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Review Article

A REVIEW ON WOUND HEALING PROPERTIES OF INDIAN MEDICINAL PLANTS

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ABSTRACT
In India a huge percentage of population depends upon the use of traditional medicine because of the easy availability of common medicinal plants and also due to the lacks of better health care alternatives. Several medicinal plants can play significant role in healing of wounds which is a prominent disease of all time. The present article enumerates 30 different medicinal plants having wound healing properties as evident by the research article published in various research journals. The details about the useful plant part and the metabolite are also compiled. The present review will certainly increase the knowledge about the medicinal plants and their uses in healing variety of wounds.

INTRODUCTION

Wounds are physical injuries that results in an opening and break of the skin that cause disturbance in the normal skin anatomy and function. They result in the loss of continuity of epithelium with or without the loss of underlying connective tissue. Wound may be produced by physical, chemical, thermal, microbial or immunological insult to the tissues. The process of wound healing consist of integrated cellular or biochemical events leading to the building of structural and functional integrity with regain of strength of injured tissues.

The medicinal plants and has a rich tradition of plant-based knowledge on healthcare. Nearly 2000 of natural drugs have reported various pharmacological activities, out of these 1600 are from plant origin (Mukherjee, 2008 and Sandhya *et al*., 2011). Medicinal plants have a vital role in the management of various diseases and which are found in the forest areas throughout South Asia, in the high Himalayan region of tropical and sub-tropical belts and arid regions of Thar Desert. India recognizes more than 2500 plant species have medicinal value, Srilanka about 1400 and Nepal about 700.

Current estimation indicate about 6 million people are suffering from chronic wounds worldwide (Kumar *et al*., 2007). The prevalence of chronic wounds in the community was reported as 4.5 per 1000 population, whereas an acute wound was about 10.5 per 1000 populations (Gupta *et al*., 2004). Plant products are potential agents for wound healing, and largely preferred because of their widespread availability and effectiveness as crude preparations. A large number of plant extracts and their pastes are equally used by tribes and folklore traditions in India for treatment of cuts, wounds, and burns. Many herbal plants have a very important role in wound healing process because they promote their repair mechanism in the natural way. The healing process is measured by the assessment of wound contraction. The herbal medicines for wound healing are very cheap and affordable and are safe as hypersensitive reactions (Vekatanarayana *et al*., 2010). A lot of people are developing diabetes at a very younger age due to stressful life. It was reported that a lot of children having this chronic and fatal disorder. Long occurrence of these fatal disorders increases the chance of non healing wounds. Hence, this encouraged to develop a list of plants having the power to heal these conditions (Sandhya *et al*., 2011).

Epidemiology

Some diseases like diabetes, immune-compromised conditions, ischaemia and conditions like malnourishment, ageing, local infection, local tissue damage due to burn or gunshot often leads to delay

in wound healing. Infection is the major complications of burn injury and is responsible for 50-75% of hospital deaths (James et al., 2010). Chronic wounds are non-healing wounds will continue to rise with increasing the population ages, chronic diseases, and the poor nutrition available. Most chronic wounds are ulcers that are associated with ischemia, diabetes mellitus, venous stasis disease, or pressure. About 3 to 6 million people suffer with chronic wound in the United States in which persons are 65 years and older accounting for 85% of total cases. Non-healing wounds result in enormous health care expenditures, with the total cost estimated at more than $3 billion per year (Mathieu *et al*., 2006; Menke *et al*., 2007).

