

## Potential Wound Healing Agents from Medicinal Plants: A Review

Yogesh Sharma, G. Jeyabalan and Ramandeep Singh

Department of Pharmacy, Sunrise University, Alwar, Rajasthan, India

### ABSTRACT

Wound is defined as the disruption of the cellular and anatomic continuity of a tissue. Wound may be produced by physical, chemical, thermal, microbial or immunological insult to the tissues. The process of wound healing consists of integrated cellular and biochemical events leading to re-establishment of structural and functional integrity with regain of strength in injured tissues. Naturally, the investigative curiosity to promote healing continues since ages. A lot of research has been envisaged to develop better healing agents and it has been a challenging task to generate them and keep pace with the problems encountered. Several drugs of plant, mineral and animal origin are described in the ayurveda for their wound healing properties. In the present review, attempts are made to understand various aspects of wounds and discuss about wound healing potential of plants, its botanical name, common name, family, part used, extract used, dose, study duration and references, which are helpful for researcher to development new wound healing formulations for human use.

**Key words:** Wound healing, wounds, burns, plant extract, ayurvedic medicinal plants, wound pharmacology

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### INTRODUCTION

Wounds generally termed as physical injuries that result in an opening or breaking of the skin. There are different types of wounds which range from mild to potentially fatal. Wound healing is impaired in diabetic patients with infection or hyperglycemia. Diabetes mellitus is one of the major contributors to chronic wound healing problems. The diabetic patients with ulcer become at high risk for major complications which include infection and amputation. In traditional medicine plants are generally used for treatment of various acute and chronic diseases and abnormalities in the body. Due to the present fast life of the humans a drastic increase in chronic disease conditions mainly diabetes has been determined. Most of these patients tend to face a tremendous problem when they get an infected wound<sup>1</sup>. Wound healing is a complex series of interrelated events that are mediated through the phases by a wide range of chemically co-ordinate cellular processes as well as hormonal influences. Medicinal plants have been shown to possess wound healing activity in animal studies<sup>2</sup>.

### CLASSIFICATION OF WOUNDS

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

### OPEN WOUND

Though an open wound blood escapes the body and bleeding is clearly visible. Open wound is further classified in various types according to the object that occur the wound<sup>3</sup>.

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

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

**Laceration wound or tears wounds:** This is the nonsurgical injury in conjunction with some type of trauma, resulting in tissue injury and damage.

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

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

**Corresponding Author:** Yogesh Sharma, Department of Pharmacy, Sunrise University, Alwar, Rajasthan, India Tel: +91-9805708728

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

### CLOSED WOUND

In closed wounds blood escapes the circulating system but remain in the body. It includes Contusion or bruises, hematomas or blood tumor, Crush injury etc.<sup>3</sup>.

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

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

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

**Acute wounds:** Acute wound is a tissue injury that normally proceeds through an orderly and timely reparative process that result in sustained restoration of anatomic and functional integrity. Acute wounds are usually caused by cuts or surgical incisions and complete the wound healing process within the expected time frame<sup>4</sup>.

**Chronic wounds:** Chronic wounds are wounds that have failed to progress through the normal stages of healing and therefore enter a state of pathologic inflammation chronic wounds either require a prolonged time to heal or recur frequently. Local infection, hypoxia, trauma, foreign bodies and systemic problems such as diabetes mellitus, malnutrition, immunodeficiency or medications are the most frequent causes of chronic wounds<sup>5,6</sup>.

### FACTORS AFFECTING WOUND HEALING:

- Improper diet
- Infection at the wound site
- Insufficient oxygen supply and tissue perfusion to the wound area
- Drugs
- Elderly age
- Diabetes and other diseases conditions

Wound healing is normal biological process in the human body. Many factors can adversely affect this process and lead to improper and impaired wound healing. A thought understanding of these factors and their influence on wound healing is essential for better therapeutic option for wound treatment<sup>7</sup>.

**Improper diet:** Wound healing is anabolic process that requires both energy and nutritive substrates. It is reported that serum albumin level of 3.5 gm dL<sup>-1</sup> or more is necessary for proper wound healing<sup>8</sup>. Protein is essential for collagen synthesis on wound site. A state malnutrition may provide an inadequate amount of protein and this can decreased the rate of collagen synthesis wound tensile strength or increased chance of infection<sup>9,10</sup>.

**Infection at the wound site:** Wound infection is probably the most common reason of impaired wound healing<sup>11</sup>. *Streptococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli* and *Pseudomonas aeruginosa*<sup>12</sup>.

**Insufficient oxygen supply and tissue perfusion to the wound area:** Adequate blood supply and tissue perfusion is extremely important for wound healing. Excessive pain, cold and anxiety can cause local vasoconstriction and increased healing time<sup>13</sup>. Smoking and use of tobacco decreased tissue perfusion and oxygen tension in wound<sup>14</sup>.

