Medicinal Plants and their Role in Wound Healing

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ABSTRACT

Plants and their extracts have immense potential for the management and treatment of wounds. The phyto-medicines for wound healing are not only cheap and affordable but are also purportedly safe as hyper sensitive reactions are rarely encountered with the use of these agents. These natural agents induce healing and regeneration of the lost tissue by multiple mechanisms. However, there is a need for scientific validation, standardization and safety evaluation of plants of the traditional medicine before these could be recommended for healing of the wounds.

KEY WORDS

Wound healing, plant extract, phyto-medicine

INTRODUCTION

Wound is defined simply as the disruption of the cellular and anatomic continuity of a tissue (Bennet, 1988). Wound may be produced by physical, chemical, thermal, microbial or immunological insult to the tissue. The process of wound healing consists of integrated cellular and biochemical events leading to reestablishment of structural and functional integrity with regain of strength of injured tissue. Clinically, one often encounters non-healing, under-healing or over healing. Therefore the aim of treating a wound is to either shorten the time required for healing or to minimize the undesired consequences (Myers et al, 1980). Attention should be directed towards discovering an agent, which will accelerate wound healing either when it is progressing normally (Mather et al, 1989), or when it is suppressed by various agents like corticosteroids (Ehrlich & Hunt, 1968), anti-neoplastics (Raju & Kulkarni, 1986), or non-steroidal anti-inflammatory agents.

Medical treatment of wound includes administration of drugs either locally (topical) or systemically (oral or parenteral) in an attempt to aid wound repair (Savanth & Shah, 1998). The topical agents used include antibiotics and antiseptics (Chulani, 1996), desloughing agents (chemical debridement, e.g. hydrogen peroxide, eusol and collagenase ointment) (Savanth & Mehta, 1996), wound healing promoters (e.g. Tretinoin, aloe vera extract, honey, comfrey, benzoyl peroxide, chamomilia extract, dexpanthenol, tetrachlordecaxide solution, clostebol acetate and the experimental cytokines.

Various growth factors like platelet derived growth factor, macrophage derived growth factor, monocyte derived growth factor (Mather et al, 1989) etc. are necessary for the initiation and promotion of wound healing. Many substances like tissue extracts (Udupa et al, 1991), vitamins & minerals and a number of plant products (Dahanukar et al, 2000) have been reported by various workers, to possess pro-healing effects. Wound healing herbals encourage blood clotting, fight infection and accelerate the healing of wounds. Plants or chemical entities derived from plants need to be identified and formulated for treatment and management of wounds. In this direction a number of herbal products are being investigated at present. Various herbal products have been used in management and treatment of wounds over the years. A few plants/plant products with promise are discussed in this paper.

Aloe vera

Aloe, a native to Africa, is also known as “lily of the desert” or the plant of immortality. Its name was derived from the alloeh meaning “bitter” because of the bitter liquid found in its leaves. Egyptians recorded use of this...
scar contracture and deformities. Therefore, the plant can be of much therapeutic value in minimizing post burn wounds and burn wounds. Aqueous extracts of *Chromolaena odorata* decoction from leaves of this plant have been used throughout Vietnam for the treatment of soft tissue injuries. It stimulates granulation tissue and re-epithelization processes (Lee, 1995). The extract also inhibits wound healing in both normal and immuno-compromised (steroid treated) rats in dead space wound models. Compared to various extracts, the whole plant extract has the greatest pro-healing activity with increase in tensile strength and lysyl oxidase activity. Aqueous extract was also effective in increasing lysyl oxidase but to a lesser degree (Udupa et al, 1991). The extract also inhibits inflammatory activity. They also stimulate wound healing. Some clinical reports suggest topical *Aloe vera* gel is useful in healing minor burns and that such application of the gel is harmless as hypersensitive reactions to it are rare. However, in some severe burns, aloe gel may actually impede healing (Schmidt & Greenspoon, 1991).

**Azardica indica**

It is commonly called as Neem and the plant has diverse medicinal properties. Neem oil contains margosic acid, glycerides of fatty acids, butyric acid and trace of valeric acid. Various active principles are nimbidin, nimbidal, azadirachthin, nimbin, azadirine, gedunin, salalin. They have diverse medicinal activities. Neem oil is especially beneficial for curing skin ailments. Oil is used for dressing for foul ulcers, eczema and skin diseases like ringworm, scabies and mange in dogs. It is a powerful insect repellant, anti-bacterial, anti-fungal, anti-viral, anti-inflammatory and also strengthens the body’s overall immune responses. Neem oil contains fatty acids which build collagen, promote wound healing and maintain the skin’s elasticity. The active ingredients of neem oil help in the process of wound healing and the skin is able to retain its suppleness as the wounds heal. Neem oil has a high content of essential fatty acids. They keep the site moist and give a soft texture to the skin during the healing process. 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.