Diabetes mellitus is one of the most common factors for chronic wound due to metabolic disorders and 2.8% of the population suffers from this disease throughout the world and it may cross 5.4% by the year 2025. According to Indian epidemiological data chronic wounds was reported as 4.5 per 1000 population whereas that of acute wounds was nearly doubled at 10.5 per 1000 population (Gupta *et al*., 2004). It has been reported that only 1–3% of drugs listed in Western pharmacopoeia for the use of skin and wounds; and at least one third of herbal remedies are for such use (Balick and Cox., 1996). In America 3–5% of all hospitalized patients have spinal cord injuries which suffer from ulcers. According to epidemiological data 225,000 spinal cord injury patients in the United States with about 9,000 new patients each year. Approximately 60% of diabetic patients develop pressure ulcers, and the range of annual cost estimate from $14,000 to $25,000 per patient for medical, surgical, and nursing care. The national expenditure cost of pressure ulcers is over $1.3 billion per year. Overall it is estimated that after 15 years the population will increase from 4 million to over 17 million individuals. Therefore, this health care problem is increasing at a dramatic rate (Diegelmann and Evans, 2004). In America the cost of institutional care on the same is supposed to be US$ 1000 per day while no such estimates are available for Indian institutions, the same demographic study has projected market expenditure of over US$ 7 billion worldwide for provisions of wound healing properties.

In India wound care is very expensive and especially with the diabetic population. The challenge was not only to improve wound care and treatment facilities but also stress on prevention among the population and heath care practitioners.

Classification of Wound

Wounds are classified on the basis of wound creation are open and closed wound and on the basis of physiology of wound healing are acute and chronic.

Open Wound

An open wound is a break in the skin or in a mucous membrane that bleed severely but are relatively free from the danger of infection to those that bleed little but have a greater potential for becoming infected. It is further classified as: Excision wound is a soft-tissue wound which includes excision of a minimum of skin, muscle which does not bleed or contract and any damaged subcutaneous fat, i.e. removal of the bacterial culture medium; Incision wound is an injury with no tissue loss and minimal tissue damage caused by a sharp object like scalpel or knife; laceration or tear wound is nonsurgical injury in conjunction with some type of trauma resulting in loss and damage of tissue; abrasions or superficial wounds caused by a sliding fall onto a rough surface then epidermis is scraped off that exposes nerve endings resulting in a painful injury; puncture wounds are caused by an object puncturing the skin, such as a nail or needle, Penetration wounds and gunshot wounds (Schultz, 1999).

Closed Wound

A closed wound involves underlying tissues without a break in the skin or a mucous membrane which are identified by swelling and bruises. There are following types of closed wounds: Contusions which are commonly known as bruises, caused by a blunt force trauma that damages tissue under the skin; hematomas also called a blood tumor, caused by damage to a blood vessel that in turn causes blood to collect under the skin; crush injury, caused by a great or extreme amount of force applied over a long period of time.

Acute Wound

Acute wound is a tissue injury that normally proceeds through an orderly and timely reparative process that results in sustained restoration of anatomic and functional integrity. These types of wounds are usually caused by cuts or surgical incisions and complete the wound healing process within the expected time frame. Many physiologic and mechanical factors may results in the development of chronic wound due to impairment of wound healing process that takes much longer time to heal (Alam *et al*., 2011; Lazarus *et al*., 1998).

Chronic Wounds

Chronic wounds or non healing wounds are failed to progress through the normal stages of healing and therefore enter a state of pathologic inflammation chronic wounds require a prolonged time to heal frequently. Local infection, hypoxia, trauma, foreign bodies and systemic problems such as diabetes mellitus, malnutrition, immunodeficiency or medications are the most common causes of chronic wounds (Alam *et al*., 2011; Menke *et al*., 2007; Krishnan *et al*., 2006). Non-healing wounds are surgical, diabetic, arterial, burns, dermatitis, vasculitis, and radiation. The cases of neuropathic treatment and pressure ulcers proportionately increase in diabetic cases. In this cases healing can be affected due to high levels of inflammatory cytokines, proteases and low levels of growth factors.

Now a day chronic wounds are major problem for both the patients and practitioners which affect a large number of patients and seriously reduce their quality of life. Wound healing has been the subject of intense research for a long time. Pharmacological reports available on Indian medicinal plants which are used in various wound healing models.

