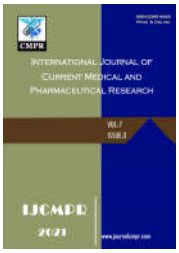
INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH
ISSN: 2395-6429, Impact Factor: 4.656
Available Online at www.journalcmpr.com
Volume 7; Issue 03(A); March 2021; Page No.5665-5671
DOI: http://dx.doi.org/10.24327/23956429.ijcmpr202103986



Case Report

EFFICACY OF PLANTS CONSTITUENTS FOR WOUND HEALING: A REVIEW

Bhanoo Pratap Singh and Ranjeet Singh

School of Pharmacy, Monad University, Hapur, U. P., India

ARTICLE INFO

Article History:
Received 13th December, 2020
Received in revised form 11th January, 2021
Accepted 8th February, 2021
Published online 28th March, 2021

Key words:
Wound healing, Indian medicinal plants

ABSTRACT

Wound healing can be defined as a complex dynamic process results in the restoration of anatomic continuity and function. Wound healing process is known as interdependent cellular and biochemical stages which are in trying to improve the wound. India has a rich tradition of plant-based knowledge on healthcare. Wound may be produced by physical, chemical, microbial, thermal insult to the tissue. The herbal extracts of plants promote blood clotting, fight infection, and accelerate the healing of wounds. The different mechanisms have been reported to improve the wound healing by medicinal plants. Indian medicinal plants is very limited and a large number of plants used in tribal and folklore with enormous potential have not been validated for their wound healing activity Ayurvedic medicinal plants, namely, *Ficus racemosa*, *Glycyrrhiza glabra*, *Curcuma longa*, *Lantana camara Linn*, *Euphorbia nerifolia*, *Ampelopsis japonica, Cinnamomum zeylanicum Nees, Ocimum sanctum Linn*, *Allium cepa Linn* and *Aloe vera*, were found to be effective in experimental models.

INTRODUCTION

A wound may be defined as a break in the epithelial integrity of skin or loss of cellular anatomic or functional continuity of living tissue. Wounds are a major case of physical disabilities [1]. When skin is torn, cut, or punctured it is term as an open wound & when blunt force trauma causes a contusion, it is called closed wound, whereas the burn wounds are caused by fire, radiation, chemicals, heat, sunlight or electricity. Normal wound healing begins immediately after the tissue injured. In undamaged skin, the epidermis (surface layer) and dermis (deeper layer) form a protective barrier against the external environment. When the barrier is broken, a regulated sequence of biochemical events is set into motion to repair the damage. The wound healing involves different phases including hemostasis, inflammation, fibrogenesis, granulation, wound constraction, neo-vascularization and epithelisation [2]. The various natural & synthetic drugs are available for the treatments of wounds and are commonly known as wound healing agents.

Classification of Wound

Wounds are classified on the basis of wound creation are open and closed wound and on the basis of physiology of wound healing are acute and chronic [3, 15].

Open wound

An open wound is a break in the skin or in a mucous membrane that bleeds severely but is relatively free from the danger of infection to those that bleed little but have a greater potential for becoming infected [4]. It is further classified as:

Excision wound

It is a soft-tissue wound which includes excision of a minimum of skin, muscle which does not bleed or contract and any damaged subcutaneous fat, i.e. removal of the bacterial culture medium.

Incision wound

It is an injury with no tissue loss and minimal tissue damage caused by a sharp object like scalpel or knife; laceration or tear wound is nonsurgical injury in conjunction with some type of trauma resulting in loss and damage of tissue; abrasions or superficial wounds caused by a sliding fall onto a rough surface then epidermis is scraped off that exposes nerve endings resulting in a painful injury; puncture wounds are caused by an object puncturing the skin, such as a nail or needle (Schultz, 1999).

