INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Research Article

A RECENT UPDATE OF BOTANICALS FOR WOUND HEALING ACTIVITY

Himesh Soni[1*] and Akhlesh Kumar Singhai[2]
[1]Suresh Gyan Vihar University, Jaipur-302025, India
[2]Lakshmi Narain College of Pharmacy, Bhopal, Madhya Pradesh-462021, India

Article Received on: 02/04/12 Revised on: 10/05/12 Approved for publication: 25/05/12

*Email: himeshsoni@rediffmail.com

ABSTRACT
Healing of wounds, whether from accidental injury or surgical intervention, involves the activity of an intricate network of blood cells, tissue types, cytokines, and growth factors. This results in increased cellular activity, which causes an intensified metabolic demand for nutrients and active drug therapy. There are various Phyto-active compounds which required for wound repair may improve healing time and wound outcome**.** This article represents detail survey of the plants used for wound healing activity. A total of 46 plants belonging to 44 genera and 26 families have been documented for their therapeutic use against wounds and related injuries such as cuts, burns, bruises caused by external injury, boils, sores, abscess and wounds created during delivery. It was found that all the plant parts or extracts used in wound healing were applied locally and was found to possess good healing property. The detailed study is needed to explore the ethno-botanical uses of medicinal plants and further clinical experimentation is also needed to scientifically evaluate these widely used herbal remedies for possible bioactive effects.
Keywords: Traditional uses, Wound healing, Medicinal plants

INTRODUCTION

An herbal drug constitutes a major part in all traditional systems of medicine. There are approximately 1250 Indian medicinal plants which are used in formulating therapeutic preparations according to Ayurvedic and other traditional systems of medicine[1].Plants provide varieties of resources that contribute to the fundamental need of food, clothing and shelter. Among plants of economical importance, Medicinal and Aromatic plants have played vital role in alleviating human sufferings[2].Plants are utilized as therapeutic agents as since times immemorial in both organized (Ayurveda and Unani) and unorganized (folk, tribal, native) forms[3]. Pharmacological activity of medicinal plants is often known as a result of millennia of trial and error but they have to be carefully investigated if we wish to develop new drug that meet the criteria of modern treatment. Since time immemorial man has used various parts of plants in the treatment and prevention of many ailments[4]. Historically all medicinal preparations were derived from plants, whether in the simple form of plant parts or in the more complex form of crude extracts, mixtures, etc. Today a substantial number of drugs are developed from plants[5] which are active against a number of diseases. The majority of these involve the isolation of the active ingredient (chemical compound) found in a particular medicinal plant and its subsequent modification. In the developed countries 25 percent of the medical drugs are based on plants and their derivatives and the use of medicinal plants is well known among the indigenous people in rural areas of many developing countries. In the past our ancestors made new discoveries of the healing power of plants through trial and error. Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and thousands of years[6].Wound infection is one of the most common diseases in developing countries because of poor hygienic conditions[7]. Wounds are the physical injuries that result in an opening or breaking of the skin and appropriate method for healing of wounds is essential for the restoration of disrupted anatomical continuity and disturbed functional status of the skin[8]. In other words wound is a break in the epithelial integrity of the skin and may be accompanied by disruption of the structure and function of underlying normal tissue and may also result from a contusion, haematoma, laceration or an abrasion . Healing of wounds starts from the moment of injury and can continue for varying periods of time depending on the extent of wounding and the process can be broadly categorized into three stages; inflammatory phase, proliferate phase, and finally the remodeling phase which ultimately determines the strength and appearance of the healed tissue[9].The objective in wound management is to heal the wound in the shortest time possible, with minimal pain, discomfort, and scarring to the patient. At the site of wound closure a flexible and fine scar with high tensile strength is desired. Understanding the healing process and nutritional influences on wound outcome is critical to successful management of wound patients.

The Four Phases of Wound Healing

Tissue injury initiates a response that first clears the wound of devitalized tissue and foreign material, setting the stage for subsequent tissue healing and regeneration. The initial vascular response involves a brief and transient period of vasoconstriction and hemostasis. A 5-10 minute period of intense vasoconstriction is followed by active vasodilation accompanied by an increase in capillary permeability. Platelets aggregated within a fibrin clot secrete a variety of growth factors and cytokines that set the stage for an orderly series of events leading to tissue repair. The second phase of wound healing, the inflammatory phase, presents itself as erythema, swelling, and warmth, and is often associated with pain. The inflammatory response increases vascular permeability, resulting in migration of neutrophils and monocytes into the surrounding tissue. The neutrophils engulf debris and microorganisms, providing the first line of defense against infection. Neutrophil migration ceases after the first few days post-injury if the wound is not contaminated. If this acute inflammatory phase persists, due to wound hypoxia, infection, nutritional deficiencies, medication use, or other factors related to the patient's immune response, it can interfere with the late inflammatory phase[10]. In the late inflammatory phase, monocytes converted