Wound Healing Process

Wound healing is a complex process that results in the restoration of anatomic continuity and function by several processes which involve following phases:

Hemostasis

- vascular constriction
- platelet aggregation, degranulation, and fibrin formation (thrombus)

Inflammatory Phase

- neutrophil infiltration
- monocyte infiltration and differentiation to macrophage
- lymphocyte infiltration

Proliferative Phase

- re-epithelialization
- angiogenesis
- collagen synthesis
- ECM formation

Remodelling Phase

- collagen remodeling
- vascular maturation and regression

During hemostasis a fibrin plug is formed and cytokines and growth factors are released from the aggregated platelets. This process lasts for 2-3 hours. Then neutrophils enter the wound site and begin phagocytosis to remove foreign particles, bacteria and damaged tissues. In inflammatory phase, the characteristic signs have been seen like erythema, heat, oedema, pain and functional disturbance. The predominant cells work here are the phagocytic cells ‘neutrophils and macrophages’. They appear and continue the process of phagocytosis as well as releasing more PDGF (Platelet derived growth factor) and TGF-ß (Transforming growth factor-β). Once the wound site is cleaned out, fibroblasts migrate in and to begin the proliferative phase. In proliferative phase the wound is rebuilt with new granulation tissue

which is comprised of collagen and extracellular matrix and into which a new network of blood vessels develop, a process known as angiogenesis and epithelial cells are finally resurface the wound known as epithelialisation. Remodeling phase is the final phase which occurs once the wound has been closed. During this phase the new collagen matrix becomes cross-linked and organized (Diegelmann *et al*., 2004).

Table 1: List of factors affecting wound healing

	Local factors
Oxygenation	• Wound sites have depleted oxygen due to vascular disruption. • Metabolically active cells required high oxygen consumption. • Essential for energy production by ATP for wound healing. • Prevents wound from infection. • Induces angiogenesis, keratinocytes differention, fibroblast proliferation, collagen synthesis, re-epithelialization and wound contraction.
Infection	• Delays healing by: • mechanical separation of wound edges • decreasing blood supply • prolonging inflammatory and debridement phase • bacteria produce proteolytic enzymes
Foreign body/ Contamination	• Contaminated wounds can progress to infection when: • foreign body present • excessive necrotic tissue in the wound • excessive bleeding • immune-suppression • decreased blood supply
Blood loss/supply	• Blood loss leading to hypovolemia can cause a decrease in the blood supply to the wound leading to local tissue hypoxia; oxygen is required for cell migration, multiplication, and protein synthesis
	Systemic factors
Patient Age	• Usually, younger patients heal faster and are less susceptible to infection than are older patients. • Healing is delayed in older due to an altered inflammatory response, such as delayed T-cell infiltration into the wound area, alterations in chemokine production and reduced macrophage phagocytic capacity (Gosain and DiPietro, 2004; Keylock *et al*., 2008; Swift *et al*., 2001).
Sex hormones	• Compared with aged females, aged males have been shown to have delayed healing of acute wounds. • Female estrogens, male androgens, and their steroid precursor dehydroepiandrosterone (DHEA) appear to have significant role on the wound-

