

An overview of medicinal plants as wound healers

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ABSTRACT

Wound healing is an integrated cellular and biochemical process of restoring normal structure functions of damaged tissue. Healing is a natural phenomenon by which body itself overcome the damaged to the tissue but the rate of healing is very slow and chance of microbial infection is high. Improvement in healing process can be accomplish either shorten the time required for healing or to minimize the undesired consequences. India has a rich tradition of plant-based knowledge on healthcare system. Several herbs and medicinal plants proved to be a wound healers were identified and formulated for treatment and management of wounds. Various herbal products have been used in management and treatment of wounds over the years. The present review attempt to highlight some herbs and medicinal plants proved to be scientifically used for the treatment of cuts and wounds as a wound healer.

INTRODUCTION

Wound may be defined as a disruption of the cellular and anatomic continuity of a tissue, with or without microbial infection and is produced due to any accident or cut with sharp edged things. It may be produced due to physical, chemical, thermal, microbial or immunological exploitation to the tissues. Wound healing is a process of restoring normal structure functions of damaged tissue. Healing is a natural phenomenon by which body itself overcome the damaged to the tissue but the rate of healing is very slow and chance of microbial infection is high. This creates demand of a substance that speeds up the rate of healing. Wound healers are one of the most critical requirement in the essential medicaments for soldier and may help in putting injured soldier back on the war field as quickly as possible. A wound healer also minimizes demand of other drugs like antibiotics and also their probable side effects by their use. (Lazarus., *et al* 1994). India has a rich tradition of plant-based knowledge on healthcare. A large number of plants/plant extracts/decoctions or pastes are equally used by tribals and folklore traditions in India for treatment of cuts, wounds, and burns.

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Besides this, there is not a single synthetic drug formulation in the market which can claims for its wound healing properties. The drugs available are either bacteriostatic or bactericidal and in these cases healing is by a natural phenomenon only (Lawrence *et al* 1994; Nguyen., *et al* 2009).

Classification of Wound

Wounds may be classified by several methods; their aetiology, location, type of injury or presenting symptoms, wound depth and tissue loss or clinical appearance of the wound. 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.

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 (Strodtbeck *et al* 2001).

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 that 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 (Kumar *et al* 2007).

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 (Kumar *et al* 2007; (Robert *et al* 1998).

Physiology of Wound Healing

Cellular activity

The process of healing which restores normal structure and function involves two different processes (Thomson, 2006).

Regeneration

proliferation of parenchyma cells which results in complete restoration of original tissue.

On the basis of capacity to divide cells are of three types. They are labelled in table-1.

Table. 1: Regeneration of parenchymal cells.

Sr. No.	Type	Situation	Regeneration
1	Labile cells	Epidermis, g.i.t. respiratory tract, urinary tract, cells of lymph node and spleen.	Under normal physiological condition, they are continuously dividing.
2	Stable cells	Parenchymal cells of liver, kidney pancreas, smooth muscles and cartilage cells.	Cells are in G0 phase and enter cell cycle after situation.
3	Permanent cells	Nervous system, skeletal system, cardiac muscle.	Can't regenerate.

In order to maintain proper structure of tissue cells enter the cell cycle under the constant regulatory control of growth factors like epidermal growth factor, fibroblast growth factor, platelet derived growth factor and endothelial growth factor. Regeneration of parenchymal cells involves two processes.

(1) Proliferation of original cells from the margin of injury with migration so as to cover the gap.

(2) Proliferation of migrated cells with subsequent differentiation and maturation so as to reconstitute the original tissue.

Repair

Proliferation of connective tissue element resulting in healing. Repair takes place by participation of mesenchymal cells, fibrocytes, endothelial cells and platelets of injured organ (Mutsaers *et al.*, 1997). Two processes are involved in repair,

1. Granulation tissue information

In this process after inflammation, cleaning of debris, in growth of granular tissue takes place. In growth takes place by angiogenesis (formation of new blood vessels by proliferation of endothelial cells) and fibrous tissue formation as a result of mitotic division of fibroblast.