**Drugs:** Many drugs are known to impair wound healing. Chemotherapeutic drugs are used in cancer are the largest group well known to delay wound repair<sup>15</sup>. Systemic glucocorticoids interfere normal healing process by reducing collagen synthesis and fibroblast proliferation.

**Elderly age:** Elderly age is found to associated with delay wound healing. It is reported that the fibroblast growth and activity diminishes and collagen production, wound contraction is slow in older individuals<sup>16</sup>.

**Diabetes and other diseases conditions:** Diabetic patients are more susceptible to wound healing. In study wound infection rate was found 11% higher in diabetic patients than in general patient's population<sup>17</sup>. Acute and chronic liver diseases also associated with delay wound healing. Patients with altered immune faction have an increased susceptibility to wound infection.

### PHASES OF WOUND HEALING

**Inflammatory phase:** The inflammatory phase starts immediately after the injury that usually last between 24 and 48 h 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<sup>18</sup>.

**Fibroblastic phase:** The second phase of wound healing is the fibroplastic phase that lasts upto 2 days to 3 weeks after the inflammatory phase. This phase comprises of three steps viz., granulation, contraction and epithelialisation. In the granulation step fibroblasts form a bed of collagen and new capillaries are produced. Fibroblast produces a variety of substances essential for wound repair including glycosaminoglycans and collagen. Under the step of contraction wound edges pull together to reduce the defects in the third step epithelial tissues are formed over the wound site<sup>19</sup>.

**Epithelization 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. Transected hair follicles also contribute to the number of migrating epithelial cells. Epithelial cell migrating across wound usually move along the basal lamina or fibrin deposits, this phenomenon is called contact guidance and is an important factor in epithelial migration. Epithelial migration is followed by increased mitosis of epithelium. Recent evidence suggests that a water soluble heatlabile substance called chalone which is secreted at the wound site is responsible for regulation for mytosis<sup>20</sup>.

**Proliferative phase:** Proliferative Phase (2 days to 3 weeks) includes: Granulation stage: Fibroblasts lay bed of collagen Fills defect and produces new capillaries Contraction stage: Wound edges pull together to reduce defect. Epithelialization stage: Crosses moist surface cell travel about 3 cm from point of origin in all directions<sup>21</sup>.

**Contraction phase:** Wound contraction is caused by the action of differentiated fibroblasts (myofibroblasts) in the granulation tissue, which contain filaments of smooth muscle actin. Contraction of these fibroblasts makes the wound margins move toward the center of the wound<sup>22,23</sup>. 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. As a result, second intention wound healing was significantly faster in ponies than in horses and significantly faster in body wounds than in metatarsal wounds<sup>24</sup>. Histology showed that myofi-broblasts 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 cells were orientated perpendicular to the vessels and parallel to the wound surface. This appears to be a more favorable condition for wound contraction to occur. In the horses, myofibroblast organization took much longer. No differences were found in the number of fibroblasts, the amounts of smooth muscle actin and collagen<sup>25</sup>. Further research was performed to investigate whether the differences in wound contraction between horses and ponies were caused by differences in the inherent contraction capacity of fibroblasts or the local environment of the fibroblasts. It was found that no differences existed in the inherent contraction capacity of fibroblasts from ponies and horses *in vitro*<sup>26</sup>. However, the level of Transforming Growth Factor, the most important instigator of wound contraction, was significantly higher in the granulation tissue of pony wounds compared with horse wounds.

**Remodeling 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<sup>27,28</sup>. 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 repair mechanisms in the natural way. Extensive research 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<sup>29</sup>.

**Parameters used in assessing wound healing activity:** For the Study of wound healing activity many *in vitro* and *in vivo* Models have been used.

*In vitro* models keratinocytes assay, fibroblasts assay. *In vivo* models incision models, excision models, dead space models, burn models can be performed. Wound healing property can be checked by measuring tensile strength of skin, measurement of wound area, percentage of contraction, collagen content, protein estimation, Period of epithilization.

**Wound healing management:** The most important clinical endpoint in wound management is wound closure. Given that wound closure is critically important,

it is argued that any agent demonstrating significant wound healing activity should be seriously considered in conventional practice. A wound healing agent may facilitate wound healing by increasing wound angiogenesis and collagen, nucleoprotein and glycoprotein metabolism, leading to improvements in both local circulation and granulation tissue formation. Several experimental studies lend support to these claims, demonstrating that the daily application of a wound healing agent to paravertebral incisions in rats facilitates collagen maturation and epithelialization within 10-25 days. Plants and their extracts have immense potential for the management and treatment of wounds. The phytomedicines for wound healing are not only cheap and affordable but are also purportedly safe as hypersensitive 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 traditional medicine before these could be recommended for healing of the wounds. Plants or chemical entities derived from plants need to be identified and formulated for the 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 the management and treatment of wounds over the years<sup>30, 31, 32, 33, 34, 35</sup>.

