Role of Medicinal Plants in Wound Healing

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ABSTRACT

Wounds are a major cause of physical disabilities. Wound healing consists of orderly progression of a series of events that establish the integrity of the damaged tissue. Normal wound healing can be adversely affected by many factors. If the healing fails to progress in the usual stepwise manner then it may lead to development of chronic wound. Many medicinal plants are found useful in treating wounds. This study describes role of Alternanthera sessilis, Morinda citrifolia, Lycopodium serratum, Sesamum indicum, Catharanthus roseus, Cecropia peltata, Euphorbia hirta, Ginkgo biloba, Clerodendrum serratum, Pierocarpus santalinus, Lawsonia alba, Napoleona imperialis, Kaempferia galangal, Radix paeoniae, Prosopis cineraria and Trigonella foenum-graecum in wound healing. A review of some patents on herbal products for wound treatment is provided to through light on the recent technical advancements in this area.

Key words: Wound, medicinal plant, extract, patent

INTRODUCTION

According to the Wound Healing Society, wounds are physical injuries that result in an opening or break of the skin that causes disturbance in the normal skin anatomy and function (Strodthoeck, 2001). They result in the loss of continuity of epithelium with or without the loss of underlying connective tissue.

Wounds represent a significant burden on the patients and health care professionals worldwide. They not only affect physical and mental health of millions of patients but also impose significant cost on them. Current estimates indicate that worldwide nearly 6 million people suffer from chronic wounds (Kumar et al., 2007). Unhealed wounds constantly produce inflammatory mediators that produce pain and swelling at the wound site. Wounds are a substrate for infection and prolong the recovery of injured patients. Chronic wounds may even lead to multiple organ failure or death of the patient (Roberts et al., 1998).

Wound healing is a normal biological response to the injury that sets into motion a sequence of events. Although wound healing is a familiar process but its underlying biology is very complex and it is still only partially understood (Sherratt and Dallon, 2002).

Many medicinal plants have been reported to possess wound healing activity and found useful in the treatment of wounds. This article outlines types of wound, factors affecting wound healing, mechanism of wound healing and properties of some medicinal plants that exhibit wound healing activity. The paper presents discussion of some patents relating to herbal products for wound healing management.
CLASSIFICATION OF WOUNDS

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

Open wounds: Through an open wound blood escapes the body and bleeding is clearly visible. Open wounds can be further classified into various types (Schultz, 1999) according to the object that causes the wound.

Incised wounds: It is an injury with no tissue loss and minimal tissue damage. It is caused by a sharp object such as a scalpel or knife. Bleeding in such cases can be profuse, so immediate action should be taken.

Laceration wounds or tear wounds: This is nonsurgical injury in conjunction with some type of trauma, resulting in tissue loss and damage.

Abrasions or superficial wounds: Abrasion is caused by a sliding fall onto a rough surface. During abrasions the topmost layer of the skin i.e., epidermis is scraped off that exposes nerve endings resulting in a painful injury. Blood loss similar to a burn can result from serious abrasions.

Puncture wounds: They are caused by an object puncturing the skin, such as a nail or needle. Chances of infection in them are common because dirt can enter into the depth of the wound.

Penetration wounds: Penetration wounds are caused by an object such as a knife entering and coming out from the skin.

Gunshot wounds: They are caused by a bullet or similar projectile driving into or through the body.

Closed wounds: In closed wounds blood escapes the circulatory system but remains in the body. This is visible in the form of bruises. Closed wounds have fewer categories, but are just as dangerous as open wounds.

Contusions or bruises: Bruises are caused by a blunt force trauma that damage tissue under the skin.

Hematomas or blood tumor: They are caused by damage to a blood vessel that consequently causes blood to collect under the skin.

Crush injury: Crush injury is caused when great or extreme amount of force is applied on the skin over a long period of time.

Acute wounds: 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 (Lazarus et al., 1994). Acute wounds are usually caused by cuts or surgical incisions and complete the wound healing process within the expected time frame. However, various physiologic and
mechanical factors may impair the healing process and wound fails to proceed through the usual stepwise progression of healing. It results in the development of chronic wound that takes much longer time to heal.

**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 (Menke et al., 2007). Chronic wounds either require a prolonged time to heal, do not heal, or recur frequently (Krishnan, 2006). These wounds are a major cause of physical disability.