in the tissue to macrophages, which digest and kill bacterial pathogens, scavenge tissue debris and destroy remaining neutrophils. Macrophages begin the transition from wound inflammation to wound repair by secreting a variety of chemotactic and growth factors that stimulate cell migration, proliferation, and formation of the tissue matrix. The subsequent proliferative phase is dominated by the formation of granulation tissue and epithelialization. Its duration is dependent on the size of the wound. Chemotactic and growth factors released from platelets and macrophages stimulate the migration and activation of wound fibroblasts that produce a variety of substances essential to wound repair, including glycosaminoglycans (mainly hyaluronic acid, chondroitin- 4-sulfate, dermatan sulfate, and heparan sulfate) and collagen[11]. These form an amorphous, gel-like connective tissue matrix necessary for cell migration. New capillary growth must accompany the advancing fibroblasts into the wound to provide metabolic needs. Collagen synthesis and cross-linkage is responsible for vascular integrity and strength of new capillary beds. Improper cross-linkage of collagen fibers has been responsible for nonspecific post-operative bleeding in patients with normal coagulation parameters[12]. Early in the proliferation phase fibroblast activity is limited to cellular replication and migration. Around the third day after wounding the growing mass of fibroblast cells begin to synthesize and secrete measurable amounts of collagen. Collagen levels rise continually for approximately three weeks. The amount of collagen secreted during this period determines the tensile strength of the wound. The final phase of wound healing is wound remodeling, including a reorganization of new collagen fibers, forming a more organized lattice structure that progressively continues to increase wound tensile strength. The remodeling process continues up to two years, achieving 40- 70 percent of the strength of undamaged tissue at four weeks.



Fig:1 Phases of Wound Healing

India is gifted with varieties of large number of medicinal herbs because of variety of climatic conditions and seasons favorable for growth of many species of plants. Amongst the large number of herbal drugs existing in India, very few have been studied systematically so far. Many herbs have proved to possess significant prohealing properties in different types of wounds.

Role of Phytopharmaceuticals in Wound Healing

Tannins

Results revealed that tannins are one of the important phytoconstituents responsible for wound healing mainly due to their astringent and antimicrobial property[13].

Flavonoids

Flavonoids show wound healing properties due to their antibacterial and antioxidant properties. Flavones, flavonoids and flavonols are phenolic structure with one carbonyl group. They are synthesized by plants in response to microbial infection and are often found effective in vitro as antimicrobial substance against a wide array of microorganisms[14]. Tannins are polymeric phenolic substances possessing the astringent property. These compounds are soluble in water, alcohol and acetone and give precipitate with proteins. Coumarins are phenolic substances made of fused benzene and pyrone rings[15].They have a characteristic odor and several of them have antimicrobial properties.

Tragacanth Mucilage

With respect to the wound healing mechanism of tragacanth mucilage, the exact mechanism could be proposed. However, the significant differences observed with the tragacanth mucilage-treated groups suggest that it could be effective on the proliferation and remodeling phases of wound healing. It is probably capable of stimulating the myofibroblasts contraction, for a faster closure of the wound. Active ingredients of tragacanth mucilage, such as bassorin and tragacanthin, may contribute to the healing effects of tragacanth mucilage[16]. Hydrolysis of tragacanthin into arabinose and glucoronic acid may cause coagulation of surface proteins, and prevent wound infection that causes a faster wound healing.

In this review we have made an attempt to give an insight into the different herbs having potential wound healing properties which could be beneficial in therapeutic practice. This includes study of following drugs:-

***Punica granatum* Peel**

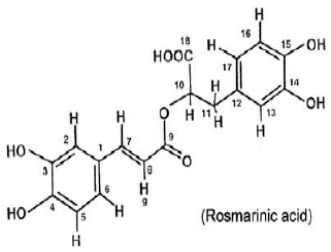
Family: Punicaceae

The study revealed that methanolic extract of dried pomegranate (*Punica granatum*) peels showed complete healing of the on 16-18 days.The presence of a high content of phenolic compounds (44.0%) along with other constituents. High-performance liquid chromatography analysis of the extract showed the presence of gallic acid and catechin as major components which promotes healing process[17].

