achilleamillefolium L.

Many different kinds of yarrow (Achillea) have long histories of usage in folk medicine. When it comes to using natural remedies for things like wounds, bleeding, stomachaches, GI problems, the common cold, the flu, and stomach difficulties, A. millefolium is among the most popular choices [30]. During the Trojan War, the Greek warrior Achilles is said to have used this plant to monitor his blood pressure and heal his wounds. It's possible that his name inspired the genus name, while "millefolium" refers to the finely divided, feathery leaves [30].

Several species of Achillea have a long history of use

in herbal therapy across many civilisations. Yarrow (Achillea millefolium L.), which is native to Europe, Asia, North Africa, and North America, is one of the most important and widely used medicinal herbs in the world [31]. Traditional medicine has used the flowering plant from its native Northern Hemisphere as an astringent, antibacterial, anti-inflammatory, and antispasmodic agent to hasten the healing of burns, ulcers, cuts, and wounds [32].

Figure 2 displays the main phytochemical components of Achillea that act as antioxidants.

The high content of flavonoids in A. millefolium has been connected to its antioxidant and anti-inflammatory properties [33]. Extracts from the Achillea plant have potent tyrosinase-inhibiting, antioxidant, and antibacterial activity [34], which makes them promising for usage as active components in skin-protecting medications and cosmetics. Two months of in vivo treatment of A. millefolium extracts resulted in thicker epidermis and increased production of cytokeratin 10, transglutaminase-1, and filaggrin in cultured skin biopsies compared to placebo [35].

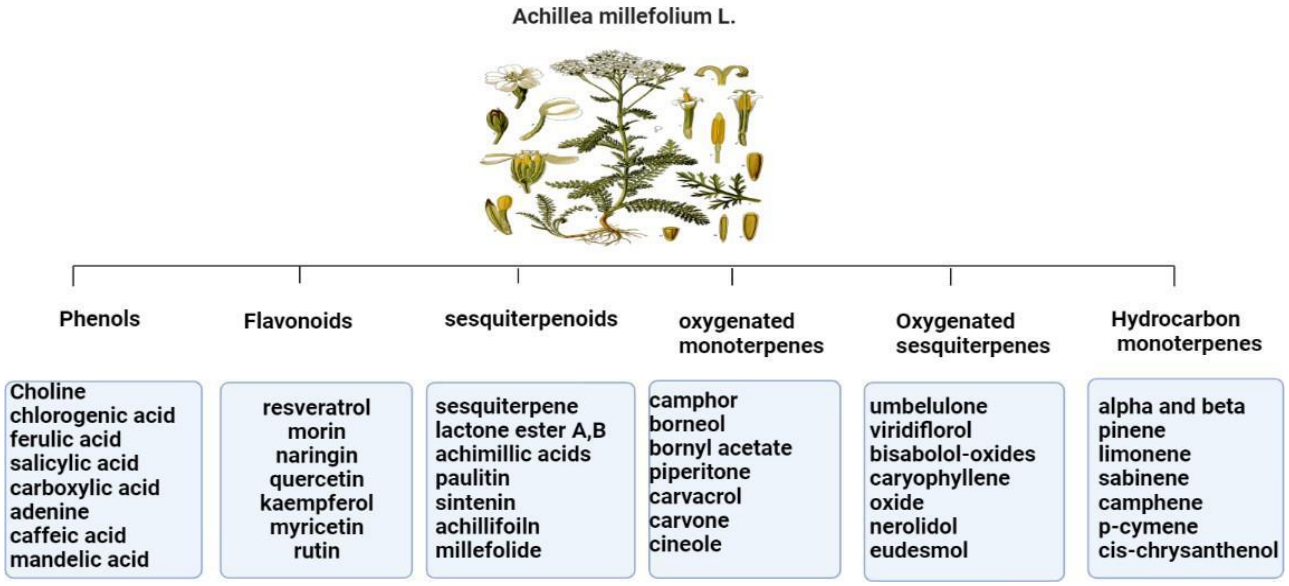


Fig.2. Bioactive phytochemicalcomponents of Achillea millefolium L. [36].

Aloe vera

The plant often known as "aloe vera" really belongs to the Lilaceae family. Aloe derives from the Arabic word "alloeh," which meaning "bitter." More and more novel food items are being made using aloevera as an ingredient because of its medicinal and functional properties [37]. For thousands of years, people in Arab, Chinese, Egyptian, Greek, Indian, Japanese, and Korean societies have relied on Aloe vera as a traditional medicine to treat a wide range of conditions, including skin problems, constipation, external and internal ulcers, hyperlipidemia, and diabetes [38].

The widespread belief in the healing properties of aloe vera has led to the rapid expansion of the sector dedicated to the plant. Products including face and hand creams, foundations, cleansers, lipsticks, lotions, shampoos and hair tonics, shaving preparations, bath products, cosmetics and scent preparations, and many more are made using this ingredient [39].