	healing process (Gilliver *et al*., 2007). • Estrogen regulating a variety of genes associated with regeneration, matrix production, protease inhibition, epidermal function, and the genes primarily associated with inflammation (Hardman and Ashcroft, 2008). • It shows that estrogen can improve the age-related impairment in healing in women, while in men androgens regulate cutaneous wound healing negatively (Gilliver *et al*., 2007).
Stress	• Psychological stress causes a delay in wound healing: • Stress up-regulates glucocorticoids (GCs) • Reduces the levels of the pro-inflammatory cytokines IL-1α , IL-1β, IL-6, IL-8 and TNF-α at the wound site. These are necessary for the inflammatory phase of wound healing (Godbout and Glaser, 2006; Boyapati and Wang, 2007).
Obesity	• Obesity has increase the risk of many diseases and health conditions, which include coronary heart disease, type 2 diabetes, cancer, hypertension, dyslipidemia, stroke, sleep apnea, frequently respiratory problems, and impaired wound healing. • Obese individuals face wound complications; including skin wound infection, dehiscence, hematoma and seroma formation, pressure ulcers, and venous ulcers (Wilson and Clark, 2004).
Medication	• NSAIDS (non-steroidal anti-inflammatory drugs): Anti-inflammatory effect has a positive influence. • Corticosteroids: Retard wound healing particularly if given before inflammation begins • Topical Insulin: Increases protein synthesis, cellular multiplication, wound contraction, and fat deposition • Antibiotics: Decrease frequency of infection but decision to use systemic, local, or any should be based on patient's condition, type, length, and environment of surgery, wound contamination, and immune status
Alcohol Consumption	• Acute alcohol exposure impairs wound healing due to • Increases the incidence of infection (Szabo and Mandrekar, 2009) • Impairing the early inflammatory response, • Inhibiting wound closure, angiogenesis, and collagen production, • Altering the protease balance at the wound site
Smoking	• Tobacco smoking causes: • Impaired white blood cell migration, resulting in lower numbers of monocytes and macrophages in the wound site, and reduces neutrophil bactericidal activity in the inflammatory phase. • Lymphocyte function, cytotoxicity of natural killer cells, and production of IL-1 are all depressed. • Macrophage-sensing of Gram-negative bacteria is inhibited (Ahn *et al*., 2008; McMaster *et al*., 2008).

	• During the proliferative phase of wound healing, yields decreased fibroblast migration and proliferation, reduced wound contraction, hindered epithelial regeneration, decreased extracellular matrix production, and upset in the balance of proteases (Ahn *et al*., 2008).
Nutrition	• A high protein diet may enhance wound healing and protein deficiency can adversely affect the repair phase of healing
	• Other deficiency concerns: zinc, copper, calcium, iron, manganese, and Vitamin A, K, E, and C
	• Energy, carbohydrate, protein, fat, vitamin, and mineral metabolism all can affect the healing process (Arnold and Barbul, 2006)
Physical Status	• Underlying disease processes, systemic infections, metabolic imbalances, or endocrine disorders can delay wound healing
Diabetes	• Hyperglycemia can cause the oxidative stress when the production of ROS increases the anti-oxidant capacity (Vincent *et al*., 2004).
	• High levels of metalloproteases are a feature of diabetic foot ulcers, and the MMP levels in chronic wound fluid are almost 60 times higher than those in acute wounds.
	• This increased protease activity supports tissue destruction and inhibits normal repair processes (Sibbald and Woo, 2008).
Trauma	• Excessive trauma at the site of the wound or related to the wound will delay the early phases of wound healing
Hematoma/Seroma	• Delay healing by mechanical separation of tissues
	• Can reduce blood supply
	• Nutrient environment for bacteria
Movement	• Movement of one portion of wound to another can disrupt healing whereas continuous passive motion of a stable wound can have a positive effect on healing
Bandaging	• Generally promotes healing:
	• Protection from contamination
	• Pressure reduces edema
	• Exudates is absorbed
	• Increase in temperature and reduction in ph
	• Adherent dressing is beneficial during debridement phase but detrimental during repair phase
	• Non-adherent dressing is most beneficial during the repair phase.