***Echium amoenum fisch* and C.A. Mey Flower**

Family: - Annonaceae

Alkannins and Shikonins (A/S) are chiral-pairs of naturally occurring isohexenylnaphthazarins. They are found in the external layer of the roots of Echium. Alkannins and Shikonins (A/S) exhibited wound-healing, anti-inflammatory, antimicrobial, antioxidant, antithrombotic and antitumor properties[18]. It also contains rosmarinic acid (flavonoids) which showed antioxidant and wound healing potential.



***Eucalyptus globules*: -** It is popular as "Karpura maram".

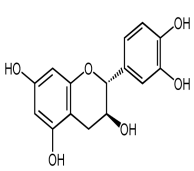
Family: - Myrtaceae.

The intra dermal administration of essential oil of E.globules increased the capillary permeability and promotes wound healing [19].

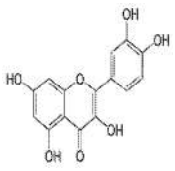
Acacia catechu: - It is popular as 'Khadira' (black catechu).

Family: - Leguminosae.

Its chemical constituents are catechin, tannic acid, quercetin, red tannin. It's a powerful astringent [20].


Catechin


tannic acid


Quercetin

The hydro alcoholic extract of *Acacia catechu* (400 mg/kg/day) was evaluated for its wound healing activity in albino rats using excision and incision wound models. The extract treated wounds are found faster epithelization [21].

***Argemone mexicana* L. (Papaveraceae)**

Local name- *Pivala dhotara*

The petroleum ether, chloroform, methanol and aqueous extracts of the leaves of *Argemone mexicana* Linn. (Family: Papaveraceae) were evaluated for their wound healing activity in rats using excision (normal and infected), incision and dead space wound models respectively. The wound healing effects of the chloroform, methanol and aqueous extracts may be attributed to the presence of phytoconstituents like alkaloids, triterpenoid, tannins and flavonoids in the extracts which are known to promote the wound healing process mainly due to their antimicrobial property. Flavonoids and triterpenoid are also known to promote the wound healing process mainly due to their astringent and antimicrobial property, which seems to be responsible for wound contraction and increased rate of epithelialisation [22].

***Brassica juncea* L. (Brassicaceae)**

Local name- *Mohari*

Crushed fruit mix in the water and then paste was applied on the wound. The screening of the wound healing activity of different leaf extracts of *Brassica juncea* Linn in excision wound model in albino rats were studied. Among different extracts, the aqueous extracts showed 94.94% maximum percentage of healing compared to control. All the extracts are found to be extremely statistical significant and comparable with control. The flavonoids counteract further decomposition of connective tissue (by collagenases and elastase) and also inhibit PG COX which produces eicosanoids that via a plasma membrane receptor and a signal chain induce the expression of protease genes [23].

***Thespesia populnea* Soland (Malvaceae)**

Local name- *Ghulbhendi*

The aqueous extract of T. populnea fruit showed significant wound healing activity in the excision wound and incision wound models in rats following topical and oral administration, respectively [24]. *Thespesia populnea* are widely used in traditional medicine to combat and cure various ailments thus appear to be rich in secondary metabolites. The anti-inflammatory, astringent, asthma and diarrhoea activities of these two plants can be attributed to their high flavonoids, steroids, alkaloids, tannins, terpenoids and saponins [25].

***Commiphora mukul* Engl. (Burseraceae)**

Local name- *Gugal*

It is an astringent of the mucous membranes and the mouth. *Commiphora mukul* is used as an effective antimicrobial agent, as a herbal remedy for sore throats, canker sores and gingivitis [26]. Exudate from the bark promotes wound healing activity.

***Terminalia chebula* Retzr (Combretaceae)**

Local name- *Harda*

The alcoholic extract of leaves from T. chebula was topically administered on dermal wounds of rats. The treated wounds healed much faster, indicated by improved rates of contraction and a decreased period of epithelization. The granulation tissue increased in total protein DNA and collagen content. The levels of hexosamine and uronic acid in these tissues also increased up to day 8 post-wounding. In addition, the extract was active against *Staphylococcus aureus and Klebsiella*. These results document the beneficial effects of T. chebula extract for the healing process [27].

***Aloe vera* L. (Liliaceae)**

Local name- *Korphad*

Clinical investigations suggest that Aloe Vera Gel preparations accelerate wound healing. In vivo studies have demonstrated that Aloe Vera Gel promotes wound healing by directly stimulating the activity of macrophages and fibroblasts. Fibroblast activation by *Aloe vera* Gel has been reported to increase both collagen and proteoglycan synthesis, thereby promoting tissue repair. Some of the active principles appear to be polysaccharides composed of several mosaccharides, predominantly mannose. It has been suggested that mannose 6-phosphate, the principal sugar component of *Aloe vera* Gel, may be partly responsible for the wound factor receptors on the surface of the fibroblasts and thereby enhance their activity. Furthermore, acemannan, a complex carbohydrate isolated from Aloe leaves, has been shown to accelerate wound healing [28].

