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PLANTS USED FOR WOUND HEALING IN SOUTH INDIA: A REVIEW

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ABSTRACT

Herbs have been used in both traditional and non-traditional medicine since 5000 years. Nowadays there is an increase in popularity of herbal medicines due to its minimal side effects. Most of the people in developing countries depend upon herbal remedies for the effective treatment of wounds. A wound is natural disruption of the normal anatomical structure and function of a tissue. Wound healing is a process by which skin repairs itself. It involves the following phases: inflammation, proliferation and remodelling. According to the WHO data and available sources, more than 80% world population depend upon herbal medical products. This indicates that despite the lack of clinical and scientific evidences, the herbal or traditional market is growing at rapid pace. In this literature review, we present the role of herbal medicine in wound healing and some of the common medicinal plants used in wound healing.

KEYWORDS: Herbal medicines, Wounds, Wound healing, Repairing, Medicinal plants.

INTRODUCTION

A wound can be defined as the disruption of a tissue's normal anatomical structure and function. In general, wounds cure in an orderly and timely repair process which is characterized by dynamic and interactive events described in 3 phases: inflammation, proliferation and remodelling. According to the Wound Healing Society, wounds are physical injuries that result in an opening or 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.[1]

Current estimates indicate that nearly 6 million people worldwide suffer from chronic wounds. 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 and death of the patients.

Types of wounds[2]

There are mainly two types of wounds: open wound and closed wound.

Open wound

Open wound can be classified according to the object that caused the wound:

- Incisions or incised wounds – caused by a clean, sharp-edged object such as a knife, razor, or glass splinter.
- Avulsions – injuries in which a body structure is forcibly detached from its normal point of insertion. A type of amputation where the extremity is pulled off rather than cut off.
- Puncture wounds - caused by an object puncturing the skin, such as a splinter, nail or needle.
- Gunshot wounds – caused by a bullet or similar projectile driving into or through the body. There may be two wounds, one at the site of entry and one at the site of exit, generally referred to as a "through-and-through."
- Abrasions (grazes) – superficial wounds in which the topmost layer of the skin (the epidermis) is scraped off. Abrasions are often caused by a sliding fall onto a rough surface such as asphalt, tree bark or concrete.
- Critical wounds - Including large burns that have been split. These wounds can cause serious hydroelectrolytic and metabolic alterations including fluid loss, electrolyte imbalances, and increased catabolism.
- Penetration wounds – caused by an object such as a knife entering and coming out from the skin.

Closed wound

- Hematomas (or blood tumour) – caused by damage to a blood vessel that in turn causes blood to collect under the skin.
  - Hematomas that originate from an external source of trauma are contusions, also commonly called bruises.

- Hematomas that originate from internal blood vessel pathology are petechiae, purpura, and ecchymosis. The different classifications are based on size.
- Crush injury – caused by a great or extreme amount of force applied over a long period of time.

Mechanism of wound healing[3]

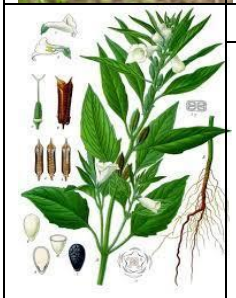
Haemostasis (blood clotting): Within the first few minutes of injury, platelets in the blood begin to stick to the injured site. They change into an amorphous shape, more suitable for clotting, and they release chemical signals to promote clotting. This results in the activation of fibrin, which forms a mesh and acts as "glue" to bind platelets to each other. This makes a clot that serves to plug the break in the blood vessel, slowing/preventing further bleeding.

Inflammation: During this phase, damaged and dead cells are cleared out, along with bacteria and other pathogens or debris. This happens through the process of phagocytosis, where white blood cells engulf debris and destroy it. Platelet-derived growth factors are released into the wound that cause the migration and division of cells during the proliferative phase.

Proliferation (growth of new tissue): In this phase, angiogenesis, collagen deposition, granulation tissue formation, epithelialization, and wound contraction occur. In angiogenesis, vascular endothelial cells form new blood vessels. In fibroplasia and granulation tissue formation, fibroblasts grow and form a new, provisional extracellular matrix (ECM) by excreting collagen and fibronectin. Concurrently, re-epithelialization of the epidermis occurs, in which epithelial cells proliferate and 'crawl' atop the wound bed, providing cover for the new tissue. In wound contraction, myofibroblasts decrease the size of the wound by gripping the wound edges and contracting using a mechanism that resembles that in smooth muscle cells.

Maturation (remodelling): During maturation and remodelling, collagen is realigned along tension lines, and cells that are no longer needed are removed by programmed cell death, or apoptosis.