Detoxification, relieving constipation, eliminating waste products, and improving digestion are just some of the many biological functions that have been attributed to aloe plants. The antibacterial and antimicrobial, anticancer, anti-inflammatory, anti-rheumatoid, and anti-arthritic properties of the aloe plant are the basis for its bioactivities [40]. There are three parts to an aloe vera plant: the green pulp, the aloe gel, and the outer leaf [41]. Antioxidant

properties have been seen in aloe gel, aloe flower extract, and aloe leaf skin [42]. Aloe vera has been used as a wound treatment for a very long time [43]. A wide variety of chronic wounds, including pressure ulcers, burns, surgical incisions, cracked lips, genital herpes, and psoriasis, have responded effectively to aloe vera [44]. The anti-inflammatory, pro-angiogenic, and wound-contraction properties of aloe vera hydrogel have led to a 29% decrease in total healing time and full wound closure in only 15 days [45]. Clinical study data showing Aloe vera's bioactive properties are shown in Figure 3 for various time periods.

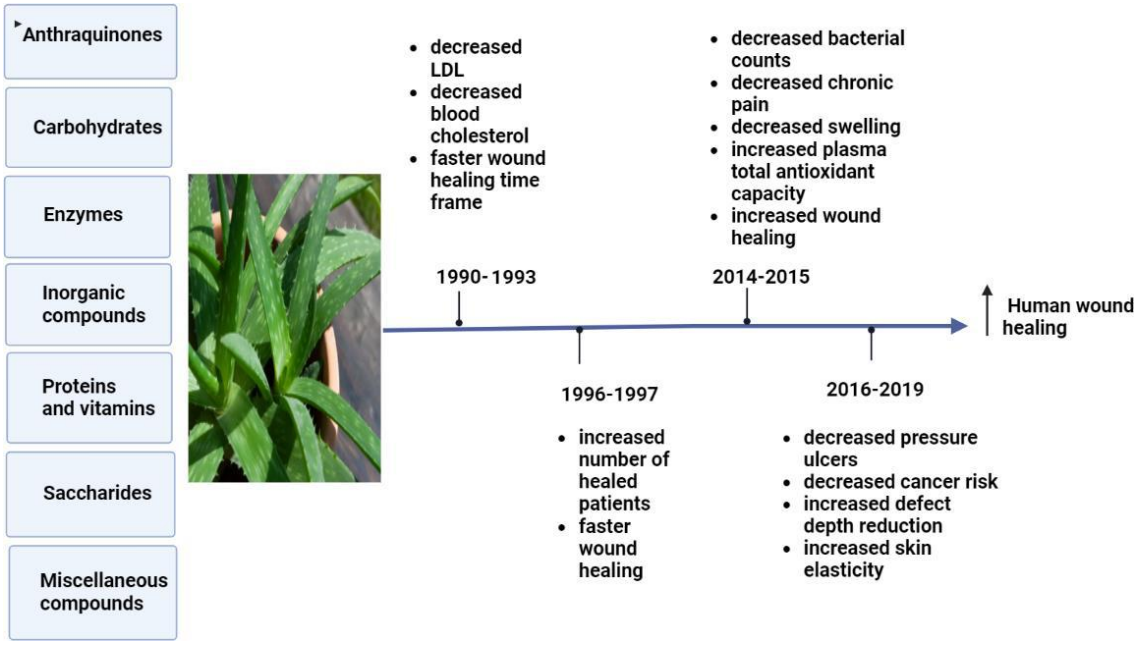


Fig.3. Effects of pharmacological bioactive components of Aloe vera on clinical trials [46].

Curcuma longa

Curcuma longa L. (turmeric) plants, which belong to the Zingiberaceae family, are the source of the brilliant yellow chemical compound called curcumin. Vogel and Pelletier, working in the Harvard College laboratory, discovered Curcumin in the Curcuma longa rhi- zomes (turmeric) almost 200 years ago [47]. Turmeric has been used to treat stomachaches, obesity, and inflammation of the intestines and skin in Ayurvedic medicine [48]. Bioactive curcuminoids like curcumin, demethoxycurcumin, and bisdemethoxycurcumin may be found in turmeric, and these compounds have been linked to anti-inflammatory effects, cancer prevention, and slowed ageing [49].

Wounds in mice treated topically with Curcumin were shown to heal more quickly, with granulation tissue that was mostly constituted of deposited collagen and a regenerated epithelium, as demonstrated in a prior research. In addition, wound healing in mice was hastened by Curcumin therapy, which worked by regulating the levels of several cytokines to lower matrix metalloproteinase-9 and tumour necrosis factor alpha [50]. Figure 4 depicts many possible outcomes associated with the use of Curcumin essential oils.