Closed wound

A closed wound involves underlying tissues without a break in the skin or a mucous membrane which are identified by swelling and bruises. Closed wound have fewer categories-

***Contusions*:** They are caused by a blunt force trauma that damage tissue under the skin

Hematomas

They are caused by damage to a blood vessel that consequently causes blood to collect under the skin

Corresponding author:* **Bhanoo Pratap Singh
School of Pharmacy, Monad University, Hapur, U. P., India

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

Acute wound

Acute wound is a tissue injury that normally precedes through an orderly and timely reparative process those results in sustained restoration of anatomic and functional integrity [5]. These types of wounds are usually caused by cuts or surgical incisions and complete the wound healing process within the expected time frame.

Chronic wound

Chronic wounds or non healing wounds are failed to progress through the normal stages of healing and therefore enter a state of pathologic inflammation chronic wounds require a prolonged time to heal frequently. Local infection, hypoxia, trauma, foreign bodies and systemic problems such as diabetes mellitus, malnutrition, immunodeficiency or medications are the most common causes of chronic wounds [6, 7]

Mechanism of wound healing

Wound healing is a complex process in which the skin or the affected organ repairs itself after injury. In normal condition the outermost layer of the skin i.e., epidermis and the inner layer i.e., dermis exists in steady-state equilibrium and forms protective barrier against the external environment. Upon injury to the skin, a set of complex biochemical events takes place in closely organized to repair the damage. In few minutes after the injury, platelets aggregates at the injury site to form a fibrin clot. This clots acts to control the bleeding and to achieve hemostasis. These phenomena include phagocytosis, the production of enzymes and reactive oxygen species, cell proliferation, cell apoptosis and migration occurring at different times. [15]

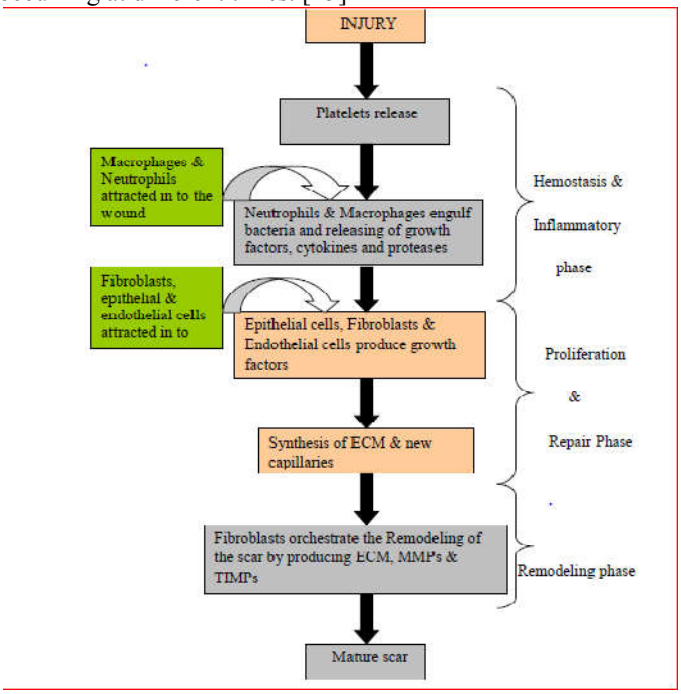


Figure 1 Mechanism of wound healing

The response to injury, either surgically or traumatically induced, is immediate and the damaged tissue or wound then passes through three phases in order to affect a final repair:

- The inflammatory phase
- The fibroblastic phase
- Epithelization phase
- Proliferative phase
- Contraction phase
- The remodelling phase

The inflammatory phase prepares the area for healing and immobilizes the wound by causing it to swell and become painful, so that movement becomes restricted. The fibroplastic phase rebuilds the structure, and then the remodelling phase provides the final form.