Table 2: Wound healing medicinal plants and their parts

Sl. No.	Common Name (Hindi)	Botanical name	Family	Habit	Plant parts used	Metabolites	Types of wound	References
1.	Neem	*Azardirachta indica*	Meliaceae	Tree	Leaves, bark and fruits	Azadirachtin, Nimbidine, Nimbin, Nimbinine	Acute, chronic, excision and incision	Shukla *et al.*,2002; Bhattarai,1992; Singh *et al.*,2001b; Mondal and Chauhan,2000
2.	Saijana	*Moringa oleifera* Lam.	Moringaceae	Tree	Root bark	Moringine, Moringinine and Pterigospermin	Excision, Incision	Singh *et al.*,2001a
3.	Haldi	*Curcuma domestica* Valeton	Zingiberaceae	Herb	Rhizome and leaves	Vit. A and Protein	Acute, open and closed	Kumar *et al.*,1993; Mondal and Chauhan, 2000; Chettri *et al.*,1992; Singh *et al.*,2001b
4.	Jaitoon/ Olive	*Olea europaea*	Oleaceae	Tree	Seed	Oil	Acute, open	Singh *et al.*,2001b
5.	Ashwagandha	*Withania sominifera*	Solanaceae	Shrub	Dried roots	Alkaloids and withanolides, Tropine	Injury, open and close	Singh *et al.*,2001b
6.	Orchid	*Ceologyne cristata*	Orchidaceae	Herb	Dried stem	Ca, P, Zn, β-sitosterol, glycoside	Excision and incision	Singh,1995a
7.	Sunflower	*Helianthus annus*	Asteraceae	Herb	Seed powder	Tannins, alkaloids, Terpenoids essential oil	Open	Alam *et al.*, 2011
8.	Sitaphal/ Sharifa	*Annona squamosa*	Annonaceae	Tree	Dried leaves, seed powder	Tannins and vit. C	Ulcer, open and close	Pal,1981; Singh,1987; Singh *et al.*,2001b; Mondal and Chauhan,2000

9.	Adusa /Adalsa	*Adhatoda vasica* Nees	Acanthaceae	Shrub	Leaf extract	Alkaloid vascicine, vit.C, and tannin	Chronic	Singh *et al*., 2001b; Vinothapooshan *et al*., 2010
10.	Dhania	*Coriandrum sativum*	Umbelliferae	Herb	Leaves and dried seed powder	Ca, P, Oxalic acid, vit. A,B,C, Iron, Protein and fat	Chronic, open	Singh *et al*., 1998a
11.	Tea tree	*Melaleuca alternifolia*	Myrtaceae	Tree	Leaves	Terpenoids (terpinen-4-ol, cineole)	Chronic, open,	Prajapati, B.G, 2007
12.	Guarpatha	*Aloe vera*	Liliaceae	Herb	Leaf	Vit.C,E and amino acid	Mild burns, open	Davis ,1992
13.	Teak	*Tectona grandis*	Verbenaceae	Tree	Leaves	Carbohydrates, tannin and anthraquinone glycosides	Ulcer, Open and closed	Chatterjee *et al*.,1997
14.	Mulberry	*Morinda citrifolia* (Linn.)	Rubiaceae	Tree	Whole plant	Saponins, tannins, triterpenes, alkaloids,flavonoids	Open, cuts and burns	Elkins,1997
15.	*Vinca rosea*	*Catharanthus roseus*	Apocynaceae	Herb	Whole plant	Monoterpenoids alkaloids, tannins, vinblastine and vincristine	Closed ,cancer	Fischhof *et al*.,1996
16.	Onion	*Allium cepa* (Linn.)	Liliaceae	Herb	Bulb extract	Kamferol,βsitosterol, ferulic acid, myritic acid, prostaglandins	Ulcer, cuts and closed	Galal and Gawad,1965
17.	Papaya	*Carica papaya*	Caricaceae	Herb	Latex,fruits	mix.of cysteine endopeptidases such as papain	Burns and open	Azarkan *et al*.,2003
18.	Salaparni	*Desmodium gangaticum*	Fabaceae	Shrub	Whole plant	Alkaloids flavonoids, iso flavonoid glycosides and terpenes	Chronic and excision	Awasthi and Tewari,1995
19	Lantana	*Lantana camara* L.	Verbenaceae	Shrub	Whole plant	Saponins, tannins, triterpenes, alkaloids, Flavonoids	Open and excision	Day *et al*.,2003
20.	Banana	*Musa sapientum*	Musaceae	Herb	Fruit	Flavonoids, sterylacl glycosides and sitoindisides I-IV	Excision, incision and ulcer	Lewis *et al*.,1999
21.	Tulsi	*Ocimum sanctum* L.	Labiateae	Herb	Leaves	Flavonoids	Excision, incision	Shetty *et al*.,2008
22.	Manjistha, Indian Madder	*Rubia cordifolia* Linn.	Rubiaceae	Herb	Roots	Purpurin, alkaloids, anthraquinone glycosides, saponins, tannins and phytosterols	Excision and incision	More *et al*., 2007; Karodi *et al*., 2009