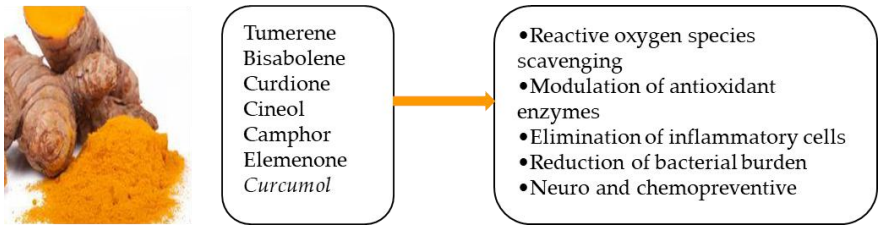


Fig.4. Some active components of curcumin essential oils and their potential effects [51].

Using a combination of Curcumin and ginger extract has been shown to improve wound healing and skin function in hairless rats with skin harmed by corticosteroids [52].

Althaea officinalis

Marshmallow, or Althaea officinalis L. (Malvaceae), has been used medicinally for a long time to alleviate laryngopharyngeal mucosal irritation and the dry cough that commonly follows. The roots, leaves, and flowers of the medicinal plant marshmallow (Althaea officinalis) are often used in traditional medicine all across the globe [53]. Starch, pectins, saccharose, mucilage, flavonoids, caffeic acid, p-coumaric acid, isoquercitrin, coumarins, phytosterols, tannins, and a number of amino acids have all been isolated from A. officinalis [54]. Lipemia, inflammation of the nasal and oral cavities, stomach ulcers, and platelet aggregation are just some of the diseases that Althaea officinalis may help remedy. Antioxidant activity in A. officinalis extract has been experimentally confirmed [55].

An Althaea officinalis extract has been used to treat wounds and inflammations for a long time. The root's ability to store water and its high polysaccharide content have been shown to have immunomodulatory effects [56]. Wound healing was much faster in the extract-treated wounds compared to the control wounds when A. officinalis extract was applied topically to a rat excision wound model (Figure 5). In addition, the hydroethanolic extract of A. officinalis contains phytochemicals that may function as antibiotics to kill gram-positive bacteria and can speed up wound healing in various ways [57].

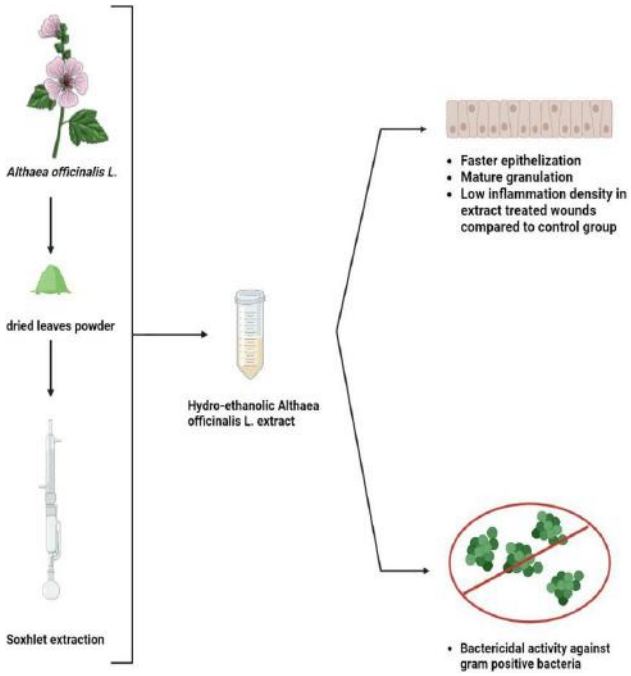


Fig.5. Efficiency of Althaea officinalis L. extract that significantly heals excision wounds on rats andinhibits gram positive bacteria compared to control group [57].

Calendula officinalis

Calendula officinalis (pot marigold) flower extracts have been used for centuries in traditional medicine. Calendula alcoholic extracts, both lipophilic and aqueous, have been used traditionally for the treatment of moderate skin irritation and the promotion of the healing of small wounds [58].

The most significant pharmacological activity associated with C. officinalis extracts are their anti-inflammatory, anti-edematous, antioxidant, antibacterial, antifungal, and immunostimulant effects. Compounds such as terpenoids, flavonoids, phenolic acids, carotenoids, coumarins, quinones, volatile oils, amino acids, and lipids dominate C. officinalis' chemical make-up [59]. C. officinalis also has antimicrobial, antiviral, effective breast

cancer treatment, antioxidant, and anti-immunomodulatory activity, as well as the ability to treat acne, prevent gastric ulcers, promote wound healing, treat bacterial infections in animals, and protect the liver and kidneys [60].

The topical and oral use of Calendula officinalis on rat excision wounds was studied. On day 8, the wounds in the extract-treated group had a 90.0% closure rate (compared to 51.1% in the control group), and the contents of hydroxyproline and hexosamine were significantly higher in the extract-treated group than in the untreated group (Figure 6) [61]. Furthermore, Calendula ointment may be used to speed up recovery after a caesarean since it helps wounds heal much more quickly after a caesarean [62].