MEDICINAL PLANTS USED IN SOUTH INDIA FOR WOUND HEALING

Scheme	Name	Botanical Name	Family	Parts Used
	Papaya	Carica papaya	Caricaceae	Fruits, Latex
	Description: Papaya fruits contain a mixture of cysteine endopeptidase such as Chymopapain A and B, papaya endopeptidase II, chinitase, papaya endopeptidase IV, protease inhibitors, papain, omega endopeptidase and proteins. Papaya fruits contain wound healing properties; papaya latex was applied to the burn wound using hydrogel as a vehicle system.[4]			
	Vasaka	Adhatoda vasica	Acanthaceae	Leaves, Stem, Root
	Description: It grows as a weed in almost all parts of India. The leaves and stem of the plant contain an alkaloid mimosine, mucilage and roots contain tannins. It shows anti-hyperglycemic, anti-diarrhoeal, anti-convulsant and cytotoxic activities. Studies have shown that the methanolic, chloroform and diethyl ether extract ointment of Adhatoda vasica has significant wound healing activity.[5]			
	Henna	Lawsonia inermis	Lythraceae	Leaves
	Description: It is commonly called as henna. The leaves of the plant are used in the treatment of burns, skin inflammations, wounds and ulcers. The leaves also possess antifungal and anti-bacterial activities.[6]			
	Drumstick	Moringa oleifera	Moringaceae	Fruit, Leaves
	Description: It is widely used in Indian diet. The plant possess anti-oxidant, anti-tumor, anti-protective, hypotensive, anti-inflammatory and diuretic properties. The aqueous extract shows significant increase in wound closure rate, skin breaking strength, granuloma breaking strength and decrease in scar area.[6]			
	Sesame	Sesamum indicum	Pedaliaceae	Seeds
	Description: It is mainly cultivated for its oil rich edible seeds. The seeds possess potent anti-oxidant effect due to the presence of sesamol. Sesame seeds are used traditionally in the treatment of wounds, especially burn wounds.[7]			
	Vinca	Catharanthus roseus	Apocyanaceae	Leaves, Flowers
	Description: It is native to the Caribbean Basin, Madagascar and has been found growing in tropical Africa. It has historically been used to treat a wide variety of diseases. Extracts from the dried or wet flowers and leaves of plants are applied as a paste on wounds in some rural communities. The fresh juice from the flowers made into a tea has been used by Ayurvedic physicians in India for external use to treat skin problems, dermatitis, eczema and acne.[8]			

	Gotu kola	Centella asiatica	Apiaceae	Leaves
	Description: It is effective in treatment of wounds, even in infected wounds, as well as burns and postoperative hypertrophic scars. Asiaticoside, isolated from Centella asiatica, has been studied in normal as well as delayed type wound healing in guinea pigs. Triterpene compounds such as asiatic acid, madecassic acid and madecassoside are the principal components that are responsible for wound healing.[9]			
	Betel pepper	Piper betel	Piperaceae	Leaves
	Description: It is extensively grown in India, Srilanka, Malaysia, Indonesia, Philippines and East African countries. Ointment of white soft paraffin containing 1% of dried residue of aqueous extract of Piper betel was found to possess wound healing activity.[10]			
	Chaulmoogra	Hydnocarpus wightiana	Achariaceae	Seeds
	Description: The oil from chaulmoogra seeds has been widely used in Indian and Chinese traditional medicine. The wound healing effect is reportedly related to improved collagenation and strength of scar tissue, as well as through promoted epithelisation.[11]			
	Marigold	Calendula officinalis	Asteraceae	Flower
	Description: In vitro pharmacological studies have shown anti-viral, anti-genotoxic, anti-inflammatory properties of marigold. It also possesss antimicrobial activity against Bacillus subtilus, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Candida albicans, Sarcina luteanand Candida monosa. In suspension or in tincture it is used topically for reducing inflammation, control of bleeding and to facilitate healing of poorly healing wounds.[12,13,14]			
	Neem	Azadirachta indica	Meliaceae	Leaves
	Description: Neem has been widely used in India due to many pharmacological activities, particularly for skin diseases. Liquid neem extracts possess anti-bacterial, anti-fungal, anti-viral and anti-inflammatory activities. Neem oil aids the building of collagen and maintains skin elasticity. It also keeps the wound moist during the healing process. All mentioned mechanisms contribute to acceleration of wound healing.[15,16,17]			
	Blume	Chromolaena odorata	Asteraceae	Leaves
	Description: Aqueous extracts and decoctions from Chromolaena leaves have been traditionally used in treatment of soft tissue and burn wounds. This liquid preparation enhance hemostatic activity, inhibit wound contraction, stimulate granulation tissue and re-epithelisation processes and can therefore aid wound healing, minimize post-burn scar contracture, as well as deformities.[18]			

