



Research Article

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Therapeutical Medicine for Wound Healing

Muhammad Waqar Mazhar^{1*}, Hamza Ali¹, Saira Saif¹, Ahmad Raza², Saleeha Kousar¹, Wajeeha Iram¹, Hira Tahir³ and Fatima Mazhar⁴

¹Department of Bioinformatics and Biotechnology, Government College University, Pakistan.

²Department of Biological Sciences, Nuclear Institute for Agriculture & Biology, Pakistan

³University of Health Sciences, Lahore, Pakistan

⁴Department of Microbiology, Muhammad Nawaz Sharif University of Agriculture, Pakistan

*Corresponding author: Muhammad Waqar Mazhar, Department of Bioinformatics and Biotechnology, Government College University, Pakistan.

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Abstract

Wounds are common external or internal damages to the body, usually caused by a physical, chemical, or biological agents. There exists natural repair wound healing repair in that includes immunological responses i.e., inflammation and necrosis. Naturally, body repairs wounds itself, but the period of healing is relatively slow. This healing process may further be delayed by the pathogens attack or weaker immune response. Wounds heal biochemically, but the time of the healing can be reduced by applying different herbs like the plant-based treatments. Sub-continent is rich in having an immense variety of medicinal plants as well. This literature review is about the role of different plants in wound healing, the efficacy of herbs on wound healing.

Keywords: Wound healing, biological agents, therapeutics plant, immune response

Introduction

The wound is defined as loss or disturbance of the proper anatomic functioning of the tissue. In this damage, microbes can reach the site of injury, and this could be very dangerous. Naturally, the healing of the wound is slow, and this slowness is very painful for the patient and for the soldiers i.e., soldier's wound should be healed rapidly, and the soldier must be returned to the field [1]. Sub-continent is rich in the plant-based knowledge of the treatment of cuts, wounds, and burns. In the pharmaceutical industry, there are a lot of drugs that are synthesized with modern techniques and have only antibacterial effects. Therefore, the healing of the wound is natural only. [2]. Nowadays, in medicine, the plants or plant parts are used extensively [3]. Besides, most of the compounds used in medicines are derived from plants [4]. The healing property of plants was identified by our ancestors through many trials and errors. That took time but after hundreds or thousands of years

of findings, the properties are well identified. [5] Developing or poorly developed countries face the issue of delayed wound healing because of an unhygienic environment. [6] The microbial attack is very frequent as well because the wounds are cuts or openings of the tissue. Therefore, injured persons are vulnerable to many diseases. Wounds can occur because of different events; thus, the appropriate method of treatment should be used. There are different stages of wound healing viz Hemostasis Phase, Inflammatory phase, Proliferative phase, and Remodeling phase. The metabolic disturbance also affects these phases resulting in delayed healing. According to a study in Colombia, people of small villages and countries make native herbal medicines and because of this treatment, there are very few chances of infection of resistant organisms [7]. That is the reason why people (traditionally using herbs) say that herbal medicines are more beneficial than modern



medicine. The purpose of treating the wound is to reduce its healing time. For this, the identification of the agent responsible for the acceleration of wound healing is required. There are different herbs and other plants used for the wound healing i.e., Aloe vera "Aloe barbadensis miller", Neem "Azadirachta indica", False Daisy "Eclipta prostrata", West Indian Lantana "Lantana camara" and tridax daisy "Tridax procumbens". [8] The purpose of this review is to investigate some herbal plants and find their role and the process of wound healing.

Wound

A wound is an injury to the bodyside cells/tissues/organs. It is usually resulted because of the physical, chemical, or microbial agent. It may also be the result of immunologic processes such as Inflammation or necrosis. Biochemically, a wound can be the loss/disturbance of the proper anatomic functioning of cells/tissues/organs. During the damage, microbial pathogens can reach the site of the wound, and this could be very unsafe. Naturally, the healing of the wound is slow, and this gradualness is very painful for the patient and for the soldiers i.e., soldier's wound should be healed rapidly, and the soldier must be returned to the field [9]. There are different factors upon which the wounds are classified and different types of wounds. Some of these are mentioned and explained in (Table 2).