***Calotropis procera* Br (Asclepidaceae)**

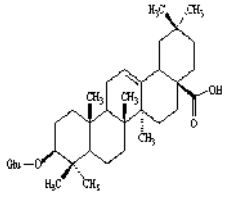
Local name- *Rui*

Calotropis procera (Asclepiadaceae) is a well known plant in the Ayurvedic system of medicine. The latex significantly augmented the healing process by markedly increasing collagen, DNA and protein synthesis and epithelization leading to reduction in wound area [29].

***Calendula officinalis* L. (Asteraceae)**

Local name- *Zendu*

Calendula oil is great to help with sore, inflamed and itchy skin conditions, for burns, eczema and nappy rash, as well as sore cracked nipples. It is also used to treat thread and spider veins as well as varicose veins. The properties of calendula are anti-inflammatory, styptic, antiseptic, anti-hemorrhagic. It is used in the treatment of ulcers and inflamed cutaneous lesions as well as slow-healing wounds and bruising. The main constituents are volatile oil, saponins, flavonoids, clendulin, sterols, fatty acids, calendic acid, oleanic acid, triterpenoids, tocopherols and flavonol glycosides. Apart from the anti-inflammatory effect that it has, it is also most effective in healing sores and wounds and in fighting fungal infections - such as Athletes foot [30].


Clendulin

***Tridax procumbens* L. (Asteraceae)**

Local name- *Dagadipala*

The Aqueous extract of whole plant of *Tridax procumbens* Linn. has ability to set the normal and immune-compromised

wound healing in rats. The plant not only increase lysyl oxidase but also, protein and nucleic acid content in the granulation tissue, probably due to increase of glycosamino glycan content[31].

***Nerium indicum* Mill (Apocyanaceae)**

Local name- *Kaneri*

The juice of the leaves is traditionally in use for application on the wound [32].

***Butea monosperma*, Fabaceae**

Alcoholic bark extract is reported to exhibit wound healing activity due to its anti oxidant effect[33]. The topical administration of an alcoholic bark extract of *Butea monosperma* on cutaneous wound healing in rats. Full-thickness excision wounds were made on the back of rat .The granulation tissue formed on days 4, 8, 12 and 16 (post-wound) was used to estimate total collagen, hexosamine, protein, DNA and uronic acid. The extract increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in DNA, total protein and total collagen content of granulation tissues. The extract treated wounds heal much faster than normal animals as indicated by improved rates of epithelialisation and wound contraction, tensile strength and histopathological examinations [34].

***Cocos nucifera* (Coconut)**

Coconut oil is useful in treatment of wounds because of its biochemical structure: unlike olive oil and animal fatty tissue, it consists of short-chained and saturated fatty acids. These qualities in coconut oil prevent it from becoming oxidized and rancid, thus making it suitable for the preservation of medicinal plants and for wound treatment [35]. Various vitamins are also found in the coconut water. They are vitamins B1, B2, B3, B5, B6, B7 and B9. Apart from that it also contains Ascorbic acid (vit.C), which promotes wound healing activity.

***Annona squamosa* (**Annonaceae**)**

Vernacular Name**:** English : custard apple, *sugar-apple, sweetsop*

Hindi : shareefa [36].

The leaves of the A.squamosa contain tannins and Vitamin C which promotes wound healing, anti-inflammatory and insecticidal activity. It enhanced the level of hydroxyproline, hexoamine and elastin in wound, which enhanced the wound healing activity [37].

***Lawsonia inermis* Linn.**

Genus Lawsonia bears one species, L. inermis (Henna, Mhendi, Shudi, Madurang, Mendi, Manghati, Madayantika and Goranti) till date, having different synonyms as alba and spinosa belonging to family Lythraceae[38].

Chloroform and aqueous extracts of leaves of the plant were capable of inhibiting the growth of microorganisms that are involved in causing burn wound infections [39-40] . Ethanol extract of the plant (200 mg/kg/day) was used to evaluate the wound healing activity on rats using excision, incision and dead space wound models. Extract of L. inermis when compared with the control and reference standard animals: a high rate of wound contraction, a decrease in the period of epithelialization, high skin breaking strength, a significant increase in the granulation tissue weight and hydroxyproline content. Histological studies of the tissue showed increased well organized bands of collagen, more fibroblasts and few inflammatory cells when compared with the controls which showed inflammatory cells, scanty collagen fibres and fibroblasts [41].