Inflammatory phase

The inflammatory phase starts immediately after the injury that usually last between 24 and 48 hrs and may persist for up to 2 weeks in some cases .The inflammatory phase launches the haemostatic mechanisms to immediately stop blood loss from the wound site. Clinically recognizable cardinal sign of inflammation, rubor, calor, tumor, dolor and function-laesa 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. [8, 10]

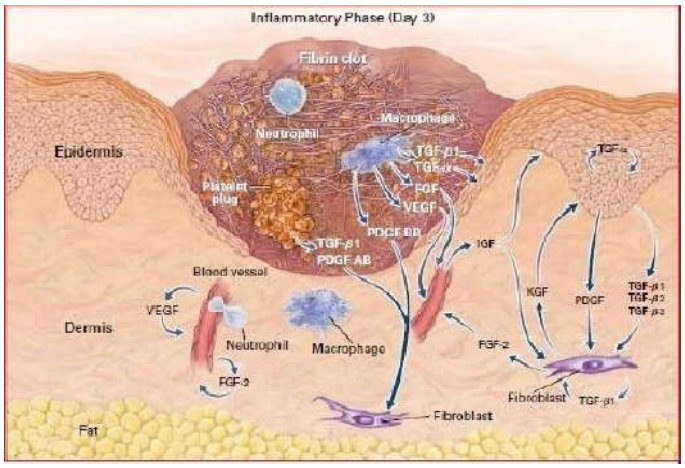


Figure 2

Fibroblastic phase

The second phase of wound healing is the fibroblastic phase that lasts upto 2 days to 3 weeks after the inflammatory phase. This phase comprises of three steps viz. granulation, contraction and epithelialization in the granulation step fibroblasts form a bed of collagen and new capillaries are produced. Fibroblast produces a variety of substances essential for wound repair including glycosaminoglycans and collagen. [8] Under the step of contraction wound edges pull together to reduces the defects in the third step epithelial tissues are formed over the wound site.

Epethelialization phase

Epithelial cell migration is one of the vital processes of wound healing. The stem cells of epithelium must detach from the edges of the wound and migrate into wound. Normally dermal basal cells adhere to each other and to the underline basal layer of the dermis. Following mobilization, epithelial cells begin to enlarge and migrate down and across the wound. [11]

Proliferation Phase

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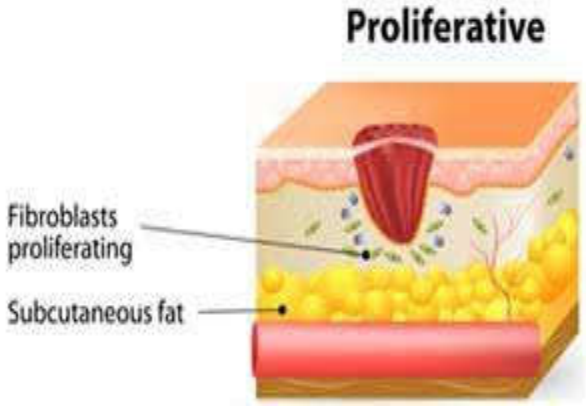

Figure 3

Contraction phase

Wound contraction is caused by the action of differentiated fibroblasts (myofibroblasts) in the granulation tissue, which contain filaments of smooth muscle action. Contraction of these fibroblasts makes the wound margins move toward the center of the wound. Wound contraction started sooner in ponies than in horses and it was significantly more pronounced in ponies. Additionally, it was significantly more pronounced in body wounds compared with the limb wounds. The wound healing was significantly faster in ponies than in horses, and significantly faster in body wounds than in metatarsal wounds. Histology showed that myofibroblasts were more organized in the wounds of the ponies: the myofibroblasts in the newly formed granulation tissue were transformed into a regularly organized pattern within 2 weeks, in which the cell were orientated perpendicular to the vessels and parallel to the wound surface.[12]

Remodelling phase

This phase last for 3 weeks to 2 years. New collagen is formed in this phase. 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. The wound healing activities of plants have since been explored in folklore. Many Ayurvedic herbal plants have a very important role in the process of wound healing. Plants are more potent healers because they promote the has been carried out in the area of wound healing management through medicinal plants. Herbal medicines in wound management involve disinfection, debridement and providing a moist environment to encourage the establishment of the suitable environment for natural healing process. [9, 14]