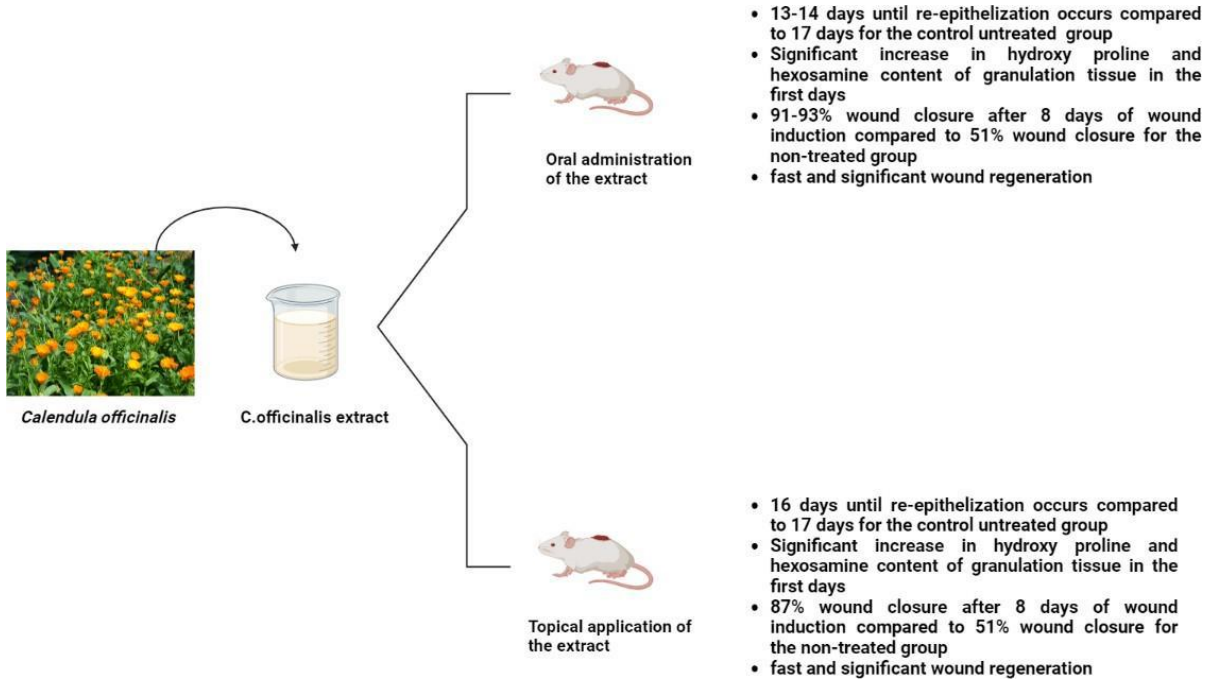


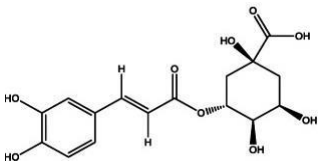
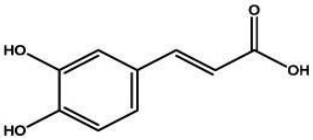
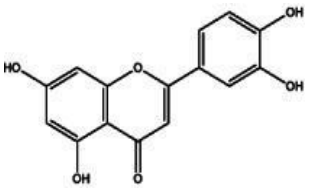
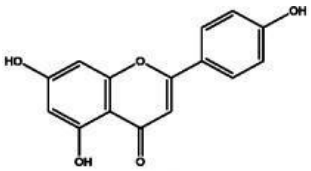
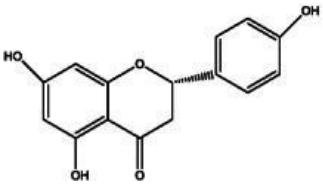
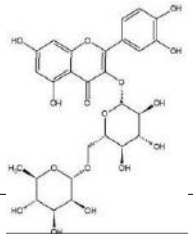
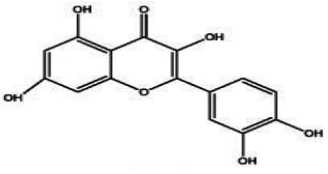
Fig.6. Effects of Calendula officinalis extract on wound closure, regeneration, hydroxyl proline, and hexosamine content in rat models [61].

Matricaria chamomilla

The camomile flower (Matricaria chamomilla L.) is a member of the Asteraceae family of plants. German camomile (M. chamomilla) is a popular star herb due to its medicinal and aromatic properties. M. chamomilla, or German camomile, is a perennial plant native to the warmer climates of south-east Europe and the Asian countries to the east. Traditional medicine makes use of both the flower heads and the essential oils [63]. M. chamomilla has a large variety of secondary metabolites and active chemicals, such as Sesquiter- penes, polyacetylenes, coumarins, and flavonoids. Extracts of camomile also include bioactive phenolic components as luteolin and luteolin-7-Oglucoside, quercetin and rutin, apigenin and apigenin-7-O-glucoside, and naringenin (Table 2) [64].