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. Some common examples of chronic wounds are diabetic foot ulcer, pressure ulcer and the venous leg ulcer.

**FACTORS AFFECTING WOUND HEALING**

Wound healing is a normal biological process in the human body. Many factors can adversely affect this process and lead to improper and impaired wound healing. A thorough understanding of these factors and their influence on wound healing is essential for developing better therapeutic options for wound treatment (Kerstein, 2007).

**Improper diet:** Wound healing is an anabolic process that requires both energy and nutritive substrates. It is reported that serum albumin level of 3.5 g/dl or more is necessary for proper healing (Hanna and Giacopelli, 1997). Protein is essential for collagen synthesis on wound site. A state malnutrition may provide an inadequate amount of protein and this can result in the decreased rate of collagen synthesis wound tensile strength or an increased chance for infection (Albritton, 1991; Rosen and Cleary, 1991).

**Infection at the wound site:** Wound infection is probably the most common reason for impaired wound healing (Lazarus et al., 1994). *Staphylococcus aureus*, *Streptococcus pyogenes*, *Corynebacterium* sp., *Escherichia coli* and *Pseudomonas aeruginosa* are some important organisms causing wound infection (Kumar et al., 2003).

**Insufficient oxygen supply and tissue perfusion to the wound area:** Adequate blood supply and tissue perfusion is extremely important for proper wound healing. Excessive pain, cold or anxiety can cause local vasoconstriction and increased healing time (Cuzzell and Stotts, 1990). Smoking and use of tobacco decrease tissue perfusion and oxygen tension in wounds (LaVan and Hunt, 1990).

**Drugs:** Many drugs are known to impair wound healing. Chemotherapeutic drugs used in cancer are the largest group well known to delay wound repair (Franz et al., 2007). Systemic glucocorticoids interfere in the normal healing process by reducing collagen synthesis and fibroblast proliferation.

**Elderly age:** Elderly age is found associated with delayed wound healing. It is reported that fibroblast growth and activity diminishes and collagen production and wound contraction are slowed in injured older individuals (Sherman, 1997).
Diabetes and other disease conditions: Diabetic patients are more susceptible to wound infection. In a study wound infection rate was found 11% higher in diabetic patients than in the general patient population (Greenhalgh, 2003). Acute and chronic liver diseases are also associated with delays in wound healing. Patients with altered immune function have an increased susceptibility to wound infection.

THE WOUND HEALING MECHANISM

Wound healing is a complex process in which the skin or the affected organ repairs itself after injury. In normal conditions the outermost layer of the skin i.e., epidermis and the inner or deeper layer i.e., dermis exists in steady-state equilibrium and forms a protective barrier against the external environment. If this protective barrier is broken due to any injury the normal physiologic process of wound healing is immediately instigated. Upon injury to the skin, a set of complex biochemical events takes place in a closely organized cascade to repair the damage. Within few minutes after the injury, platelets aggregate at the injury site to form a fibrin clot. This clot acts to control the active bleeding and to achieve hemostasis. The entire wound healing process that begins at the moment of injury can continue for even months or years.

There are three main phases of wound healing viz., inflammatory phase, proliferative phase and remodeling phase. These phases are briefly described here.

Inflammatory phase: The inflammatory phase starts immediately after the injury that usually lasts between 24 and 48 h and may persist for up to 2 weeks in some cases (Li et al., 2007). The inflammatory phase launches the hemostatic mechanisms to immediately stop blood loss from the wound site. Clinically recognizable cardinal signs of inflammation, rubor (redness), calor (warmth), tumor (swelling), dolor (pain) and functio laesa (loss of function) appear as the consequence. This phase is characterized by vasoconstriction and platelet aggregation to induce blood clotting and subsequently vasodilatation and phagocytosis to produce inflammation at the wound site.

Proliferative phase: The second phase of wound healing is the proliferative phase that lasts upto 2 days to 3 weeks after the inflammatory phase. This phase comprises of three steps viz., granulation, contraction and epithelialisation. In the granulation step fibroblasts form a bed of collagen and new capillaries are produced. Fibroblasts produce a variety of substances essential for wound repair including glycosaminoglycans and collagen (Stadelmann et al., 1998). Under the step of contraction wound edges pull together to reduce the defects. In the third step fresh epithelial tissues are formed over the wound site.

