



WOUND HEALING POTENTIAL OF HERBAL DRUGS: A MINI REVIEW

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ABSTRACT

Wound healing is a dynamic and normal biological process involving fibroblast activation and migration, re-epithelization, proliferation of endothelial cells, and angiogenesis, which are accompanied by inflammatory response and oxidative reactions in the damaged area. Herbs have been integral to both traditional and non-traditional forms of medicine dating back at least 5000 years. The enduring popularity of herbal medicines may be explained by the perception that herbs cause minimal unwanted side effects. More recently scientists increasingly rely on modern scientific methods and evidence-based medicine to prove efficacy of herbal medicines and focus on better understanding of mechanisms of their action. Preparations from traditional medicinal plants are often used for wound healing purposes covering a broad area of different skin related diseases. The main aim of this review article is potential of herbs for effective treatment of wound.

INTRODUCTION

Wounds are major case of physical disabilities. A wound which is disturbed state of tissue caused by physical, chemical, microbial (or) immunological insults (or) typically associated with loss function. According to the wound healing society wounds are physical injuries that results in an opening (or) break of the skin that cause disturbance in the normal skin anatomy and function. Wound healing is an interaction of complex cascade of cellular and bio- chemical actions healing to the restoration of structural and functional integrity with regain of strength of injured tissues. Involves continuous cell – cell interaction and cell matrix interactions that allow the process to proceed in different overlapping phases and process including inflammation, wound contraction, Re epithelialization tissue, re modeling and formation of granulation tissue with angiogenesis. Several factors delay (or) reduce the wound healing process including bacterial infection, necrotic tissue and interference with blood supply, lymphatic blockage and diabetes mellitus, generally if the above factors could be altered by any agent, an increased healing rate could be achieved. Many Ayurvedic plants have a very important role in the process of wound healing. Plants are more potent healers because they promote the repair mechanisms in the natural way.^[1]

Classification of wounds

Wounds are classified as open and closed wound on the underlying cause of wound creation and acute and chronic wounds on the basis of physiology of wound healing.^[2]

Open wounds

In this case blood escapes the body and bleeding is clearly visible. It is further classified as: Incised wound, Laceration or tear wound, Abrasions or superficial wounds, Puncture wounds, Penetration wounds and gunshot wounds.

Closed wounds

In closed wounds blood escapes the circulatory system but remains in the body. It includes Contusion or bruises, hematomas or blood tumor, Crush injury etc.

Acute wounds

Acute wound is a tissue injury that normally precedes through an orderly and timely reparative process those results in sustained restoration of anatomic and functional integrity. Acute wounds are usually caused by cuts or surgical incisions and complete the wound healing process within the expected time frame.

Chronic wounds

Chronic wounds are wounds that have failed to progress through the normal stages of healing and therefore enter a state of pathologic inflammation chronic wounds either require a prolonged time to heal or recur frequently. Local infection, hypoxia, trauma, foreign bodies and systemic problems such as diabetes mellitus, malnutrition, immunodeficiency or medications are the most frequent causes of chronic wounds.

Mechanism of wound healing^[3]

The response to injury, either surgically or traumatically induced, is immediate and the damaged tissue or wound

then passes through three phases in order to affect a final repair:

- The inflammatory phase
- The fibroblastic phase
- The remodeling phase

The inflammatory phase prepares the area for healing and immobilizes the wound by causing it to swell and become painful, so that movement becomes restricted. The fibroblastic phase rebuilds the structure, and then the remodeling phase provides the final form.

Wound healing activity

M. elengi

Roqaiya *et al.* investigated the methanolic extract from bark of *M. elengi* for wound healing activity in the form of ointment in three types of wound models on mice: the excision, the incision and dead space wound model. The extract ointments showed considerable response in all the wound models compared to standard drug betadine ointment in terms of wound contracting ability, wound closure time, tensile strength and dry granuloma weight. The methanolic extract ointment of *Mimusops elengi* effectively stimulated wound contraction; increase tensile strength of incision & dead space wounds as compared to control group.^[4]

Punica granatum peel

Murthy *et al.* investigated that methanolic extract of dried pomegranate (*Punica granatum*) peels showed complete healing of on 16-18 days. In this high content of phenolic compounds (44.0%) along with other constituents are presents. High-performance liquid chromatography analysis of the extract showed the presence of Gallic acid and catechin as major components which promotes healing process.^[5]

Aloe vera Linn.