Table 2. The phytochemistry of the major bioactive components of Matricaria chamomilla L. [64].

Molecule Name	**Chemical Structure**

Chlorogenic acid	
Caffeic acid	
Luteolin	
Apigenin	
Naringenin	
Rutin	
Quercetin	

Medicinally, camomile is most often used for its antispasmodic, antibacterial, anti-inflammatory, and antiseptic properties [65]. Within 10 days, camomile extract ointment has been shown to speed up re-epithelialization and the creation of collagen fibres [66]. The antibacterial, antioxidant, biocompatibility, and mechanical properties of a chamomile-loaded mat make it an ideal choice for use in wound healing. Mats loaded with 15, 20, and 30% camomile showed outstanding antibacterial activity, and inhibitory zones expanded with increasing camomile concentration. Furthermore, the antibacterial activity of these nanofibers was shown to be superior to that of a commercial silver-coated wound dressing [67].

Eucalyptus

High-quality woody biomass from eucalyptus plantations reduces pressure on tropical forests and the biodiversity they support [68]. Fast-growing and very adaptable, Eucalyptus trees are well recognised as an effective reforestation tree species [69]. Numerous Eucalyptus species exist now [70]. The antibacterial properties and soothing effects of Eucalyptus globulus essential oil have led to its widespread usage [71]. The oil is derived from the leaves of the Eucalyptus globulus tree.

For wound healing research, collagen estimation, and histological assessment in rats, the optimised nanoemulsion of EEO was selected as a viable alternative to both pure EEO and conventional gentamycin. Wound healing in rats was significantly enhanced by the optimised EEO nanoemulsion [72]. Other studies have shown that for the best wound-healing effects and increased cell proliferation, Eucalyptus alba leaves should be dried at a temperature of no more than 30 C before being extracted in ethanol [73].

Jojoba

Jojoba, a plant that thrives in warm, dry climates, is now commercially farmed in regions where there is a severe shortage of water and where traditional agricultural techniques would be too expensive. This shrub is heat- and drought-resistant [74], as well as requiring little soil fertility and hydration. Jojoba, or Simmondsia chinensis, is a dioecious plant native to the desert. Seeds of the S. chinensis plant provide liquid wax esters, which are utilised as an important component of industrial and cosmetic lubricants [75].

Natural jojoba oil is a light yellow oil that may be used topically to treat skin damage and restore the skin's protective barrier. Jojoba oil is composed of 97% linear long-chain esters and 3% bioactive compounds such polyphenols, flavonoids, and alkaloids. The effectiveness of Jojoba oil dry nanoemulsion powders (JND) as natural oil-based anti-inflammatory and free radical scavengers in the treatment of acute lung injury (ALI) was shown by a decrease in haemorrhage and inflammatory cell infiltrations in ALI models [76]. Additionally, jojoba liquid wax (JLW) has been shown to significantly speed up wound closure in both keratinocytes and fibroblasts. It was also shown that JLW stimulated fibroblasts to produce collagen I (Figure 7). Because of its pharmacological effects on skin cells, JLW may find use in therapeutic settings for the treatment of wounds [77]. Because it is composed of more than 98% pure waxes (mainly wax esters, with a minor amount of free fatty acids, alcohols, and hydrocarbons), sterols, and vitamins, jojoba oil is more accurately described as liquid wax than oil due to its many bioactive qualities. [78]