Remodeling phase: This phase lasts for 3 weeks to 2 years. New collagen is formed in this phase (Madden and Peacock, 1968; Proekop et al., 1979). Tissue tensile strength is increased due to intermolecular cross-linking of collagen via vitamin C-dependent hydroxylation. The scar flattens and scar tissues become 80% as strong as the original tissue.

SOME MEDICINAL PLANTS USEFUL IN WOUND HEALING

Medicinal plants are important sources of new chemical substances that have beneficial therapeutic effects. Extensive research has been carried out in the area of wound healing management through medicinal plants. Recent studies with significant findings involving Alternanthera sessilis, Morinda citrifolia, Lycopodium serratum, Sesamum indicum, Catharanthus
roseus, Cecropia peltata, Euphorbia hirta, Ginkgo biloba, Clerodendrum serratum, Pterocarpus santalinus, Lawsonia alba, Napoleona Imperialis, Kaempferia galangal Radix paeoniae, Prosopis Cineraria and Trigonella foenum-graecum are emphasized here.

**Alternanthera sessilis:** *Alternanthera sessilis* Syn. *Alternanthera triandra* belongs to Amaranthaceae plant family. It is a prostrate herb mainly used as a lactagogue and febrifuge. The seeds of the plant contain many fatty acids such as myristic, palmitic, stearic, oleic and linoleic acid (Hosamani et al., 2004). Leaves of the plant were reported to have wound healing activity by Jalaipure et al. (2008). They studied wound healing activity of the chloroform extract of the plant through excision, incision and dead space wound models. The test group of animals showed significant wound healing activity as compared to the control group in all the models.

**Morinda citrifolia:** *Morinda citrifolia* L., the “noni” (Rubiaciae) is an evergreen shrub. The leaves, fruits and roots of the plant are very nutritious. Blanco et al. (2006) reported the nutritional and therapeutic properties of the noni fruit. The ethanolic extract of the plant leaves in an oral dose of 150 mg/kg/day was used by Nayak et al. (2007) to evaluate the wound healing activity in an experiment on rats. Reduction in the wound area was found to be 71% in the test animals as compared to 57% in the controls. Significantly lower complete epithelialization time was observed in test animals than in the control animals.

**Lycopodium serratum:** *Lycopodium serratum* (Lycopodiaceae) is commonly known as Club moss. The plant is used to increase efficiency of learning and memory and in the treatment of Alzheimer’s disease. The plant is reported to contain many alkaloids (Takayama et al., 2003). Wound healing activity of aqueous and ethanolic leaf extracts of *L. serratum* was studied by excision, incision and dead space wound models on rats (Manjunatha et al., 2007). As compared to the aqueous extract and controls the ethanolic extract showed significant decrease in the period of epithelialisation and an increase in wound contraction rate, tissue breaking strength and hydroxyproline content at the wound site.

**Sesamum indicum:** *Sesamum indicum* L. is a member of family Pedaliaceae. Sesame oil obtained from the seeds of the plant is highly nutritive as it is a rich source of natural oxidants such as sesamin and sesamol (Rajeswari et al., 2010).

The methanolic extract of roots of *Sesamum indicum* was obtained and was incorporated in gel and ointment bases. These preparations were evaluated for in vivo wound healing activity on rats using excision wound model (Dhumal and Kulkarni, 2007). The test preparations exhibited faster contraction of wound diameter as compared to the control. The ointment showed a comparable wound healing potential to the povidone-iodine ointment.

**Catharanthus roseus:** *Catharanthus roseus* plant is a key source of monoterpenoid indole alkaloids, vinblastine and vincristine which are found useful in the treatment of cancer (Magnotta et al., 2006). In a study ethanolic extract of *Catharanthus roseus* flowers in a dose of 100 mg/kg/day demonstrated to possess wound healing property (Nayak et al., 2006).