23.	Balam Kheera	*Kigelia pinnata*	Bignoniaceae	Tree	Bark, fruits	Kigelione,Tannin, alkaloids, stigmasterol, β-sitosterol, p-coumeric acid and 6-methoxymelenin	Chronic, acute, open and close	Sharma *et al*., 2010
24.	Broom weed	*Scoparia dulcis* L.	Scrophulariaceae	Herb	Leaves	Scoparinol (a triterpene) scoparic acid A, B &C, scopadulic acid A &B, scopadulin, friedelin and glutinol	Excision and incision	Ayyanar *et al*., 2009; Ahmed *et al.*, 2001
25.	Bombay Aloe, Cantala	*Agave cantala* Roxb. LF	Agavaceae	Herb	Leaves	saponins, spirostanol glycoside, 3-O-[β-d-glucopyranosyl]-6O- [β-d-glucopyranosyl]-(25R)-5α-22α-O-spirostan-3β, 6α-diol	Excision incision, burns	Jain (1991), Upadhyaya *et al.* (1998)
26.	Banayan tree/Vad	*Ficus benghalensis* Linn.	Moraceae	Tree	Bark, leaf	Leucodelphinidin andleucopelargonin	Open and close	Garg and Paliwal., 2011
27.	Sarwa Wranvishapaka	*Tephrosia purpurea* Linn.	Leguminosae	Herb	Root and seeds	glycosides, rotenoids, isoflavones, flavnones,chalcones, flavonoids and sterols	Cancer, ulcer, chronic, open	Alam *et al*., 2011
28.	Bush tea	*Hyptis suaveolens* Linn.	Lamiaceae	Herb	Leaves	steroids, alkaloids, carbohydrates, proteins, flavonoids, tannins, glycosides	Chronic, burns and open	Alam *et al*., 2011
29.	Dhaman grass	*Tridax procumbens* Linn.	Asteraceae	Herb	Leaves	Alkaloids, carotenoids, flavonoids, tannins, and minerals of Ca, K & Mg	Excision and incision	Alam *et al*., 2011; Talekar et al., 2012
29.	Chaulmugra	*Hydnocarpus wightiana*	Achariaceae	Tree	Seed	Hydnocarpic acid, chaulmoogric acid, lower myristic acid, palmitic acid, stearic acid, palmitoleic acid, oleic acid, linoleic acid and linolenic acid	Acute, chronic and open	Oomen *et al*.,2000; Alam *et al*., 2011

Factors Affecting Wound Healing

On the basis of sources wound healing affecting factors may be of two types: Extrinsic factors and Intrinsic factors. Extrinsic factors have effect on the patient from the external environment, whereas Intrinsic factors directly affect the body functions through the patient's own physiology or condition. Wounds may fail to heal or have a greatly increased healing time when unfavorable conditions are allowed to persist. An optimal environment must be provided to support the essential biochemical and cellular activities required for efficient wound healing and to remove or protect the wound from factors that impede the healing process.

The phases of wound healing process may be impaired by two factors such as local factors and systemic factors (Table 1). Local factors which include Oxygenation, Infections, foreign body/contamination, blood loss/supply are directly influence the characteristics of the wound itself, while systemic factors include patient age and gender, sex hormones, stress, ischemia, obesity, medication (non-steroidal anti-inflammatory, drugs, glucocorticoid, steroids, chemotherapy), alcoholism and smoking, nutrition, and disease (diabetes, keloid, fibrosis, jaundice, uremia, hereditary healing disorder) are overall healthy or disease having individual that affect his or her ability to heal.

Ethano-Medicinal Information In Wound Healing

Some identified ethno-medicinal wound healing plants and their parts are listed in table 2. Various herbal products are formulated for the treatment and management of wound healing over the years.

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