**Lantana camara**

*Lantana camara* Linn, a shrub native of tropical America has completely been naturalized in many parts of India as an ornamental plant. The plant has abortificient, antimalarial, anti-inflammatory and wound healing properties. The hydro-alcoholic extract and fresh juice of leaves have favoured wound contraction (Kurian, 1995). The plant is potentially toxic and its toxicities include nephrotoxicity, hepatotoxicity, photosensitization, dermatitis, intestinal haemorrhage, therefore, the use of this plant in whole or any part thereof needs to be carefully regulated until the alarming toxic principles of the plant are properly identified and removed.

**St. John’s Wort (Hypericum spp.)**

St. John’s wort is a bushy perennial plant with numerous yellow flowers. It is native to many parts of the world including Europe and the United States. It has an age old history of safe and effective usage in many folk and herbal remedies. It is claimed to be useful in mental depression, anxiety, sleep disorders, menstrual cramping, sciatica and arthritis. The blossoms have been used in folk medicine to relieve patients suffering from ulcers, gastritis, diarrhea and nausea. This plant has an antiseptic action, relieves inflammation and promotes healing when used externally on cut surfaces of the body. The tincture of *Hypericum* spp. when given orally has a remarkable effect in lacerated and suppurated wounds with restoration of tissue vitality (Fayazuddin, 1981). Pro-healing action of *Hypericum* spp. tincture is evidenced by enhanced epithelization phase with an increase in wound contraction rate and granulation tissue breaking strengths (Rao et al, 1991).

**Tridax procumbens**

The plant is a native of tropical America and naturalized in tropical Africa, Australia and Asia including India. Leaf of *Tridax procumbens* mainly contains crude protein (26%), crude fiber (17%), soluble carbohydrate (39%) and calcium oxide (5%) (Chadha, 1976). The juice of the leaves of this plant is used by villagers to arrest bleeding from cuts and bruises in animals. This juice accelerates two phases of healing namely epithelization and collagenization; however it retards scar formation and granulation (Diwan et al, 1983). *Tridax procumbens* antagonized anti-epithelization and tensile strength depressing effect of dexamethasone without affecting its anti-contraction and anti-granulation action. (Diwan et al, 1983). The effect of various extracts (whole plant extract, aqueous extract, butanol extract and ether fraction) of this plant has been studied in dead space wound models. Compared to various extracts, the whole plant extract has the greatest pro-healing activity with increase in tensile strength and lysyl oxidase activity. Aqueous extract was also effective in increasing lysyl oxidase but to a lesser degree (Udupa et al, 1991). Leaf extracts of this plant also promote wound healing in both normal and immuno-compromised (steroid treated) rats in dead space wound model. The plant increased not only lysyl oxidase but also, protein and nucleic acid content in the granulation tissue, probably as a result of increase in glycosaminoglycan content (Udupa et al, 1998).

**Chromolaena odorata**

*Chromolaena odorata* was first identified in Central America and Vietnam. The aqueous extract and the decoction from leaves of this plant have been used throughout Vietnam for the treatment of soft tissue wounds and burn wounds. Aqueous extracts of *Chromolaena odorata* enhances hemostatic activity (Akah, 1990) and stimulates granulation tissue and re-epithelization processes (Lee, 1995). The extract also inhibits wound contraction reversibly. Therefore, the plant can be of much therapeutic value in minimizing post burn scar contracture and deformities.
Hydnocarpus wightiana

The oil of Hydnocarpus spp. has been used for several years as anti-leprosy drug and as an anti-parasitic drug in the treatment of guinea worm infestation. The oil of Hydnocarpus spp. when given orally or administered topically helped to heal the wounds and gangrene faster in leprosy and diabetic patients (Manjrekar, 1996). The wound healing effect of oil of Hydnocarpus spp. was studied with reference to collagenation and the strength of scar tissue (Oomen et al. 1999). The drug treated group showed a significant increase in strength of scar tissues in the incision wound model and also increased the strength of collagen tissue and hydroxyl-proline content in the dead space wound model. Hydnocarpus oil administered orally promoted epithelization, but not wound contraction (Oomen et al., 2000). External application of oil of Hydnocarpus spp. and its paste significantly shortened the epithelization period when compared to control group. Oil may act as adjuvant in healing of wounds and ulcer in leprosy patients and therefore, may be clinically useful.

Helianthus annus Linn.