### MEDICINAL PLANTS HAVING WOUND HEALING ACTIVITY

***Aloe vera*:** *Aloe vera* is one of the oldest healing plants known to mankind Also acemannan ( $\beta$ -(1,4)-acetylated polymannose)-the major polysaccharide of *A. vera*-stimulates expression of VEGF and other wound healing-related factors (e.g., keratinocyte growth factor-1 and type I collagen) in gingival fibroblasts. *Aloe*, a native to Africa, is also known as "lily of the desert" or the plant of immortality. Its name was derived from "alloe," meaning "bitter," because of the bitter liquid found in its leaves. Egyptians recorded use of this herbal plant in treating burns, infections and parasites as early as 1500 B.C. Its clear gel has a dramatic ability to heal wounds, ulcers and burns by forming a protective coating on the affected areas and speeding up the healing process. This can be especially beneficial in the case of oral wound healing. Thus, crude *Aloe vera* extract or isolated proangiogenic components may have potential pharmaceutical applications for the management of wounds<sup>36, 37</sup>.

***Quercus infectoria*:** *Quercus infectoria* is a small tree (Fagaceae). It is mainly used for the treatment of anti-inflammatory disorders and also used as dental powder, toothache treatment, gingivitis.

Pharmacologically it acts as a astringent, antidiabetic, antiviral, antitremorine, local anaesthetic, antibacterial, antifungal, anti-inflammatory and larvicidal activities. It mainly contains tannin (50-70%) and small amounts of gallic acid ellagic acid<sup>38, 39, 40</sup>.

***Chromolaena odorata*:** *Chromolaena odorata* aqueous extract and the decoction from the leaves of this plant have been used throughout Vietnam for the treatment of soft tissue wounds and burn wounds. The aqueous extracts of *Chromolaena odorata* enhance hemostatic activity and stimulate granulation tissue and re-epithelization processes. The extract also inhibits wound contraction reversibly<sup>41</sup>.

***Helianthus annuus*:** In a study, the alcoholic extract of the whole plant of *Helianthus annuus* applied in the form of an ointment on the excised wound of rats led to a significant reduction in the total healing period. This has been confirmed by histology, where earlier appearances of fibroblasts were seen. Early appearance and higher accumulation of mucopolysaccharides has been stated as indicators of hastened repair<sup>42</sup>.

***Ginkgo biloba*:** *Ginkgo biloba* exhibits a variety of interesting pharmacological activities, such as increase in blood fluidity, antioxidant, membrane stabilizing, improvement in cognition and pro-healing. 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 the granulation tissue. The main constituents of *Ginkgo biloba* are flavonoids and terpene trilactones and the pro-healing action of *Ginkgo biloba* is due to the presence of flavonoids<sup>43, 44</sup>.

***Catharanthus roseus*:** *Catharanthus roseus* plant is a key source of monoterpene indole alkaloid, vincristine and vinblastine which found useful in treatment of cancer. In a study of ethanolic extract of flower of this plant in a dose of 100 mg<sup>-1</sup> kg<sup>-1</sup> day<sup>-1</sup> demonstrated to possess wound healing property<sup>45, 46</sup>.

***Lycopodium serratum*:** *Lycopodium serratum* is commonly known as club moss. Wound activity of aqueous and ethanolic leaf extract of *Lycopodium serratum* was studied by excision, incision and dead space wound model on rats. as compared to the aqueous extract and controls the ethanolic extract showed significant decrease in the period of epithelialization and an increase in wound contraction rate, tissue breaking strength and hydroxyl proline content at the wound site<sup>47</sup>.

**Curcuma longa:** Commonly known as turmeric and haldi in Hindi. Turmeric has been used for treating wounds in the rats. The anti-inflammatory property and the presence of vitamin A and proteins in turmeric result in the early synthesis of collagen fibers by mimicking fibroblastic activity. Juice of the fresh rhizome is commonly applied to recent wounds, bruises and leech bites. A paste of turmeric and leaves of *Justica adhatoda* with cow urine is rubbed on skin affected with prurigo and eczema. It can also be mixed with ginger oil to prevent skin eruptions<sup>48,49</sup>.

**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<sup>50</sup>.

**Horse chestnut:** *Horse chestnut* contains a compound called aescin that acts as an anti-inflammatory agent and reduces edema (swelling with fluid) following trauma, particularly sports injuries, surgery and head injury. A topical aescin preparation is popular in Europe for the treatment of acute sprains during sporting events<sup>51</sup>.

**Echinacea purpurea:** *Echinacea* is used among European practitioners of herbal medicine to promote wound healing and is approved by the German government for this use<sup>52</sup>.