**Cecropia peltata:** *Cecropia peltata* (Cecropiaceae) leaves are used traditionally in Mexico to treat a variety of disorders including type 2 diabetes. Infusion prepared by the dried leaves of the plant is drunk as agua de uso (Andrade-Cetto and Vázquez, 2010). Aqueous and ethanolic leaf extracts
of this plant were screened for wound healing properties (Shivananda, 2006). Wound areas reduced statistically significantly in all treatment groups as compared to respective controls (p<0.001). Protein, hydroxyproline and hexosamine contents were increased significantly in extract treated animals as compared with the controls.

**Euphorbia hirta**: *Euphorbia hirta* (Euphorbiaceae) is a weed commonly found in tropical countries and has been used traditionally for cough, asthma, bronchitis bowel complaints, worm infestation, kidney stones, bronchial affections and conjunctivitis (Loh et al., 2009). The aqueous extract of the plant shows analgesic, anti-pyretic, anxiolytic, sedative, anti-inflammatory activities and also inhibitory action on platelet aggregation.

Ethanolic extract of the entire herb of *Euphorbia hirta* was employed for exploring its wound healing activity in an investigation (Jaiprakash et al., 2003). Wistar Albino rats were used in the experiment and excision wounds, incision wounds and dead space wounds were studied. It was found that the ethanolic extract of the entire herb of *E. hirta* possesses significant wound healing activity.

**Ginkgo biloba**: *Ginkgo biloba* is used as an herbal medicine from the ancient times. In recent experiments the plant has been reported to be effective in ischemic brain injury, cerebrovascular insufficiency, cognitive speed, dementia and Alzheimer's disease, peripheral vascular disease and aging damages (Satoh and Nishida, 2004).

Healing suppressant effect of cyclophosphamide by *Ginkgo biloba* was evaluated by Bairy et al. (2006). Cyclophosphamide significantly reduced (p<0.05) and *Ginkgo biloba* significantly increased (p<0.05) the breaking strength and hydroxyproline content of granulation tissue. This effect of *Ginkgo biloba* may be attributed to its antioxidant property.

**Clerodendrum serratum**: The roots and leaves of *Clerodendrum serratum* (Bharangi) have great medicinal value. It is found useful in cephalalgia, ophthalmia, glandular swellings and in wound healing.

Ethanolic extracts of root and leaves of *Clerodendrum serratum* were obtained and their wound healing potency was evaluated on Albino rats (Vidyai et al., 2005). The results showed higher wound healing potency of the root extract as compared to the leaf extract. On comparison with the control both the extracts demonstrated significant wound healing potency.

**Pterocarpus santalinus**: *Pterocarpus santalinus* L. belongs to the family Fabaceae. The wood of the plant possess astringent, tonic and diaphoretic properties. A paste of the wood is used externally in inflammations and headache (Kameswara et al., 2001). The wound healing potency of ethanolic extracts of leaf and stem bark of *Pterocarpus santalinus* was evaluated by Manjunatha et al. (2005). The extracts demonstrated significant decrease in the period of epithelialisation, increase in the rate of wound contraction, skin breaking strength, granulation tissue dry weight, hydroxyproline content and breaking strength of granulation tissue. Histopathological study of granulation tissue also evidenced the increased collagenation when compared to control group of animals.

**Lawsonia alba**: *Lawsonia alba* (Lythraceae) has been shown to possess antimicrobial, antifungal and antitubercular activities. Its bark is reported to be useful in jaundice and in the enlargement of the spleen (Ahmed et al., 2000).
Wound healing potential of the leaf extract of *Lawsonia alba* was evaluated through oral and topical routes of administration. Results indicated that the extract exhibited better efficacy upon topical administration as compared to the oral administration (Mandawade and Patil, 2003).

**Napoleona imperialis:** *Napoleona imperialis* is a Nigerian folklore medicinal plant. Chah et al. (2008) demonstrated antibacterial and wound healing properties of this plant in rats. In another experiment Esimone et al. (2005) prepared an herbal ointment of the methanolic extract of *Napoleona imperialis* and evaluated its wound healing effect by the excision wound model on guinea pigs. The result of the experiment indicates that *Napoleona imperialis* extract possess a better wound healing property as compared to the standard antibiotic used as control.

**Kaempferia galanga:** This medicinal plant has been extensively used for treatment of various disorders including hypertension, rheumatism and asthma (Zakaria and Mustafa, 1994). In Thailand the rhizome of *Kaempferia galanga* (Zingiberaceae) is traditionally used for relieving toothache, abdominal pain, muscular swelling and rheumatism (Ridtitid et al., 2008).