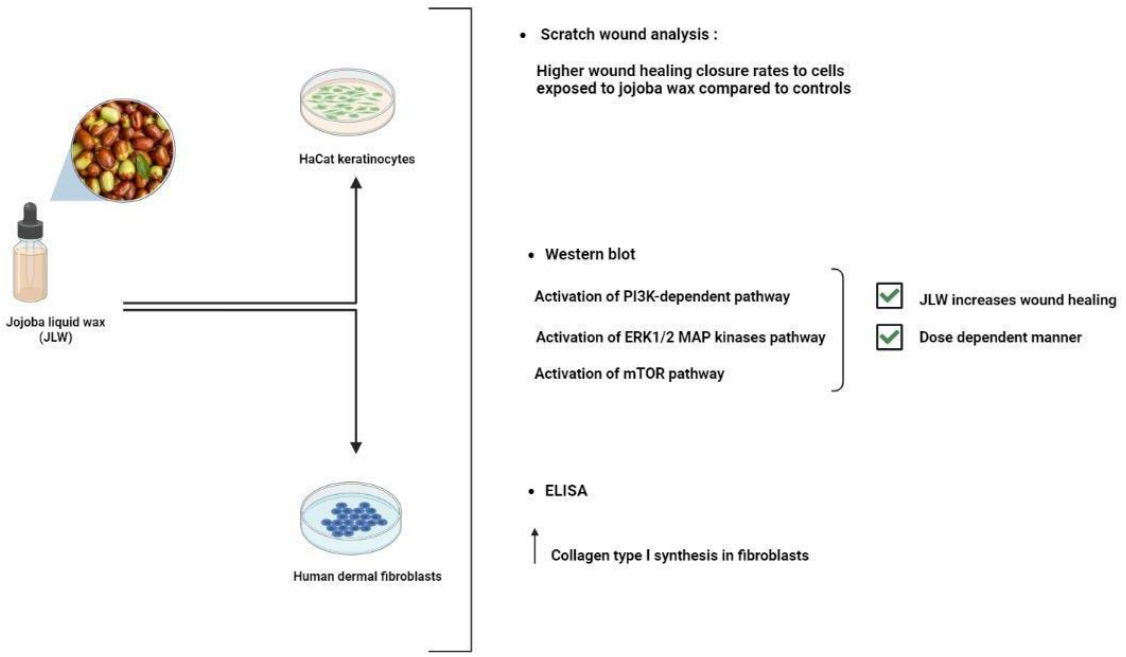


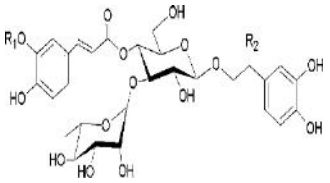
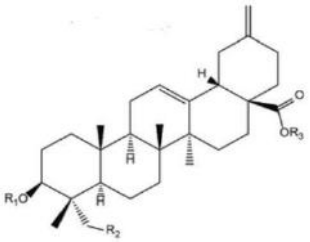
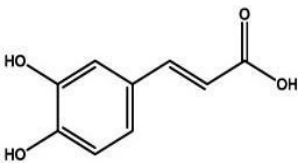
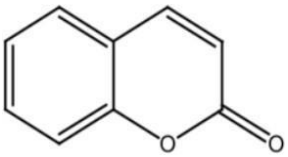
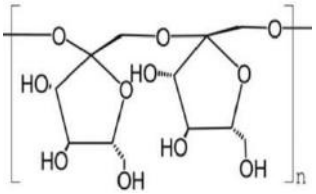
Fig.7. Jojoba liquid wax (JLW) wound healing properties examined by western blot, ELISA andscratch wound analysis on in vitro human dermal fibroblasts and keratinocytes [77].

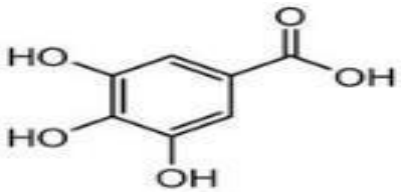
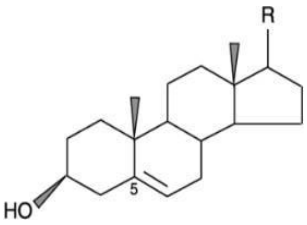
Plantago major

Plantago major L., a member of the family Plantaginaceae, is often referred to as plantain. It is a perennial herb with rosette-shaped leaves that grow to be 15 to 30 cm in diameter [79]. Plantago major, often known as plantain, may be found growing in a wide range of environments, from disturbed roadside ditches to cultivated fields to canal water to landfills [80]. The leaves and seeds of this plant have been used traditionally in folk medicine to cure a broad range of conditions, from digestive difficulties to breathing problems. Wounds have been treated with it because of its anti-inflammatory, anti-microbial, and anti-tumor properties. Internal and external poisons may be neutralised by the chemicals found in plantains [81].

Table 3 [82] lists the many bioactive compounds found in Plantago major. These compounds include polysaccharides, terpenoids, lipids, and flavonoids in addition to caffeic acid derivatives. P. major ointment is an analgesic and antibacterial agent in addition to being a wound-healing herb, making it an ideal therapy for second-degree burns [83]. P. major extract was also shown to significantly outperform other therapy in speeding the recovery of rats with dorsal cervical injuries [84]. The leaves of P. major have been shown to hasten wound healing in an ex vivo pig wound-healing model. P. major may be a good source of various bioactive chemicals with wound healing potential, since extracts of freeze-dried leaves prepared from both ethanol and water have showed a stimulating effect. The most effective concentration for both extract types is 1.0 mg/mL (dry weight) [85].

Table 3. The phytochemistry of the major bioactive components of Plantago major [82].

Molecule Name	**Chemical Structure**
Phenylethanoid glycosides	
Triterpenoids	
Caffeic acids	
Coumarins	
Polysaccharides	

Phenolic acids	
Sterols	

Inula

Flowering plants belonging to the genus Inula may be found all over the world, including in Europe, Asia, and even Africa. Several of these species are employed in medical preparations [86]. Inula has terpenoids, flavonoids, and lignins in its chemical makeup. The sesquiterpenoids of the genus Inula are extensively dispersed as well [87]. This includes the sesquiterpenoids eudesmanes, xanthanes, sesquiterpenoids dimers, and sesquiterpenoids trimers. Chemicals isolated from Inula species have shown promising biological activity against a wide range of conditions, including those caused by oxidative stress, inflammation, diabetes, cancer, and neurological disorders [88].