Wound healing

Healing of skin and soft tissue wounds involves three major steps which are inflammatory, proliferative, and remodeling stage. In the inflammatory stage, homeostasis is maintained by the platelets. [10] Platelets induce the clotting. It is the immediate response that is generated after the damage has happened. Blood vessels coagulate, thrombocytes and platelets collectively form a

fibrin network. The formation of this fibrin network depends on the action of some factors [11]. This fibrin network restores the skin's function by organizing the matrix for cellular movement at the site of the wound. The Fibrin network also protects against micro-organisms [12]. This inflammatory response is generated by the activation of pro-inflammatory cytokines e.g., IL-1 β (Interleukin 1 beta), TNF- α (Tumor necrosis factor), and INF- γ (Interferon-gamma) [13]. Then macrophages reach the site of the wound to remove the cell debris. Macrophages also attract the other inflammatory cells to the wound area by releasing the chemotactic factors e.g., cytokines, pro-angiogenic, inflammatory, and fibro genic factors [5,6]. The proliferative stage of damaged tissue starts on the 4th day of the injury and ends on the 21st day. Different cells are involved in the proliferation i.e., macrophages, lymphocytes fibrocytes, neurocytes, and amniocytes. These cells collectively re-establish the function of skin and fill the defects (closure of wound). Re-modeling of tissue is just like the interior finishing i.e., maturation. The time of re-modeling starts from the 21st day and lasts for 2 years. Fibrocytes play their role the re-modeling fibrocytes to develop tensile strength. Now the healed tissue exactly looked like the undamaged tissue. [7].

Causes of wounds

The cause of the wound must be identified before the initiation of treatment so that it can be controlled accordingly. There are different causes of the wound which are listed in (Table 1). Underlying causes of tissue damage Trauma (initial or repetitive) Scalds and burns (thermal and chemical) Animal bites or insect stings Malignancy Pressure Vascular compromise (arterial, venous, lymphatic, or mixed) Immunodeficiency Adverse effects of medications Psychosocial disorders Nutritional deficiencies Metabolic disease, including diabetes Connective tissue disorders.

Table 1: The cause of the wound must be identified before the initiation of treatment so that it can be controlled accordingly. There are different causes of the wound which are listed.

Underlying Causes of Tissue Damage		
Trauma [initial or repetitive]	Scalds and burns [thermal and chemical]	Animal bites or insect stings
Malignancy	Pressure	Vascular compromise [arterial, venous, lymphatic, or mixed]
Immunodeficiency	Adverse effects of medications	Psychosocial disorders
Nutritional deficiencies	Metabolic disease, including diabetes	Connective tissue disorders

Table 2: Some types of wounds and their explanation.

Type of Wound	Explanation	References
Open Wound	<p>Blood comes out of the body, which results in bleeding.</p> <p>Different wounds come in this category:</p> <ul style="list-style-type: none"> • Incised wound • Laceration • Tear wound • Abrasions • Puncture wound • Penetration wound • Gunshot. 	[48]

Closed Wound	In this type of wound, the blood comes out of the circulatory system due to vessel injury, but the blood remains in the body and cannot get out. There is no bleeding and can be of the following types: <ul style="list-style-type: none"> • Contusion • Bruises • Hematomas crush injuries 	[49]
Acute Wound	The wounds heal timely through routine processes like Inflammation, regeneration, and remodeling of wounded cells/tissue/organs.	[50]
Chronic Wound	These are the wounds that cannot be healed through the normal wound healing process.	[51]

Stages of wound healing

There are some stages of healing that are given in the (Figure 1).

Figure 1: Homeostasis is the first response generated within minutes. Platelets play their role in clotting. The period of 1-4 days of injury is Inflammation. during this period neutrophils

and macrophages remove cell debris and involve in the process of phagocytosis. Proliferation is the period of the 4th-21st day of injury. Proliferation involves the re-establishment of skin function and different cells (Macrophages, Lymphocytes, Fibroblasts, Neurocytes, and Angiocytes) perform their function to re-establish the function of the skin.