Lantana Camare., Verbenaceae

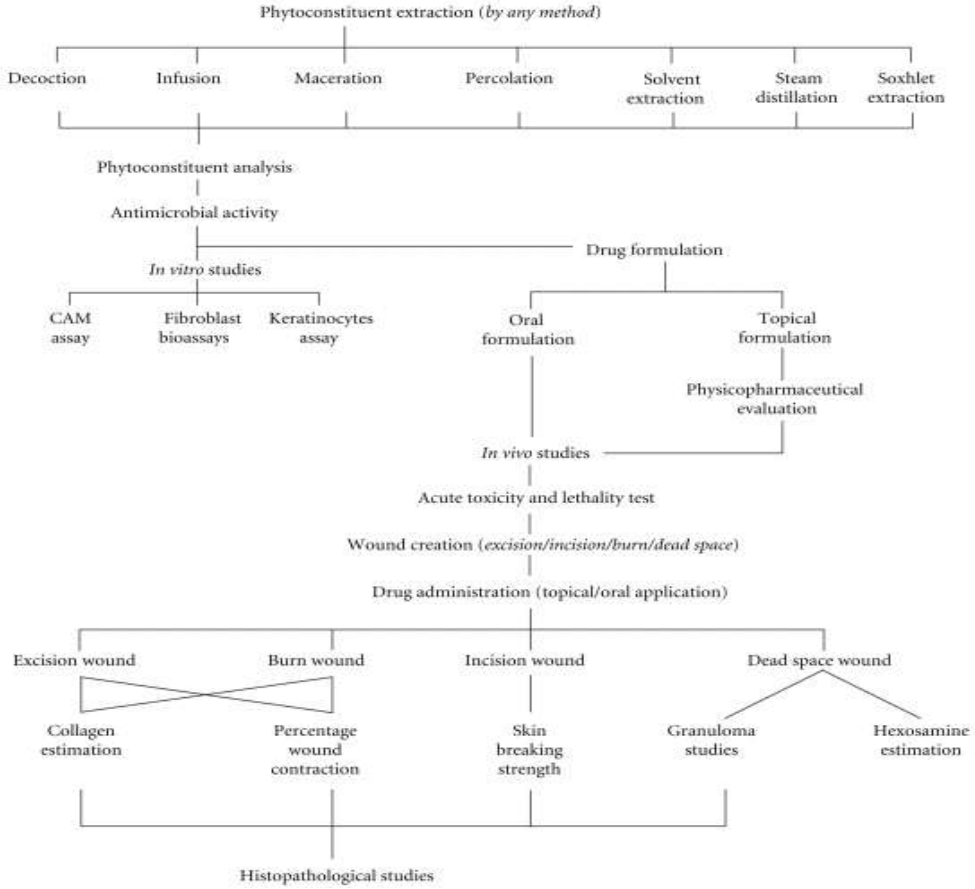
Lantana camara is used in herbal medicine for the treatment of skin itches, as an antiseptic for wounds, and externally for leprosy and scabies Ethanolic extract of the leaves showed wound healing effect[42].