2. Contraction of wound

Contracted wound heals rapidly as less surface area is there contraction involves activities like dehydration, contraction of collagen and myofibroblast appearance.

Extra cellular matrix

It is responsible to strengthen the wound. In addition they also direct cell migration, differentiation and organization. Extracellular matrix has five main components. These are labelled in table-2.

Steps Involved In Wound Healing

Steps involved in healing depends on the characteristics of the wound and wound are of two types on the basis of the character (Falanga *et al.*, 2005).

Primary union of wound

This is seen when wound is characterized by small, clean and uninfected condition without much loss of cells. Steps in primary union include (a) haemorrhage (b) inflammation (c) proliferation and migration of basal cells of epidermis towards incision (d) fibroblast and new collagen fibers invasion.

Secondary union of wound

Characters of secondary union include open with large tissue defect having excessive loss of cells and tissues. First three steps in secondary union is same as the primary union. There after following step is seen. In fourth step main bulk of secondary healing is formed by granulation and granulation tissue is formed by proliferation of fibroblast and angiogenesis. In final step, wound contraction takes place by the action of myofibroblasts. In the first type of wound sutures can be used but for the second type. Wound healers are the only option.

Factors influencing healing

two types of factor influencing the wound healing (Thomas, 2011).

1. Local factors: includes

- Infection by tissue organization which delays healing

- Poor blood supply which shows healing
- Movement of affected part of delay healing
- Exposure to ionizing radiation delay granulation
- Exposure to ultraviolet light facilities healing
- Foreign bodies including sutures interferes in healing

2. Systematic factors : includes

- Wound healing is rapid in young and slow in aged people
- Nutritional deficiency of vitamin C and zinc delay healing
- Haematological abnormalities also affects healing
- Diabetics are more prone to infection and hence delay healing
- Administration of glucocorticoids (anti-inflammatory) delay healing.

Table. 2: Components of extracellular matrix in cell repair.

S. No.	Component	Function	Comments
1	Collagen	Structural support	Proteinous nature Synthesized and secreted by Ribosomes.
2	Glycoproteins	Adhesive for cells and support material	Following types are presents Fibronectin Tenasein Thromboplastin
3	Basement membrane	Acts as a base	Consists of Collagen IV and laminin.
4	Elastic fibres	Provide ability To recoil	Consist of two Components elastin glycoprotein elastin micro fibril
5	Protoglycan	Helps in Formation of collagen	Have two components Carbohydrate polymer protein bound to it.

Commonly Used Medicinal Plants as Wound Healers

Aloe Vera

Aloe Vera commonly known as Kumari is a perennial herb belonging to liliaceae family. It has short stem and shallow root system with large fleshy, rosettes sessile leaves. It can be seen as wild herb in dried parts of India (Heggars *et al.*, 1996). Today aloe vera gel is an active ingredient in hundreds of skin lotions, sun blocks and Cosmetics (Grindlay *et al.*, 1986). *Aloe Vera* is an excellent remedy for minor burns, cuts and sunburns. Both juice and aqueous extract from the leaves shows significant healing properties. It is also reported that it not only speeds up healing but also prevents injured surface from getting infected (Chitra *et al.*, 1998).

Aloe Vera was studied for burn wounds by routine dressing by *A. Vera* extract every 3rd day in chemically produced burn on healing subjects. The wound healing time and bacteriological control was significantly in Aloe group (Udupa *et al.*, 1994). The working mechanism of *Aloe Vera* for wound healing is reported to be enhancing collages turnover rate and increased level of lysyl oxidase (responsible for cross linking of newly synthesized collages (Chitra *et al.*, 1998). Beside wound healing effect, it is reported to have ulcer healing property (when taken internally) and protective action on skin.

Gingko biloba

It belongs to the family Gingkoaceae and commonly known as Kew tree. It is widely planted in Korea and China.