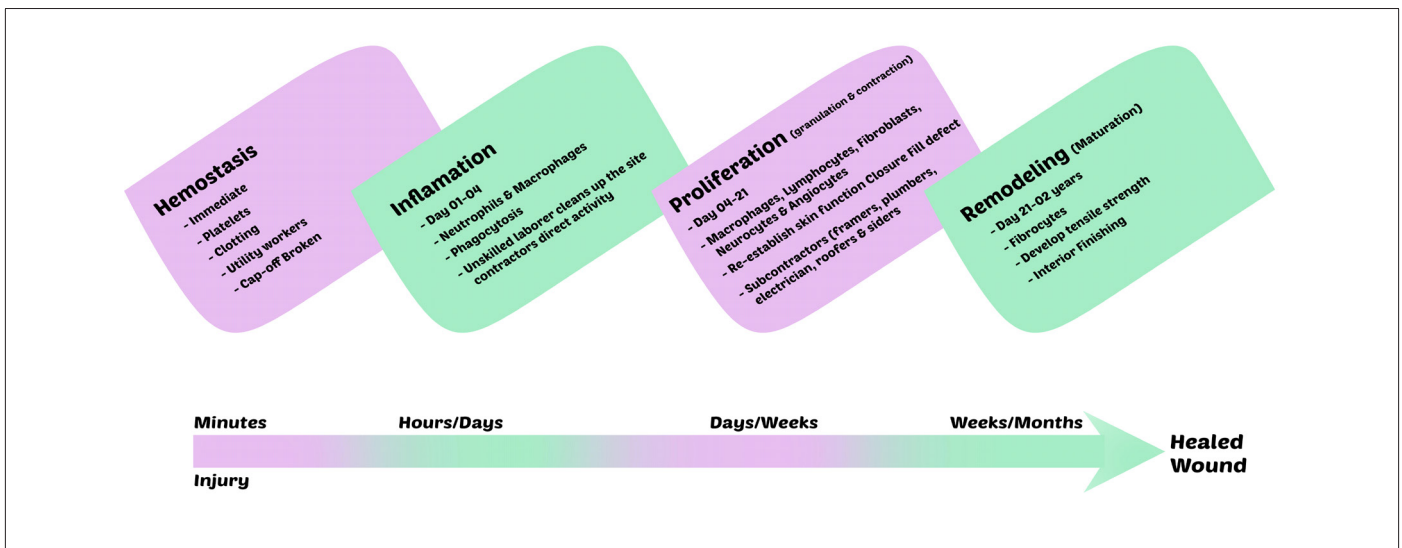


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Therapeutic plants: A remedy for wounds

As mentioned earlier, different plant species can be used as a remedy for wounds. The mode of action of some plants to wound healing is mentioned in (Table 3). Some of these plant species are described below:

Table 3: Some plants having different modes of action are mentioned in this table.

Name of plants	Role	References
Astragalus propinquus and Rehmannia glutinosa	Treatment of Urinary Retention	
	Edema	[10]
	Hemorheology	[11]
	Diabetes-Related Diseases Treatment of Diabetic Foot Ulcers	[12]
	Promote Diabetic Wound Healing	

Ampelopsis japonica	Effective Against Burns Antimicrobial	[13] [14]
Andrographis paniculata.	Treatment of Wounds, And Itchiness	[15] [16]
Angelica sinensis	Anti-inflammatory	[17]
Caesalpinia sappan	Reduce Oedema and Pain	[18]
	Antiallergic Anti-inflammatory	[19]
Blumea balsamifera	Treatment of Eczema, Dermatitis, Skin Injury, Bruises,	[20]
Calendula officinalis	Wounds Burns Dermatitis Anti-inflammatory Antioxidant Antibacterial Antiviral Antifungal Anticancer Activities	[21]
Boswellia sacra	Treatment of Trauma	[22]
	Treatments of Inflammatory Diseases	[23]
Camellia sinensis	Antioxidant	[24]
	Anti-inflammatory	[25]
	Antimicrobial	[26]
	Anticarcinogenic	[27]
	Antiaging	[28]
	Anti-Obesity	[29]
Neuroprotective Activities.	[30]	
Carthamus tinctorius	Anti-inflammatory	[31]
Cinnamomum cassia	Anti-inflammatory	[32]
Celosia argentea	Treat Skin Sores Eruptions Ulcers Mouth Ulcers, Other Skin Diseases	[33]
Commiphora myrrha	Antioxidant Anti-inflammatory Antibacterial Analgesic Clean Wounds Reduce Oedema Provide Pain Relief [Analgesia]	[E. Y. H. Nomicos, 2007]
Curcuma longa	Treat Inflammation, Respiratory Disorders, Liver Disorders, Diabetes Abdominal Pain.	[34]