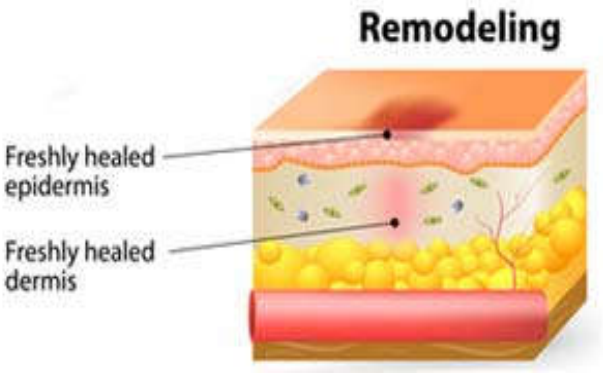

Figure 4

Medicinal plants having wound healing activity

Aloe vera (Liliaceae): *Aloe vera* is indigenous medicinal plant found throughout India. *Aloe vera* is a native plant in Africa. There are over 100 active constituent are found in Aloe vera plant which possesses astringent, haemostatic, antidiabetic, antiulcer, purgative, antiseptic, antibacterial, anti-inflammatory, antioxidant, anticancer, antidiarrhoeal, and wound healing properties [18]. The active constituent of aloe is a mixture of glycoside, termed aloin. *Aloe vera*, or one or more of its constituents promote wound healing in various animal models. Gels have been traditionally found which contain 96% of water and essential oil, amino acids, minerals, vitamins, enzymes and glycoproteins. It contains many natural bioactive compounds, including pyrocatechol, saponins, acemannan, anthraquinones, glycosides, oleic acid, and phytol, as well as simple and complex water-soluble polysaccharides [26]. *Aloe vera* gel is used for various cosmetics and medical applications [19, 20]. The mucilage is cooling and is used as a poultice for application on inflamed parts. [23]

Ocimum sanctum Linn. **(Labiaceae):** *Ocimum sanctum Linn.* commonly known as „Tulsi‟ is widely distributed plant throughout India and different parts of the world. The *Ocimum sanctum Linn.* Which possess antifertility, anticancer, antidiabetic, antifungal, antimicrobial, hepatoprotective, cardioprotectiveanti-inflammatory, analgesic, immunostimulatory, free radical scavenging, antimicrobial, antiemetic, antispasmodic, analgesic, adaptogenic and diaphoretic activity. The leaves of *Ocimum sanctum* contain a volatile oil composed of limonene, borneol, copaene, caryophyllene, and elemol, phenolic compounds (rosmarinic acid, apigenin, cirsimaritin, and isothymusin), flavonoids (orientin and vicenin), and aromatic compounds (methyl chavicol and methyl eugenol) [29]. Eugenol the active constituent present in *Ocimum sanctum Linn*, has been found to be largely responsible reported to for pharmacological activities [30]. Wound healing was found to be faster *in Ocimum sanctum* extract treated rats as compare to control group due to elevating TNF-α production. [32]

Cinnamomum zeylanicum Nees **(Lauraceae**): Cinnamon is one of the most important spices used daily by people all over the world. Overall, approximately 250 species have been identified among the cinnamon genus, with trees being scattered all over the world. [33,34]. Cinnamon bark is used as spice, condiment and flavoring agent. *Cinnamomum zeylanicum Nees* has some properties such as antioxidant, antiulcer, antimicrobial, antidiabetic, hypoglycemic, anticancer, cardiovascular disease, hypolipidemic, neurological disorders, and anti-inflammatory activity, which

can be beneficial in types of wound such as diabetic and infected wounds. *Cinnamomum zeylanicum Nees* consists of a variety of resinous compounds, including cinnamaldehyde, cinnamate, cinnamic acid, and numerous essential oils such as trans-cinnamaldehyde, cinnamyl acetate, eugenol, L-borneol, caryophyllene oxide, b-caryophyllene, L-bornyl acetate, E-nerolidol, α-cubebene, α-terpineol, terpinolene, and α-thujene. [35, 36]