Propagation type includes seeds and vegetative methods.⁶ *Gingko biloba* has found to have significant activity against both dead space and excision wound models in male rats. A 50 mg/kg of dose has significantly promoted the breaking strength and hydroxyproline content of granulation issue in dead space wounds and in case of excision wound model, it is found to shorten the epithelization period (Bairy *et al.*, 2001). It is also reported that the activity of G.B. is due to its high amino acid content which absorbs rapidly in blood stream and in combination with vitamins; they provide essential nutrients to the wound area to promote healing. Beyond wound healing, it is used as an anti-inflammatory and antiallergic agent in ancient Chinese medicine.

Centella asiatica

Centella asiatica is a small trailing herb bearing white to reddish flowers which normally grows widely in the wet places. Commonly it is known as Brahmi and it is propagated by seeds and vegetable propagation. Clinical studies of the formulation (ointment, cream & gels) of aqueous extracts of *Centella asiatica* reports that, when it is applied topically thrice daily for 24 days on open wound site. The treated wound epithelized faster and the rate of wound contraction was higher as compared to control wound. Gel formulation produce better results as compared to other two formulations (Kumar *et al.*, 1998). It is reported that the active constituents responsible for the activities of *Centella asiatica* are found to be asiaticosides and madicassoides (Shetty *et al.*, 2006).

Nelumba nucifera

Nelumba nucifera belonging to family Nymphaeaceae is called as Kamal in Hindi and Lotus in English. It is perineal aquatic herb embedded in mud with large flower. It is commonly cultivated in ponds and swamps by using rhizomes for propagation. *Nelumba nucifera* is very common among natural and traditional healers. They collect leaves and rhizomes, dry them and burn to produce ash which acts as wound healer. But now it is reported that the methonolic extract of rhizomes of *Nelumba nucifera* in the formulation of ointment is effective in different types of wound model in rats. The effect were studied on excision wound model, incision wound model and dead space wound model by using two different concentrations i.e. 5 % w/w & 10 % w/w ointment. The ointment in both the concentration responded significantly in all the wound models. Both the extract ointment shows the significant effect in respect with wound contracting activity, wound closer time, tensile strength, regeneration of tissue at the wound site and lysyl oxidase activity. The effects produced are comparable to that of standard drug¹² (Mukherjee *et al.*, 2000).

St. John wort

Hypericum mysorens is a perennial flowering plant and has been long used in folk medicine it belongs to the family Hypericaceae and is commonly known as St. Johns Wort.

The flowering tops are commonly used as tea or fresh tincture. It is reported that the methanolic extract of *Hypericum mysorense* produces wound healing in rats. The extract, in the form of ointment (5% w/w and 10% w/w o arial part) was evaluated in excision and incision wound models in rat. Both the concentration of the ointment showed significant response in both type of wound when compare to the control. The effect is comparable with standard drugs (Mukherjee *et al.*, 2000, Harsh *et al.*, 2000).

Tulsi

This extract is derived from the plant of *Ocimum sanctum* belonging to family Labiatae. It has been widely grown throughout the world and commonly cultivated in gardens. Traditionally *Ocimum sanctum* is used in malarial fevers, gastric disorders and in hepatic infections. *Ocimum sanctum* leaves are also used in bronchitis, ringworm and other cutaneous diseases and earache. The leaves are used as a nerve tonic and to sharpen memory. *Ocimum sanctum* leaves are abundant in tannins like gallic acid, chlorogenic acid etc and also contain alkaloids, glycosides, and saponins along with the volatile oil. The major active constituent of Holy basil leaves include urosolic acid. It contains 70% eugenol, carvenol and eugenol-methyl-ether (Udupa *et al.*, 2006).

Eucalyptus

It is also called Dinkum Oil. This oil is obtained by steam distillation of fresh leaves of *Eucalyptus globules* belonging to family Myrtaceae. It is indigenous to Australia and Tasmania. It is cultivated in United States, Spain, Portugal, and in India. It contains cineole, also known as eucalyptol. It also contains pinene, camphene, and phellandrene, citronellal, geranyl acetate. In skin care it can be used for burns, blisters, herpes, cuts, wounds, skin infections and insect bites. It can furthermore boost the immune system and is helpful in cases of chicken pox, colds, flu and measles Oil is used as a counter irritant, an antiseptic, and expectorant. It is used to relieve cough and in chronic bronchitis in the form of inhalation. It is ingredient of several liniment s and ointments. Solution of eucalyptus oil is used as nasal drop (Hukkeri *et al.*, 2002).