Hibiscus rosa-sinensis	Antibacterial Wound Healing Properties Attenuate Inflammation, Enhance Fibroblast Proliferation Collagen Deposition,	[35] [36]
Ganoderma lucidum	Inflammation Modulation Anti-Infective	[37] [38] [39]
Daphne genkwa	Anticonvulsant Analgesic Diuretic Antitussive Expectorant Mild Sedative Agent	[40] [Z.-J. Zhan, 2005 [W. J. Du, 2017]
Entada phaseoloides	Analgesic Bactericide Hemostatic Anticancer Agents Topical Treatment for Skin Lesions	[41] [42]
Ligusticum striatum	Ischemic Disorders Menstrual Disorders Headache	[43] [44] [45]
Lonicera japonica	Antimicrobial Anti-inflammatory Antipyretic Antioxidant Anticancer Hepatoprotective Antihyperlipidemic Capabilities	[46] [47]
Paeonia suffruticosa	Antioxidant Neuroprotective Antitumor Anti-inflammatory Antidiabetic	[48] [49] [50] [51] [52]
Panax ginseng	Reduce Inflammation Confer Antioxidant Anticancer Antibacterial Antiallergic Antiaging	[53, 54] [55] [56] [57] [58]

Polygonum cuspidatum	Burns	
	Snake Bite	
	Anti-inflammatory	[59, 60]
	Estrogenic	[61]
	Antitumor	[62]
	Antiaging	[1, 20-23, 39, 52-120]
	Neuroprotective Cardioprotective Activities	

Aloe vera (*Aloe barbadensis miller*)

Aloe vera is a local plant found abundantly in the sub-continent. Aloe vera is being used for the treatment of wounds for the last 5000 years in many parts of the world like Egypt, Romans and by some populations of Africa, Asia, and America. Aloe vera is the most ancient plant which is being used for the clinical purpose [14]. It has a swollen root system, small and fleshy leaves. Aloe vera is present in the forests of the sub-continent as a wild herb. This plant is commonly used for the treatment of burns, cuts, and other small wounds. It is used in the cosmetics like lotions and sun blokes as well. There are many compounds in Aloe vera which play important role in wound healing e.g., Acetone plays a role in the killing of pathogens (antimicrobial) [15]. Other compounds that have the same role are saponins, acemannan, and anthraquinone derivatives [16]. Polysaccharides present in the Aloe vera have a role in the granulation [17]. According to the past study of this plant, it was applied after every 3 days on the chemically burn wound. Then the diameter of the wound was measured after the specific period. Aloe vera showed protection of skin. when orally taken then showed effectiveness on the ulcer [18].

Tumeric (*Curcuma longa*)

Curcumas belong to ginger family and has curcumin in its roots [19] which is very important in medication and reservation of current food practices showed that curcumin is used to treat respiratory and liver disorder [20]. In china, curcumin use as a traditional medicine for treatment of abdominal pain. This molecular interact at transcription, translation, and post tanscriptional changes and act as a key of these cellular pathway. Cell adhesion molecules, 5-LOX, aptosis, NF- κ B, Cyclooxygenases-2, STAT3, prostaglandin E2, C-reactive protein, Triglycerides, apoptosis, phosphorylase kinase, creatinine, AST, ALT, transforming growth factor- β , prostate specific antigen, ET-1, heme-oxygenase-1, cell adhesion molecules, and pro-inflammatory cytokines are targated pathways. [21]. in vivo studies, more than 100 studies in which curcumin as a treatment for epithelial cancer. It's very important and beneficial effects to alter extracellular and pericellular matrix. [22]. curcimum enhances

granulation tissue formation, fibroblast proliferation, and collagen deposition in cutaneous wound healing. [22].