Curcuma longa Linn. **(Zingiberaceae):** *Curcuma longa Linn.* is an oldest spice and very useful herb of Ayurvedic medicine. It has been used throughout India since thousands of years. It is also known as as Indian saffron‟ and turmeric. [37] *Curcuma longa Linn.* extract contain major amounts of mineral dyes, curcumin, curcuminoids, demethoxycurcumin, bisdemethoxycurcumi,phenolic compounds and volatile oils including turmerone, atlantone and zingiberene [40]. The Medicine use curcumin to treatment of inflammation, respiratory disorders, anti-inflammatory, skin diseases, antiseptic, carminative, antimicrobial, antiviral, antitumor, and hepatoprotective and so on liver disorders, diabetes and wound healing activity. *Curcuma longa Linn.* rhizomes have better and faster wound healing effect than standard drug Povidone Iodine ointment on excision wound model .[39]

Lantana camara Linn. **(Verbenaceae*):*** *Lantana camara Linn.* is a flowering ornamental plant found throughout in India. It is also known as lantana**.** The stem, root and leaves contain many of the bioactive compounds responsible for various therapeutic applications such as cancers, chicken pox, measles, asthma, ulcers, swellings, eczema, tumors, high blood pressure, bilious fevers, catarrhal infections, tetanus, rheumatism, malaria, antiseptic, antispasmodic, carminative and diaphoretic swellings and wound healing. The constituents of essential oil of *Lantana camara Linn.* are Sabiene (19. 6-21.5%), 1, 8- Cineole (12.6- 14.8%), ß-caryophyllene (12.7-13.4%), α-humulene (5.8-6.3%), two rare sequin terpenoids humulene epoxide-III and 8-hydroxy bicyclo-germacrene 11, 1, 8-cineol (15.8%), sabinene (14.7%) and caryophylene (8.9%)**.** [42]

Allum cepa Linn. **(Liliaceae):** *Allium cepa Linn.* belongs to the family of Liliaceae. *Allum cepa Linn.* Commonly known as onion .It N-sitosterol, ferulic acid, myritic acid, prostaglandins. These constituents used as abortifacient and bulb extract was shown to have an economic effect in rats. *Allium cepa Linn* is proved that antidiabetic, Antioxidant, antihypertensive, antithrombotic, hypoglycemic & hyperlipidemic activities. Phytochemical screening of *Allium cepa Linn* revealed the presence of tannins, flavonoids, alkaloids, proteins & other important constituents. Flavonoids have been documented which is believed to be one of the most important components of wound healing. The enhanced wound healing may be due to free radical scavenging action and the antibacterial property of the Phytoconstituents present in it which either due to their individual or additive effect fastens the process of wound healing. This could be the reason for prohealing activity of Allium cepa Linn. The plant has a variety of pharmacological activities including anticancer, antidiabetic, antimicrobial, cardiovascular, antioxidant effects. The plants *Allium cepa Linn.* are proved to show the analgesic, antidiabetic, antioxidant, antidepressant, aphrodisiac, antihyperlipedemic. [44,45,46]

Ampelopsis japonica **(Vitaceae):** *Ampelopsis japonica* growing throughout eastern Asia and eastern North America, the roots of Ampelopsis japonica are used as a traditional treatment for burns and ulcers, amongst other indications [49]. *Ampelopsis japonica* pharmacological activities, including neuroprotective [50], antimicrobial, and anticancer activities. [51] *Lee et al*. demonstrated that ethanol extracts from dried roots of Ampelopsis japonica accelerated the healing of cutaneous scald injury in rats [52]. Tumour necrosis factor-alpha (TNF-α) and TGF-β1 were observed to be elevated 2 days after injury and declined as healing progressed. In contrast, interleukin-10 (IL-10) was found to be elevated after 14 days, coincident with wound closure [52]. When compared with wounds treated with Vaseline (petroleum jelly) or silver sulfadiazine, topical treatment with ethanolic Ampelopsis japonica improved re-epithelization, granulation tissue formation, vascularization, and collagen deposition [52].