An ornamental annual herb, with erect, rough and hairy stem is common in Indian Gardens in swampy areas. In traditional medicine the plant is used by tribals for inflammation of eyes, sores, dysuria, colic, tiger bites and bone fractures (Jain & Tarafdar, 1970). In a study the alcoholic extract of whole plant of H. annus applied in the form of an ointment on the excised wound of rat led to a significant reduction in total healing period. This has been confirmed by histology where earlier appearances of fibroblasts were seen. Early appearance and higher accumulation of muco-polysaccharides has been stated as indicators of hastened repair (Deshpande et al. 1965).

Jasminum auriculatum

A small herb found in south India and the western peninsula. The alcohol free defatted extract of J. auriculatum leaves has been reported to contain lupeol and jasminol (Deshpande & Upadyaya, 1967). Juice of leaves of J. auriculatum has been shown to be beneficial in wound healing. The juice when applied in the form of jelly, locally on linear uniform excised wound in rats is found to promote wound healing. This has been assessed by histological, biochemical and contraction rate studies (Deshpande et al, 1965). Fresh juice of the leaves showed an increase and early gain of the tensile strength in the linear wounds in rats. The study indicated that collagenation contributed to improved tensile strength in the early phase of healing. Such effect was also reported by Deshpande & Pathak (1966). Ghee medicated with J. auriculatum, on topical application accelerated the healing time of second degree burn wounds in rats up to six days. The mucopolysaccharide accumulation was significantly higher in group treated with medicated ghee (Deshpande & Pathak 1966).

Ginkgo biloba

Ginkgo biloba (Salisburia aduantifolia) is also known as maiden hair tree. The genus ginkgo originated 200 million years ago and is considered as a living fossil (Hori et al, 1997). Extracts of leaves have been used therapeutically for centuries (Newall et al., 1996). Ginkgo biloba exhibits a variety of interesting pharmacological activities such as increase in blood fluidity, antioxidant, membrane stabilizing, improvement in cognition and pro-healing (Bairy & Rao, 2001). Its preparations promote epithelization without altering wound contraction. In case of dead space wounds Ginkgo biloba has increased granulation tissue breaking strength without altering granulation tissue mass weight. However, it did significantly enhance the content of hydroxyl-proline of granulation tissue. The main constituents of Ginkgo biloba are flavonoids and terpene trilactones and the pro-healing action of the Ginkgo biloba is due to the presence of flavonoids (Bairy & Rao, 2001).

Curcuma longa Linn.

Commonly known as turmeric and haldi in Hindi. C. longa has been reported to possess anti-bacterial, anti-fungal and anti-inflammatory activities (Chopra et al., 1986). The part used are rhizomes and it contains curcumin (diferuloyl methane), turmeric oil or turmerol and 1,7-bis, 6-hepta-diene-3, 5-dione. Curcumin has potent anti-inflammatory and analgesic activities (Srimal et al. 1971).

Volatile oil isolated from C. longa also exhibits antibacterial and potent anti-inflammatory activity. Curcuma longa also contains protein, fats, vitamins (A, B, C etc) all of which have an important role in wound healing and regeneration. Turmeric has been used for treating the wounds in the rats (Rao et al., 2003). The anti-inflammatory property and the presence of vitamin A & proteins in turmeric result in the early synthesis of collagen fibers by mimicking fibroblastic activity (Kumar et al, 1993). Juice of the fresh rhizome is commonly applied to recent wounds, bruises & leech bites. A paste of turmeric & leaves of Justica adhatoda with cow urine is rubbed on skin affected with prurigo & eczema. It can also be mixed with ginger oil to prevent skin eruptions.

Centella asiatica

Centella asiatica (Brahmi) also known as "gotu kola", is the main herb in Ayurveda for nervous system, it is used in the repair of nervous tissue from crushing trauma, such as spinal injury, neuromuscular disorders, and to increase general brain function and memory concentration. It is used extensively in the treatment of leprosy, a host of skin conditions including cellulites, varicose vein and wounds. The active principles of Centella asiatica are triterpenes and asiaticoside which are responsible for promotion of rapid wound healing.
(Shukla et al. 1999). Aqueous extract of Centella asiatica suspended in 5% propylene glycol promoted wound healing on topical administration in experimentally induced open wounds in rats as compared to other extracts (alcoholic, petroleum ether and chloroform). This was evidenced by the increase in collagen content and thickness of epithelium (Rao et al. 1996). However, Suguna et al. (1998) demonstrated that alcoholic extract of Centella asiatica orally or topically improved the rate of wound healing in rats. Topical administration of the aqueous extract increased cellular proliferation, promoted the collagen synthesis at the wound site as evidenced by the increase in DNA, protein, collagen content of granulation tissue and in tensile strength. The treated wound epithelialized faster as compared to control. Among the various formulations (ointment, cream and gel) of aqueous extract, the process of healing was better with gel formulation.