In a study conducted by Shanbhag et al. (2008) ethanolic extract of *Kaempferia galanga* was obtained and its effect in dexamethasone suppressed wound healing was studied in Wistar rats. When *Kaempferia galanga* extract was coadministration with dexamethasone a significant reduction in the epithelialization time with an increase in tissue breaking strength and percentage of the wound contraction was observed.

**Radix paoniae:** *Radix paoniae* (Paeonaceae) is used to treat amenorrhea, traumatic injuries, epistaxis, inflammation, boils and sores and to relieve pain (He et al., 2004).

Aqueous extract of the roots of *Radix paoniae* was screened for wound healing by excision, incision and dead space wound models on Wistar rats. Parameters studied were tissue breaking strength, epithelialisation, wound contraction and granulation tissue dry weight. The test group demonstrated significant wound healing activity as compared to Nitrofurazone ointment treated control group (Malviya et al., 2009).

**Prosopis cineraria:** *Prosopis Cineraria* (Mimosaceae) is an evergreen, small, thorny, irregularly branched tree. Aqueous paste of bark of the tree when applied externally disinfects wounds and promotes healing (Anonymous, 1914). The tree is also found to possess anti-inflammatory, analgesic and anti cancer activity (Vishnoi et al., 2005) and useful in boils and skin diseases (Parveen et al., 2007).

**Trigonella foenum-graecum:** *Trigonella foenum - graecum* (Papilionaceae), commonly known as Fenugreek is a very useful medicinal plant. Seeds of the plant show wound healing activity (Taranali and Kuppast, 1996). Fenugreek is found useful for its antihyperlipidemic activity (Issarani and Nagori, 2006). Fenugreek seeds are rich in polysaccharide galactomannan (Toppo et al., 2009) that has exhibited significant wound healing property (McAnalley et al., 1995). Issarani and Nagori (2004) demonstrated that Fenugreek galactomannan is as a potential bioactive molecule for conducting advance research in the area of wound healing management.

**SOME PATENTS ON HERBAL PRODUCTS FOR WOUND TREATMENT**

Patents are store houses of the latest technical information. Although patented products are excluded to be made or used commercially by others before the patent expiration (Nagori and
Mathur, 2008, 2009) still patent reviews are useful in many ways. Patent reviews provide a comprehensive knowledge of the latest technical advances in a particular subject area. They help researchers to identify potential areas for conducting new research work and developing better products and methods. Such reviews help manufacturers to avoid falling in patent infringement litigation by designing alternative products and methods (Nagori and Mathur, 2009).

A review of some patents that relate with the use of medicinal plants in wound healing management is done here. This review provides an insight on the recent technological advances that have taken place in the area of wound management.

**Topical gel matrix:** Costa et al. (2008) developed a gel matrix for wound healing, in which a plant oil extract is entrapped. According to their patent such plant oil may be pine, clove, coriander or Sweet Birch oil. The gel matrix comprises of about 15% w/w polyethylene glycol-150, about 37.4-45% w/w ethoxydiglycol, 1-8% w/w polysorbate surfactant and a bio compatible liquid carrier.

**Pharmaceutical compositions comprising an extract of Euphorbia prostrata:** A novel composition comprising of an extract of the plant Euphorbia prostrata was patented (Jain et al., 2008). This composition contains pharmaceutically acceptable carrier optionally with therapeutic agents useful for the treatment of wounds.

**Herbal composition for cuts, burns and wounds:** A novel herbal composition for treatment of cuts, burns and wounds was developed (Pushpangadan et al., 2008). The patented composition comprises extracts of any of the plant *Utleria solicifolia, Jatropha curcas, Clerodendrum infortunatu* and *Centella asiatica*. The herbal composition was found capable of causing at least 70% wound contraction in 10 days.

**Gel based cosmetic and wound healing formulation and method:** Knapp and DiSalvo (2007) patented a gel-based cosmetic and wound-healing formulation and methods for making this formulation. The formulation comprises of live yeast cell extract, pigment and a gel.

**Topical wound dressing and method of making same:** A patent on topical wound dressing and method of making the same was granted to Leber (2006). In this wound dressing a gauze pad is impregnated with tannin extract derived from Black pekoe tea.