Euphorbia nerifolia Linn. **(Euphorbiaceae):** There are about 45,000 medicinal plants species in India. *Euphorbia neriifolia Linn* grows widely around the dry, rocky and hilly areas of north, central and south India. It is used as laxative, carminative, improves appetite, useful in abdominal troubles, bronchitis, tumors, leucoderma, piles, inflammation, enlargement of spleen, anemia, ulcers, fever and in chronic respiratory troubles rubefacient, and expectorant as well as in treatment of whooping cough, gonorrhoea, leprosy, asthma, dyspepsia, jaundice, enlargement of the spleen, tumours, stone in the bladder, abdominal troubles and leucoderma. Leaves are brittle, heating, carminative, and good for improving the appetite and treatment of tumours, pains, inflammations, abdominal swellings and bronchial infections. Roots are used as symptomatic treatment of snake bite, scorpion sting and antispasmodic. The plant parts or whole *Euphorbia neriifolia Linn* extract and its isolates have been reported scientifically using various in-vivo and in-vitro experimental methods for anaesthetic, analgesic, anti-anxiety, anti-convulsant, anti-psychotic, anti-arthritis, anti-carcinogenic, antidiabetic, anti-diarrhoeal, anti-inflammatory, anti-thrombotic, antimicrobial, antioxidant, antiulcer, cytotoxic, death-receptor expression enhancing, dermal irritation, diuretic, haemolytic, immunomodulatory, radioprotective, scorpion venom and wound healing properties. [53]

Ficus racemosa Linn. **(Moraceae):** *Ficus racemosa Linn.* belongs to the family of Moraceae. It is a popular medicinal plant in India, which has long been used in Ayurveda. [62] The roots of this plant are useful in the treatment of dysentery. Its bark is astringent, antidiabetic, refrigerant, efficacious in threatened abortion, anti-amoebic, hypoglycaemic, antidiabetic, antioxidant, antidiarrhoeal, anti-inflammatory, antipyretic, antifungal, antibacterial, hypolipidemic, and antifilarial, and hepatoprotective and anti-diarrhoeal activities.[54] The active constituent, β-sitosterol, tetra triterpenes, glauanol acetate, racemosic acid kaempferol, stigmasterol, methyl ellagic acid isolated from the leaves and stem bark. The leaves are used as a washing agent for wounds and ulcers. The aqueous and ethanolic extract of roots of *Ficus racemosa Linn* on incision and excision wound model. Aqueous extract of root increased the percentage closure due to enhanced epithialialization and collagen synthesis. [63]

Glycyrrhiza glabra Linn **(Fabaceae):** Glycyrrhiza glabra, family Leguminosae, is a plant which grows in Egypt and other countries of the world. It is widely distributed in mountainous regions northwest of India and in the sub-Himalayan tract in India. *Glycyrrhiza glabra Linn* root

extract showed that it contains saponin triterpenes (glycyrrhizin, glycyrrhetinic acid and liquirtic acid), flavonoids (liquirtin, isoflavonoids and formononetin) and other constituents such as coumarins, sugars, amino acids, tannins, starch, choline, phytosterols . *Glycyrrhiza glabra Linn* is used as gout, asthma, sore throat, tonsillitis, flatulence, sexual debility, epilepsy, hyperdypsia, fever, coughs, skin diseases, swellings, acidity, leucorrhoea, bleeding, jaundice, hiccough, hoarseness, and vitiated conditions of vata dosha, gastralgia, cephalalgia, ophthalmopathy and pharyngodnia. [59, 60]

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How to cite this article:

Bhanoo Pratap Singh and Ranjeet Singh (2021) 'Efficacy of Plants Constituents For Wound Healing: A Review ', *International Journal of Current Medical and Pharmaceutical Research,* 07(03), pp 5665-5671.

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