**Cedrus deodara**

Its oil has been reported to possess anti-inflammatory and anti-microbial activities. Cedrus deodara has also shown wound healing properties and is particularly useful in infective wounds (Dikshit & Dixit, 1982).

**MISCELLANEOUS PRO-HEALERS FROM PLANTS**

The healing effects of Ocimum sanctum, and Begia odorata on infected experimental wounds in laboratory animals have been reported. All these plants, notably Ocimum sanctum promote healing (Thaker & Anjaria 1986). The aqueous extract Euphorbia nerritofilia when applied topically facilitates the healing of surgically produced cutaneous wounds in guinea pigs. It increases the gain in tensile strength, DNA content and promoted epithelization (Rasik et al. 1996). Alcoholic extract of Indigofera aspalathoides has analgesic, anti-inflammatory and wound healing effect. The crude betal nut extract and its polyphenols promoted healing of incision and dead space wounds (Padmaja et al., 1996). Fresh leaves of Kalanchoea integra showed encouraging results in healing inflammatory conditions associated with wounds. Mango butter which is extracted from the seeds of Mangifera indica is known to have wound healing properties. It is commonly applied in ulcers, fissures of lips, hands and on chapped skin. Anecdotal evidence, some clinical observations, animal model studies and few randomized clinical trials support the efficacy of honey in treating Gram negative and Gram positive infections. These herbal preparations have been reported to have wound healing properties. Various combinations like extracts of Balsamodendron mukul (guggul), Maharasanadi kwath, Phyllanthus emblica, Tinospora cordifolia, Rubia cordifolia, Glycyrrhiza glabra and shanka bhasma which are claimed to have wound healing action. Poly-herbal preparations containing these herbs have been claimed to be useful in treating Gram negative and Gram positive infections. These herbal preparations have been reported to promote gain in tensile strength in incision wound model, but do not modify the granulation phase of healing (Udupa et al. 1989). These herbs have also been reported to promote epithelization and wound contraction in cases of excision wound models (Nadakarni & Nadakarni, 1954). This property may be due to the effect of these herbs on migration and mitosis of epithelial cells and promotion of contraction of myo-fibroblasts. These myo-fibroblasts are responsible for wound contraction (Gibbiani et al., 1972).

**POLY HERBAL PREPARATION**

Various combinations like extracts of Balsamodendron mukul (guggul), Maharasanadi kwath, Phyllanthus emblica, Tinospora cordifolia, Rubia cordifolia, Glycyrrhiza glabra and shanka bhasma which are claimed to have wound healing action. Poly-herbal preparations containing these herbs have been claimed to be useful in treating Gram negative and Gram positive infections. These herbal preparations have been reported to promote gain in tensile strength in incision wound model, but do not modify the granulation phase of healing (Udupa et al. 1989). These herbs have also been reported to promote epithelization and wound contraction in cases of excision wound models (Nadakarni & Nadakarni, 1954). This property may be due to the effect of these herbs on migration and mitosis of epithelial cells and promotion of contraction of myo-fibroblasts. These myo-fibroblasts are responsible for wound contraction (Gibbiani et al., 1972).

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But the benefits of medicinal plants are being rediscovered in many developed countries, where consumers are turning to such therapies in place of, and in addition to, Western medical treatments. And, all over the world, the drive to lower the cost of health care has made herbals and botanicals an attractive alternative to more expensive synthetic remedies. In 1978, the World Health Organization responded to increased interest in medicinal plants by convening a series of international consultations, seminars, and symposia to explore and promote the use of medicinal plants. Medicinal Plants Diversity and their Conservation. Conservation and sustainable use of medicinal plants are issues on which immediate focus is. Herb. Various pharmacological reports are available on plants employing different wound healing models and its underlying molecular mechanism for the validation of their traditional claims and development of safe and effective and globally accepted herbal drugs for wounds. The schematic illustration of practices in wound healing studies of plants is shown in Figure 1. Figure 1: Schematic illustration of practices in wound healing studies of plants. 5. Phytoconstituent Extraction. Medicinal Plants Diversity and their Conservation. Conservation and sustainable use of medicinal plants are issues on which immediate focus is. Herb. These natural agents induce healing and regeneration of the lost tissue by multiple mechanisms. However, there is a need for scientific validation, standardization and safety evaluation of plants of the traditional medicine before these could be recommended for healing of the wounds.