***PSIDIUM GUAJAVA* LINN**.

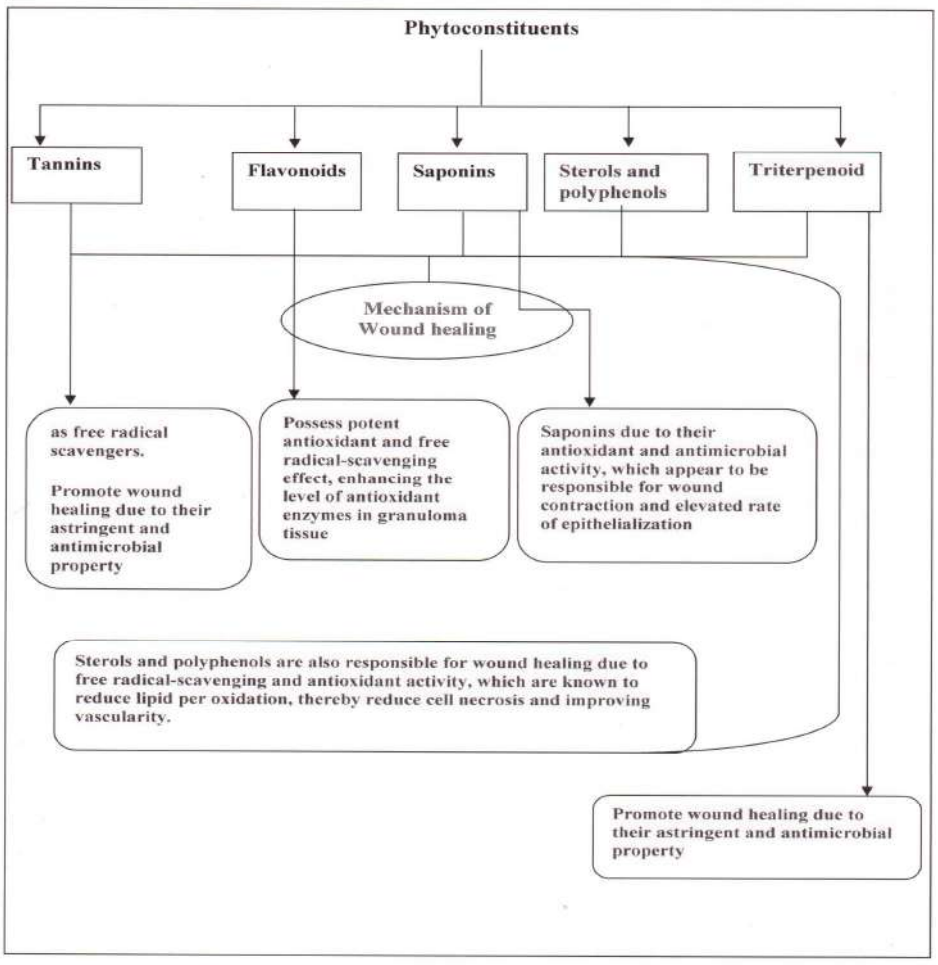
Psidium guajava, is a common plant, grown all over India for its delicious fruits “gauva’.

Its leaves & fruits have been used to enhance external wound healing in traditional medicine. Fruit extract has been reported to contain vitamin C, quercetin and Zn. Thus, the prohealing activity of *Psidium guajava* fruit extract could be attributed to its constituents like quercetin and Zn. Vit.C accelerated the healing process [43-44].

Practices in wound healing studies of plants



Mechanism of wound healing [45-46]



Several types of injuries like burn, wounds, and skin ulcers usually generate superoxides and lipid peroxidation through the activation of neutrophils. Hence, any drug that inhibits lipid peroxidation is believed to increase the viability of collagen fibrils by increasing the strength of collagen fibres, increasing the circulation, preventing the cell damage, and by promoting the DNA synthesis. Better collagenation seen under the influence of some herbal extracts may be because of improved antioxidant status. Thus, an intervention into any one of these phases by drugs could eventually lead to either promotion or depression of the collagenation phase of healing[47].

CONCLUSION

The study of ethno medical systems and herbal medicines as therapeutic agents of a paramount importance in addressing health problems of traditional communities and third world countries as well as industrialized societies[48]. In Indian traditional medicine, the species of the following genera are commonly used to treat wound and related injuries; *Abutilon, Achyranthes, Acorus, Aegle, Aerva, Aloe, Azadirachta, Bambusa, Bidens, Boerhaavia, Butea, Caesalpinia, Calotropis, Carissa, Cassia, Cucumis, Curcuma, Cynodon, Datura, Dodonaea, Eclipta, Euphorbia, Ficus, Hyptis, Lantana, Leucas, Morinda, Ocimum, Opuntia, Pavetta, Pergularia, Plumbago, Pongamia, Sida, Smilax, Terminalia, Tridax, Vitex* and *Zizyph*us[49].India revealed that wound healing natural products usually localized in root (27%) > leaves (20%) > stem > seed > whole plant > fruit > flower > rhizome > tuber > shoot > stamen > grain > gall > filament and plant product like latex (46%), oil (40%) , gum and resin (7%).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 inhibits wound healing, enhancing the healing process and lowering the incidence of wound infections. Many botanicals have been found useful in wound healing. Botanicals provides leads to find therapeutically useful compounds, thus more efforts should be made towards isolation and characterization of active compounds and their structure elucidation. The combination of traditional and modern knowledge can produce better drugs for proper wound care with fewer adverse effects.