Bael

It is also called a Bael fruits, Indian bael. It consists of unripe or ripe fruits of the plant knowns as *Aegel marmelos* belonging to family Rutaceae. It is indigenous to India and found in Mynmar and Sri Lanka. The pulp is red in colour with mucilaginous and astringent taste. The chief constitute of drug is marmelosin which is furocoumarin. The drug also contains carbohydrates, protein, volatile oil and tanines. The pulp also contains vitamin C and vitamine A. two alkaloids O-methylhalfordional and isopentylhalfordinol have been isolated from fruits. It is used as digestive, appetizer and also used in the treatment of diarrhea and dysentery. It is also a tonic and it has a wound healing properties (Jaswanth *et al.*, 2001).

Myrobalan (Harde)

It also called Haritaki, chebulic myrobalan. It consists of dried, ripe, and fully matured fruits of *Terminalia Chebula* belonging to family Combretaceae. It is found in sub-Himalayan tracks from Ravi to West Bengal, Asam and all forest in India. It is found growing at an altitude of 1800 m. it is not cultivated and fruits are collected from wild grown forest plants. It is a tree, 15 to 25 m in height, and 1.5 to 2.5 m in diameter. It has yellowish-white flowers in the terminal spike. It contains hydrolysable tannins which upon hydrolysis yield chebulic acid and d-galloyl glucose. it also contains chebulagic, chebulinic, ellagic and gallic acids. It is used mainly as a astringent, laxatives, stomachic and tonic, anthelmintic. Fruit plup used to cure bleeding. It is an ingredient of ayurvedic preparation 'Triphala'. It is also used in piles and external ulcers (Suguna *et al.*, 2002).

Neem

Alcoholic extract of neem is useful in eczema, ringworm and scabies. Neem leaf extracts and oil from seeds has proven anti-microbial effect. This keeps any wound or lesion free from secondary infections by microorganisms. Clinical studies have also revealed that neem inhibits inflammation as effectively as cortisone acetate; this effect further accelerates wound healing. Neem oil contains margosic acid, glycerides of fatty acids, butyric acid and trace valeric acid.

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Turmeric

It is also called Indian saffron, curcuma. It consists of dried as well as fresh rhizomes of the plant known as *curcuma longa* belonging to family zingiberaceae. It contains not less than 4% of volatile oil. India account for as much as 90% of the total output of the world.

Curcuma longa is the main species of commerce and is cultivated for its rhizomes in India, China and in Sri Lanka. India is the major grower with almost 80,000 hectares under the crop producing 1, 44,000 tonnes per annum. The plants are grown for 7 to 9 months after which the rhizomes are harvested, cooked, dried and then processed for powder, oleo-resin and curcumin. The extraction of powder is carried out by using solvents, water or both. It contains about 5% of volatile oil, resin. Starch grains and curcuminoids which is the chief constitutes of curcumin, Volatile oil, content sesquiterpenes such as α and β pinene, α -phellandrene, camphor, zingiberene. It is used as a condiment or spices, and colouring agent, especially for ointments and creams. It is used for the detection of boric acid. Traditionally it has been proved as antiinflammatory, anticancer, antiseptic (Mehra *et al.*, 1984).

Table 3: Medicinal Plants with wound healing activity.