Oryan *et al.* evaluate the wound healing properties of *Aloe vera* (*Aloe barbadensis*) on cutaneous wounds. Forty rats were randomly divided into two equal groups (control and experimental). 1.5 mL of filtered *Aloe vera* aqueous extract was used on the lesions of the experimental group. Wound contraction was measured planimetrically on day 5, 10, 15 and 20. Twenty rats (10 of each group) were sacrificed on day 10 and then histopathological and biomechanical samplings were done. The remaining animals were sacrificed on day 20. Treated animals showed a non-significant improvement in wound contraction and histopathology on day 10. Wound contraction started showing significant differences between groups from day 15 onwards. The lesions of the treated animals showed a better alignment, fewer inflammatory cells infiltration and significantly improved biomechanical properties on day 20 ($P < 0.05$). These results suggested that application of *Aloe vera* aqueous extract on open wounds induces significant wound contraction and accelerates healing.^[6]

Curcuma longa

Rhizomes of *Curcuma longa* (Turmeric) are used for various medicinal purposes. It possesses antibacterial, anti-inflammatory, anti-arthritic, anti-hepatotoxic (liver protective) and anti-allergic properties. Ayurvedic texts have additionally described it to be good for skin ailments and also as a blood purifier, wound cleanser, healer, remover of body toxins, killer of abdominal worms and a wind-repellent agent etc. Purohit *et al.* evaluated the ethanolic extract of *Curcuma longa* (Turmeric) rhizomes for wound healing activity through topical route on excision wound model. The activity was compared with standard drug Povidone Iodine ointment (5% w/w). Ethanolic extract of *Curcuma longa* (Turmeric) rhizomes was found to have better and faster wound healing effect than standard drug Povidone Iodine ointment on excision wound model.^[7]

Sesame Oil

Sharif *et al.* examined the characteristics of sesame oil extract in healing dermal wounds in rats and observing if there is a dosage to response relation. The results of present study indicated that sesame oil extract promotes significant wound healing activity. This was demonstrated by a significant increase observed in the rate of wound contraction in the case groups compared with olive oil and standard treatment group and also a dosage-response relation was observed.^[8]

Catharanthus roseus

Singh *et al.* observed that the methanolic extract of *Catharanthus roseus* L significantly speed up the healing process and provide the strength to collagen tissue. The preliminary phytochemical analysis of the leaf extract showed the presence of tannins, triterpenoids and alkaloids. Any one of the observed phytochemical constituents present in Leaf of *Catharanthus roseus* L may be responsible for the wound healing activity. Recent studies have shown that phytochemical constituents like flavanoids and tri-terpenoids are known to promote the wound-healing process mainly due to their astringent and antimicrobial properties, which appear to be responsible for wound contraction and increased rate of epithelialisation. Further phytochemical studies are in progress to isolate, characterize and identify the specific active compounds in this plant responsible for wound healing activity. The results of this study can be justified by the facts that the methanolic extract of leaf of *Catharanthus roseus* L enhances the faster lay down of collagen fibres and improves the antioxidant status in the wound of diabetic animals.^[9]

Morinda citrifolia L.

Nayak *et al.* investigated that *Morinda citrifolia* L. (noni) is one of the most important traditional Polynesian medicinal plants. The primary indigenous use of this plant appears to be of the leaves, as a topical treatment for wound healing. The ethanol extract of noni leaves (150mg kg⁻¹ day⁻¹) was used to evaluate the wound-healing activity on rats, using excision and dead space

wound models. Animals were randomly divided into two groups of six for each model. Test group animals in each model were treated with the ethanol extract of noni orally by mixing in drinking water and the control group animals were maintained with plain drinking water. Healing was assessed by the rate of wound contraction, time until complete epithelialization, granulation tissue weight and hydroxyproline content. On day 11, the extract-treated animals exhibited 71% reduction in the wound area when compared with controls which exhibited 57%. The granulation tissue weight and hydroxyproline content in the dead space wounds were also increased significantly in noni-treated animals compared with controls ($P < 0.002$). Enhanced wound contraction, decreased epithelialization time, increased hydroxyproline content and histological characteristics suggest that noni leaf extract may have therapeutic benefits in wound healing.^[10]

Ocimum kilimandscharicum

Paschapur et al. evaluate the wound healing potential of aqueous extract of leaves of *Ocimum kilimandscharicum*. It is a well-known plant in Indian traditional medicine. On the basis of traditional use and literature references, this plant was selected for evaluation of wound healing potential. An aqueous extract of leaves was examined for wound healing activity at two different doses (200 and 400 mg/kg) in three types of wound models on rats: the excision, the incision and dead space wound model. Significant increase in skin breaking strength, granuloma breaking strength, wound contraction, dry granuloma weight and decreased in epithelialization period was observed in animals of both the treatment groups compared to control. Granuloma tissue was subjected to histological examination to determine the pattern of lay-down for collagen using Van Gieson and Masson Trichome strains. Biochemical parameters viz; L-Hydroxyproline, Hexose amine, Ascorbic acid and Malondialdehyde also confirmed its potential wound healing activity at either dose. Thus, the enhanced wound healing may be due to free radical scavenging action and the antibacterial property of the phytoconstituents present in it which either due to their individual or additive effect fastens the process of wound healing.^[11]