REFERENCES

1. Mukherjee PK. Quality Control of Herbal Drugs: An approach to evaluation of botanicals. 1st ed. New Delhi: Business Horizons; 2002 :114-124.
2. Baqar SR. "Textbook of Economic Botany", First edition, Rawalpindi, Published in Pakistan by Ferozsons (Pvt) Ltd., Lahore; 2001,23.
3. Girach RD, Khan H, Ahmad M. "Botanical Identification of Thuhar, seldom used as Unani medicine". Hamdard Medicus. 2003;vol XLVI, No.1: 27-23.
4. Chah KF, Eze CA, Emuelosi CE, Esimone CO.Antibacterial and wound healing properties of methanolic extracts of some Nigerian medicinal plants.J Ethnopharmacol. 2006; 104: 164 -167.
5. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environ Health Pers.2001;109:69-75.
6. Gurib-Fakim A. Review – Medicinal plants: Traditions of Yesterday and drugs of tomorrow. Mol Asp Med. 2006; 27: 1- 93.
7. Senthil Kumar M, Sripriya R, Vijaya Raghavan H, Sehgal P. Wound Healing Potential of *Cassia fistula* on Infected Albino Rat Model. J Surg Res. 2006; 131: 283–289.
8. Meenakshi S, Raghavan G, Nath V, Ajay Kumar SR, Shanta M. Antimicrobial, wound healing and antioxidant activity of *Plagiochasma appendiculatum* Lehm. et Lind. J Ethnopharmacol. 2006; 107: 67–72.
9. Sumitra M, Manikandana P, Suguna L. Efficacy of *Butea monosperma* on dermal wound healing in rats. Int J Biochem Cell Biol. 2005; 37: 566–573.
10. Stadelmann WK, Digenis AG, Tobin GR. Impediments to wound healing.Am J Surg. 1998;176:39S-47S.
11. Stadelmann WK, Digenis AG, Tobin GR. Physiology and healing dynamics of chronic cutaneous wounds. Am J Surg .1998;176:26S-38S.
12. Blee TH, Cogbill TH, Lambert PJ. Hemorrhage associated with vitamin C deficiency in surgical patients. Surgery .2002;131:408-412.
13. Ya C, Gaffney SH, Lilley TH, Haslam EIn RW and Karchesy JJ. Chemistry and significance of condensed Tannins. Plenum: New York;1988,553.
14. Andrew Chevallier Fnimh. "Encyclopedia of Medicinal Plants", IInd edition, published by Dorling Kindersely in Great Britain;1996,14-15.
15. Mcgregor SE. Insect Pollination Of Cultivated Crop Plants .Usda, 1976.
16. Moghbel A, Hemmati A, Agheli H, Rashidi H, Amraee K. The effect of the Tragacanth mucilage on the healing of the full-thickness wound in the rabbit. Arch Iranian Med. 2005;8(4):257-262.
17. Murthy KN, Reddy VK, Veigas JM, Murthy UD. Study on wound healing activity of *Punica granatum* peel. J Med Food. 2004;7(2):256-9.
18. Papageorgiou VP, Assimopoulou AN, Ballis AC. Alkannins and shikonins: a new class of wound healing agents. Current medicinal chemistry. 2008; Vol:15.Issue:30.
19. Sarkar SN. Capillary permeability-increasing effect of Eucalyptus hybrid leaf and a Seseli indicum seed oils in rabbit. Indian Journal of Pharmacology. 1994 ;26(1)-55-56.
20. Naik GH, Satav JG."Comparative antioxidant activity of individual herbal components used in Ayurvedic medicine". Phytochemistry.2003; 63:97-104.
21. Karwani G, Singhvi IJ, Gupta SK and Agarwal A. Wound Healing Activity of Hydroalcoholic Extract of Acacia catechu. RJPT. 2011;4(6):905-906.
22. GK Dash and PN Murthy. Evaluation of *Argemone mexicana* Linn. Leaves for wound healing activity. J Nat Prod Plant Resour.2011;1(1): 46-56.
23. Malan R, Walia A, Saini V, Gupta S. Comparison of different extracts leaf of Brassica juncea Linn on wound healing activity. European Journal of Experimental Biology. 2011;1(2):33-40.
24. Nagappa AN, Cheriyan B. Wound healing activity of the aqueous extract of Thespesia populnea fruit. Fitoterapia . 2001;72(5):503-506.
25. Savithramma N, Rao ML and Bhum G. Phytochemical screening of Thespesia populnea (L.) Soland and Tridax procumbens L. J Chem Pharm Res. 2011;3(5):28-34.
26. Herodotus. The history of Herodotus (440 B.C.). The Internet Classics Archive; 1994-2000.
27. Suguna L, Singh S, Sivakumar P et al. Influence of Terminalia chebula on dermal wound healing in rats. Phytother Res.2008;16(3): 227-31.
28. Grindlay D, Reynolds T. The Aloe Vera phenomenon: a review of the properties and modernuses of the leaf parenchyma gel. Journal of ethnopharmacology.1986;16:17-15.
29. Rasik AM, Raghubir R, Gupta A, Shukla A, Dubey MP, Srivastava S, Jain HK, Kulshrestha DK. Healing potential of Calotropis procera on dermal wounds in Guinea pigs. Journal of ethnopharmacology .1999; 68(1-3):261-6.
30. Rao S, Udupa A, Udupa S, Rao P, Rao G, Kulkarni D. Calendula and hypericum: two homeopathic drugs promoting wound healing in rats. Fitoterapia .1991; 62:508.
31. Nazeruddin GM, Shirish S, Pingale S and Shaik S. Pharmacological review of Tridax procumbens L. Der Pharmacia Sinica.2011; 2 (4): 172-175.
32. Sandeep B Patil, *etal*. Traditional uses of plants for wound healing in the Sangli district, Maharashtra. International Journal of Pharm Tech Research. 2009;Vol.1, No.3:876-878,
33. Patil DN, Kulkarni AR, Shahapurkar AA and Hatappakki BC. Natural Cumin Seeds for Wound Healing Activity in Albino Rats. International Journal of Biological Chemistry. 2009; 3 (4): 148 – 152.
34. Sumitra M, Manikandan P and Suguna L . Efficacy of Butea monosperma on dermal wound healing in rats. The International Journal of Biochemistry & Cell Biology. 2005; 37: 66–573.
35. Nevin KG, Rajamohan T. Effect of topical application of virgin coconut oil on skin components and antioxidant status during dermal wound healing in young rats. Skin Pharmacol Physiol. 2010; 23(6):290-7.2010.
36. Soni H, Sharma S, Mishra K, Singhai AK. Qualitative and Quantitative profile of flavonoids isolated from leaves of *Annona squamosa*. IJRP.2011;2(5):24-26.
37. YL Yang, FR Chang, CC Wu, WY Wang, YC Wu. New ent-kaurane diterpenoids with anti-platelet aggregation activity from Annona squamosa. Journal of Natural Products.2002;65(10): 1462-1467.
38. Sastri BN. The Wealth of India: Raw Materials. Edn 6, Vol. (L-M), CSIR, New Delhi;1962:47-50.
39. Muhammad HS, Muhammad S. The use of Lawsonia inermis Linn. (henna) in the management of burn wound infections. African Journal of Biotechnology.2005; 4: 934-937.
40. Hamdi YP, Benazzouz M, Belkhiri H, Chari Z, Serakta M, Bensgni L. Healing effect of Lawsonia inermis L. (henna) as exemplified by the third degree burns. Revue de Medicines et Pharmacopeias Africans. 1997; 11-12:151-156.