S. No.	Common Name	Source and Family	Parts Used	Reference
1	Aleppo Oak	<i>Quercus infectoria</i> Fagaceae	Galls	Jalalpure et al., 2008
2	Aloe/kumara	<i>Aloe vera. Aloe barbadensis</i> Liliaceae	Aq. Extract & juice of leaves	Chitra et al., 1998; Udupa et al., 1994.
3	Amla	<i>Phyllanthus embilica</i> Euphorbiaceae	Ethanollic extracts of fruits	Suguna et al., 2000
4	Angelica	<i>Bryophyllum pinnatum</i> Crassulaceae	Aqueous & alcoholic extract of Leaves	Khan et al., 2004
5	Apamarga	<i>Achrynthus aspera</i> Amaranthaceae	Aqueous & ethanolic extracts of leaves	Ghosh et al., 2011
6	Aritana	<i>Bryophyllum pinnatum</i> Crassulaceae.	Aq. Alcoholic & petroleum extract of leaves	Mahmood et al., 2002
7	Bach	<i>Acorus calamus</i> Araceae	Ethanollic extract of leaves	Jain et al., 2010
8	Bael	<i>Aegle marmelos</i> (Rutaceae)	Methanollic extract of root.	Jaswanth et al., 2001; Udupa et al 1994
9	Brahmi	<i>Centella asiatica</i> Umbelliferae	Aq. Extract of flowers	Kumar et al. 1998 Shetty et al., 2006
10	Brazilian Pepper	<i>Schinus terebinthifolius</i> Anacardiaceae	Hydroalcoholic extract of leaves	Lucena et al., 2006
11	Charoli	<i>Buchanania lanzan</i> Anacardiaceae	Alcoholic Extract	Chitra et al., 2009
12	Chaturangi	<i>Lanata camara</i> Verbanaceae	The Ethanolic extract of Leaf juice	Nayak et al., 2009
13	Chaulmogra	<i>Hydnocarpus weighuana</i> Flacourtiaceae	oil	Oommen et al., 1999
14	Cumin	<i>Cuminum cyminum</i> Umbelliferae	Aqueous extract of leaves, Seed	Patil et al., 2009
15	Devadaru	<i>Cedrus deodara</i> Pinaceae	Oil	Dikshit et al., 1982
16	Eucalyptus	<i>Eucalyptus globules</i> Myrtaceae	Oil	Hukkeri et al., 2002
17	Figwort	<i>Scrophielaria nodosa</i> Scrophulariaceae	Seeds,pods	Stevenson et al., 2002
18	Gandana	<i>Achillea millefolium</i> Asteraceae	alcoholic & aqueous extracts of leaves	Nirmala et al., 2001
19	Ghamra	<i>Tridax procumbens</i> Asteraceae	Whole plants extract & alcoholic extract of leaves	Diwan et al., 1983; Raina et al., 2008
20	Ginkgo(GB)	<i>Ginkgo biloba</i> Ginkgoaceae	Ethanollic extract of stem	Bairy et al.,2001
21	Hadjod	<i>Cissus quadrangularis</i> Vitaceae	Whole plants	Inngierdingen et al., 2004
22	Indigofera	<i>Indigofera enneaphylla</i> Fabaceae	Alcoholic extract of aerial parts	Hemalatha et al., 2001
23	Jasmine	<i>Jasminum auriculatum</i> Oleaceae	Ethanollic extract of leaves & flowers	Deshpande et al., 1967
24	Kamal	<i>Neumbo nuciera</i> Nymphaeaceae	Methanollic Extract of rhizomes	Mukherjee et al., 2000
25	Leopardis bane	<i>Arnica Montana</i> Asteraceae	Flowers, Rhizomes	Karow et al., 2008
26	Liquorice	<i>Glycyrrhiza glabra</i> Leguminosae	Vacuum dried Ethanolic extract of bark & root	Kishore et al., 2001
27	Marigold	<i>Clendula officinalis</i> Compositae	Flower extract	Preethi et al., 2001
28	Mexican/prickly poppy	<i>Argemone mexicana</i> Papaveraceae	Ethanollic & aqueous extracts of leaves	Dash et al., 2011
29	Myrobalan	<i>Terminala chebula</i>	Alcoholic extract of leaves	Saguna et al., 2002;
30	harda	<i>Combretoreceae</i>	& fruit	Choudhary., 2011
30	Ndende	<i>Entoda Africana</i> Fabaceae	Ethanollic extracts of leaves	Diallo et al., 2001
31	Neem	<i>Azardica indica</i> Meliaceae	Methanol extract of leaves	Barua et al., 2007
32	Nagarmotha	<i>Cyperus rotundus</i> Cyperaceae	extract of tubers	Puratchikody et al., 2006
33	Napoleona	<i>Napoleona Imperialis</i> Lecythidaceae	Methonolic extract of Leaves	Esimone et al., 2010
34	Orange Buddleja	Ball <i>Berldlej globosa</i>	Aq.leaf extract	Minsah et al., 2001
35	Palas	<i>Butea monosperma</i> Fabaceae	Alcoholic bark extract	Sumitra et al., 2005
36	Paras-pipal	<i>Thepsia populnea</i> Malvoceae	Aq. Extract of fruit	Nagappa et al., 2001
37	Paste rubber	<i>Saba Florida</i>	Leaves extract	James et al., 2010
38	Peepal	<i>Ficus religiosa</i> Moraceae	ethanollic & aqueous extracts of leaves & plant	Roy et al., 2009; Garg et al.,2011.
39	Pepper elder	<i>Peperomia pellucid</i> Piperaceae	Ethanollic extract of leaves	Villegas et al., 2001