Inula viscosa is a perennial herbaceous plant that grows all throughout the Mediterranean basin and is often referred to as "Magramane" by its locals. Because of its anti-inflammatory, anthelmintic, antipyretic, antiseptic, and antiphlogistic characteristics [89], the plant has been used in traditional medicine to treat a wide range of ailments. Bioactive chemicals, volatile oils, and phenolic compounds may be derived from Inula viscosa leaves. Furthermore, its antioxidant, antibacterial, and antifungal properties suggest its potential for the creation of natural preservatives with applications in agro-food [90]. Many human illnesses are linked to oxidative stress, and the Inula genus provides a rich supply of antioxidant compounds with diverse structural profiles that may be used in the development of novel treatments [91, 92]. Protein expression of p53, bax, and bcl-2 is restored to near-normal levels after administration of Inula racemose (Ir) extracts, and total phenolic content is also dramatically increased. As a result, Ir extracts have shown promise as a therapeutic agent for treating hepatic damage after orthotopic liver transplantation [92].

Figure 8 shows that some common herbs, including Althaea officinalis, Calendula officinalis, Matricaria chamomilla, Eucalyptus, Plantago major, Jojoba, and Inula, include pharmacological wound healing bioactivities.

Fig.8. Pharmacological wound healing activities of some remarkable medicinal plants. 1: Jojoba,2: Calendula officinalis, 3: Eucalyptus, 4: Chamomile, 5: Inula, 6: Plantago major, 7: Althea officinalis.

Pine

Pine trees are grown all over the globe because they can be used to make so many different things. Wood and cellulose are also viable options for construction [93]. Pine resin, known as oleoresin, includes a wide range of terpenoids and is also a source of phenolic compounds. Phenolic compounds are produced by polyphenolic parenchyma cells and specialised ray cells, and resin ducts are found all throughout the wood, bark, roots, and needles. Specialised secretory tissues also produce and retain copious quantities of terpenoid resin [94].

The chemical make-up of various pine tree components, such as wood, bark, resin, needles, cones, and seeds, is shown in Figure 9 [95].

Pine pollen polysaccharides (PPPS) promote cell division, alter the cell cycle from G1 to S and G2, and upregulate Cyclin B1 expression in vitro, which speeds the healing of mouse skin wounds and the development of chicken embryo chorioallantoic vasculature. Activation of the JAK2-STAT3 signalling pathway was responsible for PPPS's effects [96]. Cones of Pinus pinea and P. halepensis yielded the most beneficial essential oils for the wound healing activity models. However, no significant anti-inflammatory or wound-healing effects were found in any other essential oils tested [97]. More than half of pine resin is abietic acid. Increased synthesis of p38 and extracellular signal-regulated kinase (ERK) is associated with abietic acid's enhanced angiogenic ability. Human umbilical vascular endothelial cells' migration and tube formation were also sped up by abietic acid. Treatment with 0.8 mM abietic acid has been shown to hasten wound closure in a mouse model of cutaneous wounds [98].

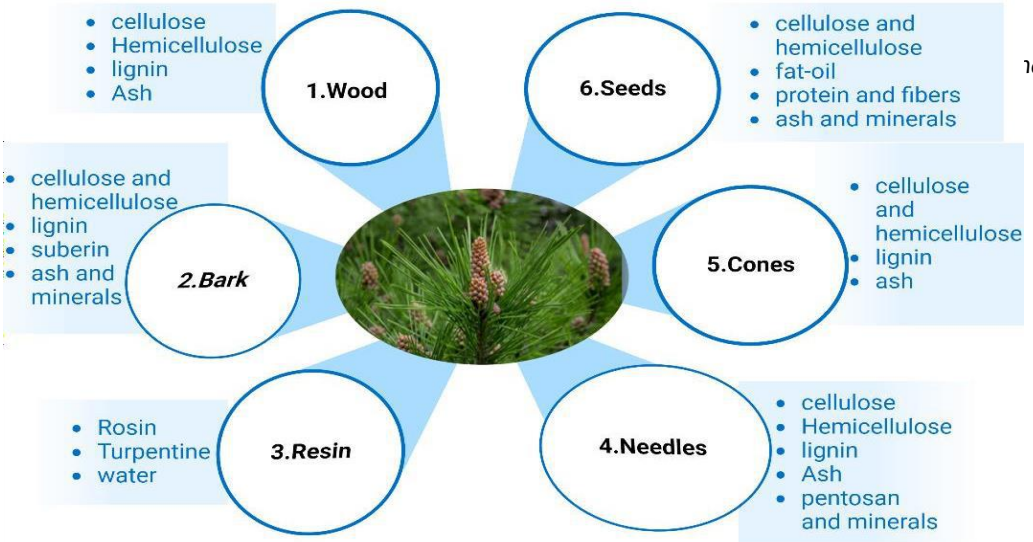


Fig.9. Chemical composition of different pine parts [99].