<table>
<tr><td rowspan="2">  </td><td>Turmeric</td><td>Curcuma longa</td><td>Zingiberaceae</td><td>Rhizomes</td></tr>
<tr><td colspan="4">Description: Tumeric possess anti-bacterial, anti-fungal, analgesic and anti-inflammatory activities (curcuminoids decrease prostaglandin formation and inhibit leukotriene biosynthesis via the lipoxygenase pathway). The anti-inflammatory activity and the presence of vitamin A and proteins in turmeric result in early synthesis of collagen fibers by mimicking fibroblastic activity. Juice of the fresh rhizome is commonly applied to fresh wounds, bruises, and leech bites.[19]</td></tr>
<tr><td rowspan="2">  </td><td>Cassia</td><td>Cinnamomum cassia</td><td>Lauraceae</td><td>Bark</td></tr>
<tr><td colspan="4">Description: It is a commonly used spice and flavouring agent, and the bark of Cinnamomum cassia is also used to increase blood circulation and as an analgesic. In vitro and in vivo studies indicate that cinnamaldehyde, a bioactive component from Cinnamomum cassia, is a natural insecticide, is an antimicrobial, antidiabetic, antilipidemic, anti-inflammatory, and neuroprotective agent, and activates PI3K/AKT and MAPK signalling pathways, increasing VEGF expression, and stimulating angiogenesis in human umbilical vein endothelial cells. Cinnamaldehyde is also reported to improve wound healing in zebrafish.[20]</td></tr>
<tr><td rowspan="2">  </td><td>Aloe Vera</td><td>Aloe barbadensis</td><td>Liliaceae</td><td>Leaves</td></tr>
<tr><td colspan="4">Description: Aloe Vera has been used for medicinal purposes in several cultures for centuries, especially in Greece, Egypt, India, Japan and China. 3500 years ago Egyptians already used aloe extracts in treating burns, infections, and parasites. Aloe gel was proven to aid wound healing, in treating ulcers, and burns by forming a protective coating on the affected areas. Various constituents of Aloe Vera stimulate wound healing and have anti-inflammatory activity.[21]</td></tr>
</table>

SOME MERITS AND DEMERITS OF TRADITIONAL HERBAL DRUG DELIVERY

Advantages	Disadvantages
The cost of herbal medicine is very low compared to pharmaceutical drugs.	Herbal medicines take a longer time to work compared to pharmaceutical drugs. Thus it can't be used in chronic conditions.
They have fewer side effects, and may be safer to use overtime.	Herbal medicines are self-administered. As a result, there is no dosage or warnings specified.
They are available without a prescription and many of them can be grown at home.	Herbal medicines when consumed with pharmaceutical drugs, the two can interact with each other resulting in injuries to health.

USE OF NOVEL DRUG DELIVERY SYSTEMS TO ENHANCE THE EFFICACY OF HERBAL DRUGS

The kind of novel herbal formulations such as polymeric nanoparticles, nanocapsules, liposome, noisome, etc. has been reported using proactive and plant selections. The novel formulations are described to have remarkable advantages over conventional formulations of

plant extracts which include enhancement of solubility, bioavailability, and protection from toxicity, enhancement of pharmacological activity, and enhancement of stability, improved tissue macrophages distribution, sustained delivery, and protection from physical and chemical degradation.

Nanoparticles are efficient delivery systems for the delivery of both hydrophilic and hydrophobic drugs. Nanoparticles are the submicron-sized particles, ranging 10–1000 mm. The nanospheres have a matrix type structure in which the active ingredient is dispersed throughout, whereas the nanocapsules have a polymeric membrane and an active ingredient core. Nanonization possesses many advantages, such as increasing compound solubility, reducing medicinal doses, and improving the absorbency of herbal medicines compared with the respective crude drugs preparations.

Liposomes are micro particulate or colloidal carriers, usually 0.05–5.0 μm in diameter which forms spontaneously when certain lipids are hydrated in aqueous media. The liposomes are spherical particles that encapsulate a fraction of the solvent, in which they freely pass around or float into their interior. They can carry one, several, or multiple concentric membranes.

Niosomes are multilamellar vesicles formed from nonionic surfactants of the alkyl or dialkylpolyglycerol ether class and cholesterol. Earlier studies in association with L'Oreal have shown that, in general, niosomes have properties as potential drug carriers similar to liposomes. Liposomes face problems such as they are expensive, their ingredients such as phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special memory and handling, and purity of natural phospholipids is variable. Niosomes do not have any of these problems.[22]

CONCLUSION

The wound healing process which includes the inflammation, proliferation, and tissue remodelling phases is the result of coordinated cellular and biochemical responses. The main aim of wound healing is to decrease the risk factors that inhibit wound healing, thus enhancing the wound healing process. Several medicinal plants have been found effective in wound healing. Medicinal plants provide leads to find therapeutically active components, thus more efforts should be made towards isolation and characterization of the active principles and elucidation of the relationship between the structure and activity. The use of NDDS in herbal drug delivery can enhance the safety and efficacy of herbal drugs. The

combination of traditional and modern knowledge can produce effective drugs for wound healing with lesser side effects.

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