40	Prickly pear	<i>Opuntia ficus indica</i> Cactoaceae	Methanolic extracts of stem	Park <i>et al.</i> , 2001
41	Quince	<i>Cydonia oblonga</i> <i>Cydonia vulgaris</i> Rosaceae	Aq. Extract Seed mucilage	Hemmati <i>et al.</i> , 2001
42	Rooirabas	<i>Pelargonium reniforme</i> <i>Pelargonium radala</i> Geraniaceae	Arial parts extract & leaves	Kayser <i>et al.</i> , 1997; Pepeljnjak <i>et al</i> 2005.
43	Rue, Pismaram Sabab	<i>Ruta graveolens</i> , <i>Ruta chalepensis</i> Rutaceae	Hydroalcoholic extract of whole plants, oil	Ivanova <i>et al.</i> , 2005
44	Sarphomka	<i>Tephrosia purpurea</i> Fabaceae	Ethanollic Extract	Lodhi <i>et al.</i> , 2002
45	Sehud, Thuhar	<i>Euphorbia nerioflia</i> Euphorbiaceae	Aquous extract of latex	Rasik <i>et al.</i> , 1996
46	St. John wort	<i>Hypericum mosorence</i> Hypericaceae	Methanolic extract of leaves.	Mukherjee <i>et al.</i> , 2000
47	Sunflower	<i>Helianthus annuus</i> Compositae	Leaves, seeds, flowers, roots	Subashini <i>et al.</i> , 2012
48	Tulsi	<i>Ocimum tenuiflorum</i> , <i>Ocimum sanctum</i> Labiateae	Ethanollic extract of whole part	Udupa <i>et al.</i> , 2006
49	Turmeric	<i>Curcuma longa</i> Zingiberaceae	Rhizomes	Mehra <i>et al.</i> , 1984
50	Yellow-berried Nightshade	<i>Solanum xanthocarpum</i> Solanaceae	Ethanollic extract of leaves & fruits.	Dewangan <i>et al.</i> , 2012.

CONCLUSION

There are a number of plants which are used traditionally used the tribal people of India are not been validated or such plants not been evaluated keeping the traditional and conventional claim in mind. Generally pharmacologist should study traditional systems of medicine in scientific way and validate by screening plant/plant extracts for pharmacological activity. This review focused on the pharmacological reports of plant/plant extracts screens the soluble extracts in the development of an acceptable wound healing preparation, which if validated properly and proven scientifically can act as substitute or may even replace the modern wound healing agents.

Considering the principle drawbacks, associated with synthetic compounds, plants which are the gift from nature having traditional knowledge, provides excellent raw material for the treatment of various diseases and disorders. As in the allopathic system of medicine, wound healers are available but traditional knowledge in the form of literature provides number of traditional and household preparations for those purposes. Preliminary scientific investigations on plants indicate that natural products could be exploited to discover some novel wound healers.

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