***Tephrosia purpurea* Linn.**

Lodhi et al. studied the wound healing potential of ethanolic extract of *Tephrosia purpurea* (aerial part) in the form of simple ointment using three types of wound models in rats as incision wound, excision wound and dead space wound. The results were comparable to standard drug Fluticasone propionate ointment, in terms of wound contraction, tensile strength, histopathological and biochemical parameters such as hydroxyproline content, protein level, etc. Histopathological study showed significant ($P < 0.05$) increase in fibroblast cells, collagen fibres and blood vessels formation. All parameters were observed significant ($P < 0.05$) in comparison to control group.^[12]

***Tectona grandis* Linn.**

Varma et al. examined the wound healing activity of *Tectona grandis* (TG) Linn. leaf extract on rats. Healthy albino rats (150-200 g) of either sex were taken for excision and incision wound model. Animals were divided into four groups of six animals in each group. For Group simple ointment served as control. The Groups 2 and 3 had 5 and 10% ointment of TG leaf extract and Group 4 soframycin ointment served as standard. In excision wound percentage of wound contraction was assessed, whereas in incision wound tensile strength was assessed. Statistical analysis was performed by one-way analysis of variance followed by *t*-test. In excision wound model, 5% ointment of TG leaf extract showed a reduction in wound area 8th day onwards. Reduction in wound area was very significant ($P < 0.01$) as compared to control. Whereas 10% ointment of TG leaf extract and standard showed a reduction in wound area fourth day onwards, which was highly significant ($P < 0.001$) as compared to control. In incision wound model, animals treated with 5% ointment of TG leaf extract showed significant ($P < 0.05$) increase in tensile strength as compare to control. However, animals treated with 10% ointment of TG leaf extract showed very significant ($P < 0.001$) increase in tensile strength as compare with control. However, animals treated with soframycin showed highly significant ($P < 0.001$) increase in tensile strength as compare with control. TG leaf extract showed significant wound healing activity.^[13]

***Carica papaya* L.**

The aqueous extract of *C. papaya* fruit (100 mg kg-1 day-1 for 10 days) was evaluated for its wound healing activity in streptozotocin-induced diabetic rats using excision and dead space wound models by Nayak et al. Extract-treated animals exhibited 77% reduction in the wound area when compared to controls which was 59%. The extract treated wounds were found to epithelize faster as compared to controls. The wet and dry granulation tissue weight and hydroxyproline content increased significantly when compared to controls. The extract exhibited antimicrobial activity against the five organisms tested. *Carica papaya* promotes significant wound healing in diabetic rats and further evaluation of this activity in humans is suggested.^[14]

***Sphaeranthus indicus* Linn.**

Jha et al. assess the wound healing activity of *Sphaeranthus Indicus* flower head by providing better tissue formation and protection against microbial invasion. Various ointments of extracts in various proportions were prepared and subjected for assessment of wound healing activity in albino rats. Based on the comparison of wound healing activity of various formulations, the formulation comprising of 2% (w/w) alcoholic extract of flower head of *sphaeranthus indicus* found to be superior to that of control and standard formulation. In addition to greater hydroxyproline

content found in healed wounds as compared to control and standard formulation.^[15]

Francis et al performed the wound healing potential of *Ocimum sanctum* (basil) to elucidate therapeutic potential of alcoholic extract of basil in wound healing in diabetic rabbit model. Animals were divided into wounded control treated with povidone Iodine and test with basil extract. Semi-quantitative and qualitative evaluation of tissue architecture and immunohistochemistry encompassing collagen I and III studies expressed swift regeneration of injured epidermis in basil extract treated wound in comparison to control. This is articulated by organized dermal collagen deposition with collagen I to III ratio resembling normal skin, wound area measurement and absence of clinical signs of wound infection.^[16]

CONCLUSION

In the present comprehensive review, we focused on the herbs as their wound healing potentials. The healing process can be physically monitored by assessing the rate of contraction of the wound, period of epithelization, tensile strength, histopathology and weight of granuloma in different wound models. The demand of herbal drugs is increasing day by day in developed as well as developing countries because they are safer and well tolerated as compared to those allopathic drugs. The combination of traditional and modern knowledge can produce novel drugs for wound healing with significantly lowered unwanted side effects.

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