Green Tea

Over two-thirds of the global population enjoys a cup of tea, with green tea made from the Camellia sinensis plant being particularly popular [100]. Green tea, or Camellia sinensis (L.), is one of the world's oldest and most popular drinks. It is cultivated mostly in Japan, China, and Taiwan. Cancer, obesity, diabetes, heart disease, infections, and neurological diseases are only some of the health problems that have been shown to be helped by drinking green tea [102].

Agricultural practises, weather, growing season, and the kind of plant used may all have an impact on the final product. Polyphenols, namely flavonoids, are the primary components of green tea. Green tea catechins account about 6- 16% of the dry leaves. About 59% of the total quantity of catechins is accounted for by epigallocatechin (EGCG), followed by epigallocatechin (EGC) at 19%, epicatechin-3-gallate (ECG) at 13.6 percent, and epicatechin (EC) at 6.4 percent [103].

It is generally known that the beneficial benefits of green tea, particularly epigallocatechin gallate (EGCG), are mostly due to its polyphenols [104]. The main bioactivities are assumed to come from EGCG, which is the most abundant component in tea leaves (Figure 10). These bioactivities include the scavenging of free radicals, the killing of microbes, reducing inflammation, and encouraging new blood vessel growth, all of which promote healthy wound closure and reduce the risk of infection [105].

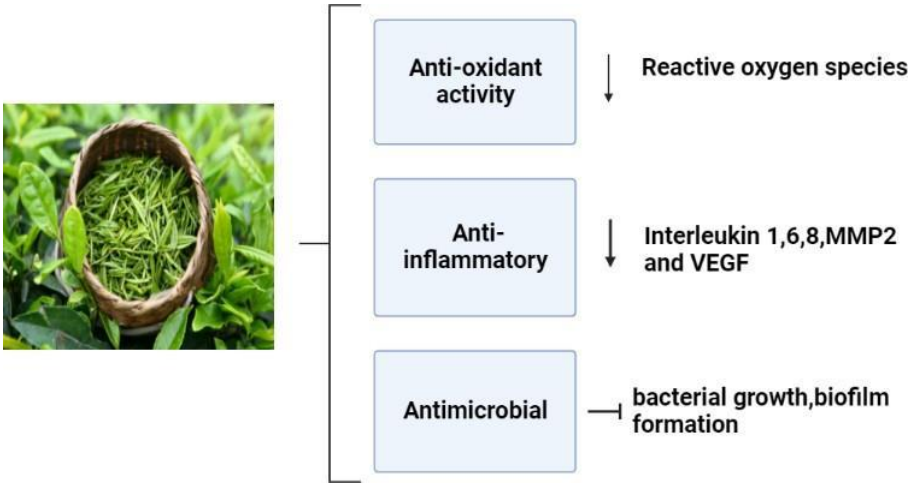


Fig.10. Pharmacological effects of green tea on the wound healing mechanism [106].

Green tea ointment seems to successfully minimise episiotomy discomfort and hasten wound healing [107]. Green tea polyphenols have been shown to hasten wound healing in diabetic rats via modulation of the PI3K/AKT signalling pathway [108], as shown in both animal experiments and analyses of the underlying molecular mechanisms.

Punicagranatum L.

The pomegranate, scientifically known as Punica

granatum L., is an ancient fruit packed with useful nutrients including protein, vitamins, and minerals. The peel makes up between 49% and 55% of a pomegranate fruit, while the arils make up between 45% and 52% (18% to 20% seeds and 26% to 30% juice) [110]. Antioxidant-rich compounds may be found in abundance in pomegranate seeds [111]. Pomegranate peel extracts showed considerable beneficial benefits in a minipig model of second-degree burns [112], which may be attributable to elevated levels of vascular endothelial growth factor A and transforming growth factor beta Previous studies have shown that 10% of standard pomegranate extracts can speed up the healing of serious second-degree burn wounds, which are characterised by angiogenesis, a complete and mature epithelium, a low number of inflammatory cells, and a high density of collagen with a good organisation [113].

In addition, P. granatum flower extract cream has been shown to hasten the healing of wounds in rats when compared to other treatments by day 25 [114]. This extract may also be used to treat burn injuries. Pomegranate peel ointment significantly enhanced the wound contraction and the period of epithelialization in excised injured mice over 10 days, as measured by mechanical (contraction rate, tensile strength), biochemical (raising of collagen, DNA, and protein synthesis), and extract evaluations [115]. Table 4 is a summary of the pharmacological bioactivities of numerous plant species used in traditional medicine.

II. CONCLUSIONS

All of the plants we looked at have complicated chemical makeups that are linked to various pharmacological effects. Anti-microbial, anti-inflammatory, and anti-oxidative activities are all features that are shared by these substances. Healing pharmaceuticals of the future may be derived from medicinal plants due to their low toxicity and high absorption. Topical or systemic use of phytotherapeutic pharmaceuticals alone or in addition to other healing therapies should be explored, especially when treating patients with chronic or resistant skin ulcers.

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