41. Nayak BS, Isitor G, Davis EM, Pillai GK. The evidence based wound healing activity of Lawsonia inermis Linn. Phytotherapy Research. 2007; 21(9):827-831.
42. Nayak BS, Raju SS, Ramsubhag A. Investigation of wound healing activity of Lantana camara L. in Sprague dawley rats using a burn wound model. International Journal of Applied Research in Natural Products.2008;1(1):15-19.
43. Mudliar VS, Patil PA, Torgal SS, Malur PR, Mittal. Influence of the fruit and leaf extract of Psidium guajava Linn. on wound healing in wistar rats. Journal of Cell and Tissue Research. 2008; Vol. 8(1) :1313-1316 .
44. Nadkarni, 1976 & Warrier et al., 1994; Nadkarni, 1976; Rastogi and Mehrotra, 1974-1994, Vol I-V &Yohanarasimhan, 2000; Wound healing compounds.
45. Baravkar AA, Kale RN, Patil RN, Sawant SD. Pharmaceutical and biological evaluation of formulated cream of methanolic extract of *Acacia nilotica* leaves. Research Journal of Pharmacy and Technology. 2008; 1(4):481–483.
46. Shenoy C, Patil MB, Kumar R, Patil S. Preliminary phytochemical investigation and wound healing activity of *Allium cepa* Linn (Liliaceae) .International Journal of Pharmacy and Pharmaceutical Sciences. 2009; 2(2):167–175.
47. Umadevi S, Mohanta GP, Kalaichelvan VK, Manavalan R. Studies on wound healing effect of *Flaveria trinervia* leaf in mice. Indian Journal of Pharmaceutical Sciences. 2006; 68(1):106–108.
48. Hutt MJ, Houghton PJ. A survey from the literature of plants used to treat scorpion stings. J Ethnopharmacol. 1998;60: 97 – 110.
49. Jain SK. Dictionary of Indian Folk Medicine and Ethnobotany. Deep publications, Paschim Vihar, New Delhi; 1991.