**Herbal extract having therapeutic activity on injuries and pharmaceutical composition and health food containing the same:** A pharmaceutical composition for treating injuries was developed by Hong (2006). The composition contains a mixture of extracts of *Astragali radix, Ginseng radix, Carthami flos, Angelicae gigantis radix, Cnidii rhizoma, Rehmanniae radix preparata, Paeoniae radix and Cinnamomi cortex spissus.*

**Wound healing antiscarring topical composition of centella and ginseng:** Mini et al. (2002) invented a wound healing antiscarring topical composition of Centella and Ginseng. It comprises of centella whole extract (0.01-1% by weight) and ginseng extract (0.01-0.5% by weight) with pharmaceutically acceptable excipients.
Antipruritic composition and wound-healing-promoting composition: Tsuchida et al. (2006) developed an antipruritic and a wound healing promoting composition which comprises Sasa albo-marginata extract in an amount 1%-10% by weight as expressed in terms of the solid content thereof. The composition is reported to show an excellent wound healing promoting effect.

Nutraceutical treatments for diabetic and non diabetic wound healing: A method for improving wound healing in a mammal was developed by Chien and Bagchi (2008). The method involves administering an effective amount of two or more of the following substances: chromium, zinc, berry extract, Polygonum cuspidatum extract, L-arginine, chlorophyll and aloe vera to the patient. It is claimed to improve wound healing.

Topical wound care product containing hyssop extract: A new composition for treating wounds containing hyssop extract combined with glycerol, salt, saccharides and water was discovered to be effective in promoting healing of wounds (Reichert, 2008).

Composition having wound curing promotive effect: A new skincare preparation for external use, a pharmaceutical and a wound masking material comprising herbal extract were prepared by Yamamoto et al. (2009) in Japan. The preparation is claimed to be safe after long term use and was found useful for diabetic patients.

Extract of Stewartia koreana and use thereof: The extract of Stewartia koreana promotes migration and multiplication of endothelial cell and shows excellent effect in angiogenesis and wound healing (Kim et al., 2010). A pharmaceutical composition for promoting angiogenesis or tissue regeneration and a cosmetic for improving wrinkles containing Stewartia koreana extract was developed.

Herbal medicinal composition for curing external wound and bedsore and method of manufacturing medicine from the composition: A new herbal medicinal composition for curing an external wound and a bedsore was prepared by Chuang et al. (2009). The composition contains herbal medicinal materials such as dried ginger root, dried aconiti tuber and cinnamon bark as the effective ingredients.

Wound healing ointment: A novel ointment composition comprising Eleutherococcus senticosus (Siberian ginseng) extract useful in the treatment of wound and burns was prepared and patented (Vladimirovich et al., 2009).

Wound healing agent containing momordicae semen extract: Momordicae semen extract possess wound healing efficiencies. A topical transdermal formulation comprising Momordicae semen extract was developed (Bongcheol et al., 2009). The formulation was capable of reducing the time required for wound treatment and wound closure.

Compound catechu ointment for healing wound and preparation method thereof: The patent relates to a new compound Catechu ointment used for wound healing and a method of preparing such ointment (Yimu, 2009).
Heidouba extract and preparation method and pharmaceutical use thereof: An herbal preparation containing Huidouba extract was developed by Lirong et al. (2009). The preparation was found useful in the treatment of trauma, incised wound, scalds and burn injuries.


A composition for the treatment of burns, cuts and like wounds: Compositions and a method for fast healing of wounds, lesions, bed sores fissures, burns, cuts and ulcers were developed by Luuia and Cipla Ltd. (2008). The herbal based compositions are in the form of creams, lotions, gels or ointments or the like.

CONCLUSION

Wound healing is a biological process that begins with trauma and ends with scar formation. The goals of wound care include reducing risk factors that inhibit wound healing, enhancing the healing process and lowering the incidence of wound infections. Many medicinal plants have been found useful in wound healing. Medicinal plants provide leads to find therapeutically useful compounds, thus more efforts should be made towards isolation and characterization of the active principles and elucidation of the relationship between structure and activity. The combination of traditional and modern knowledge can produce better drugs for wound healing with fewer side effects.

REFERENCES