Greater burdock (*Artium lappa*)

It is found in some parts of America, Europe, and Asia for the treatment of skin problems like burns, acne, and rashes and some clinical uses [23,24]. Clinically Artium lappa is antidiabetic [25] antioxidants [26] anticancer [27]. But for skin problems, the qualities that make Artium lappa useful are antimicrobial [28] and antiviral [29]. It is mostly cultivated on perennial herbs [23] it is commonly known as burdock it is used for the treatment of sore in the throat and also used for skin treatment such as skin burns, rashes, and acene [30] Recent studies showed that Artium lappa is anti-inflammatory, antimicrobial, antiviral [31-33], anti-cancer, antidiabetic, antioxidant [26] and hepatoprotective activities the roots extract of articum lappa for dermal ECM metabolism decrease wrinkles on the skin [34].

False Daisy (*Eclipta prostrata*)

This species is found in African countries and has a significant role in the wound healing. In a study, it was applied in the form of past on the wound. The diameter of the wound was measured regularly. The time of the haling was reduced to 85% than the normal conditions. (Wikipedia). Eclipta prostrata is being used locally in Pakistan but there is no pharmaceutical industry that makes medicine from this herb. An experiment was performed to check the wound healing activity of E. prostrata. Three types of extracts of E. prostrata were used i.e., aqueous, hydroethanolic extract, and vaseline. The ability of E. prostrata was observed under the microscope. E. prostrata reduced the time of all the three stages of wound healing i.e., inflammation, proliferation, and re-modeling. Different chemicals play their role in the healing process. Further work is needed to know about the chemicals that which chemicals are released, which play a role in wound healing [8,9].

Green Chiretta (*Andrographis paniculata*)

It is also commonly known as green chiretta; it is used for the treatment of fever, snakebite, dysentery wound infection itchiness

in china, Asian countries, and India [35-37]. Its extract contains antioxidant [38] anti-inflammatory, antidiabetic, antimicrobial, and antiviral activities Recent research shows that 10 percent leaf extract of *Andrographis paniculate* is used to enhance the wound closure rate in Rats animals that are treated with *Andrographis paniculata* showed reduced rate of Inflammation, reduced rate of scarring and has more androgenesis and collagen fiber for the closure of wounds. A diterpenoid is extracted from the leaves of *Andrographis paniculata* which play important role in autoimmune disorders.

Pepervine (*Ampelopsis japonica*)

It is found all over eastern Asia and northern America. *Ampelopsis japonica* roots are used to treat ulcers, burns, and other indications [39]. Like this, it is also used as a neuroprotective [40] antimicrobial and also protect from cancer [41,40] *Ampelopsis* is also used to extract ethanol, which is used for the scold injuries in rats [42], and it is also observed that treatment with *Ampelopsis japonica* is more powerful than vaseline or petroleum gel; it improved reepithelialization, vascularization, and collagen formation.

Indian pennywort (*Centella asiatica*)

In a study, rat's skin wounds were created with radiations. These wounds were healed earlier when applied with *Centella asiatica* than naturally [43] A compound derived from *Centella asiatica* known as Asiaticoside enhances the formation of collagen and epithelial layer in the guinea pig [44] A compound madecassoside derived from *Centella asiatica* when orally applied to the mouse, it was effective in collagen formation and angiogenesis [45].

Neem (*Azadirachta indica*)

Neem is present abundantly all over the sub-continent. Local people are very familiar with it. Neem has small leaves and a strong stem. The oil extracted from it and the leaves are used for treatment because neem has antimicrobial characteristic so kill the pathogens and protect the wound from further damage. It protects the patient from secondary diseases so promotes wound healing. [46]

Onion (*Allium cepa*)

Allium cepa has many uses in the medicinal field but its role in wound healing is also identified. *Allium cepa* reduces the time of healing and plays an important role by producing collagen concentration [47]. The method and the chemical composition are unknown.

Future perspectives

At present some herbal plants are used for wound healing and are safe compared to synthetic drugs.

Conclusion

This review discussed why different medicinal is used to treat serious infectious diseases and skin disorders. Over millennia human develop different ways to use botanical resources as medicine. Wounds heal naturally, but this review article tells that nature has provided so many plants to heal the wounds more rapidly. Some scientific industries use modern technology in making drugs for the treatment of wounds. However, traditional methods should be standardized.

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