**Hippophae rhamnoides L.:** *Hippophae rhamnoides* L. (family Elaeagnaceae) commonly known as Seabuckthorn (SBT). Leaves, ripe fruits and seeds from seabuckthorn have been found to be a rich source of a large number of bioactive substances including flavonoids (isorhamnetin, quercetin, myricetin, kaempferol and their glycoside derivatives), carotenoids ( $\alpha$ ,  $\beta$ ,  $\delta$ -carotene, lycopene), vitamins (A, C, E and K), tannins, triterpenes, glycerides of palmitic, stearic and oleic acids and some essential amino acids. The high content of bioactive substances has been reflected in its extensive exploitation by traditional medicine. Seabuckthorn has antioxidant and anti-inflammatory activity and has been reported to be useful in treating skin wounds<sup>53,54,55,56</sup>.

**Sesamum indicum:** *Sesamum indicum* is a member of family Pedaliaceae. Sesame oil obtained from the seeds of the plant is highly nutritive as it is rich source of natural oxidant such as sesamin and sesamol. The methanolic extract of root of *Sesamum indicum* was obtained and was incorporated in gel and ointment bases. These preparations were evaluated for *in vivo* wound healing on rat using excision wound model<sup>57,58</sup>.

**Radix paeoniae:** Aqueous extract of roots of *Radix paeoniae* was screened for wound healing by excision, incision and

dead space wound models on wistar rats. Parameters studied were tissue breaking strength, epithelialization, wound contraction and granulation tissue dry weight. The test group demonstrated significant wound healing activity as compared to nitrofurazone ointment treated control group<sup>59</sup>.

**Morinda citrifolia Linn:** *Morinda citrifolia* is also known as Indian mulberry, belongs to family; Rubiaceae. It mainly contains saponins, tannins, triterpenes, alkaloids, flavonoids. It is mainly used for the bowel disorders, including arthritis, atherosclerosis, bladder infections, boils, burns, cancer, chronic fatigue syndrome, circulatory weakness, cold, congestion, constipation, diabetes, eye inflammations, fever, fractures, gastric ulcers, gingivitis, headaches, heart diseases, hypertension, immune weakness, indigestion, intestinal parasites, kidney disease, malaria, menstrual cramps, mouth sores, respiratory disorders, ringworms, sinusitis, sprains, stroke, skin inflammation and wounds<sup>60</sup>.

**Terminalia bellirica Roxb:** *Terminalia bellirica* Roxb. belonging to the family Combretaceae, commonly known as belliricmyrobalan. Fruit is astringent, antiseptic, rejuvenative, brain tonic, expectorant and laxative. It is used in coughs, sore throat, dysentery, diarrhoea and liver disorders. It is also useful in leprosy, fever and hair care. In folk medicine it has been used for the treatment of skin diseases as antiseptic and on all types of fresh wound. An ethanol extract of *Terminalia bellirica* Fruit has properties that render it capable of promoting accelerated wound healing activity compared with placebo control<sup>61</sup>.

**Moringa oleifera Linn:** *Moringa oleifera* Linn. (Moringaceae) has been an ingredient of Indian diet since centuries. The leaves of the plant have also been reported for its anti-tumor, hypotensive, antioxidant, radioprotective, anti-inflammatory and diuretic properties. The aqueous extract was studied and it was found that there was significant increase in wound closure rate, skin-breaking strength, granuloma breaking strength, hydroxyproline content, granuloma dry weight and decrease in scar area was observed<sup>62</sup>.

**Tectona grandis Linn:** *Tectona grandis* Linn. is commonly known as Indian teak and belongs to family Verbinaceae. It contains mainly carbohydrates, tannins and anthraquinone glycosides. *Tectona grandis* is used as anti-inflammatory agents and also used topically for the treatment of burns. It is mainly used for the injuries like burn, inflicted wound and skin ulcers. The extract applied topically or given orally promoted the breaking strength, wound contraction and collagenation<sup>63</sup>.

***Tephrosia purpurea* Linn:** *Tephrosia purpurea* Linn. belongs to family Leguminosae. It also called as "Sarwa Wranvishapaka". It contains glycosides, rotenoids, isoflavones, flavones, chalcones, flavonoids and sterols. According to Ayurvedic system of medicine various parts of this plant are used as remedy for impotency, asthma, diarrhoea, gonorrhoea, rheumatism, ulcer and urinary disorders. It is also used in the treatment of bronchitis, boils, bleeding piles, pimples, roots and seeds are used as insecticidal, vermifuge, leprosy wound and the juice is used for the eruption on skin<sup>64</sup>.

***Carica papaya* Linn:** *Carica papaya* Linn. belongs to family Caricaceae. Papaya fruits contains a mixture of cysteine endopeptidases such as papain. Chymopapain A and B, papaya endopeptidase II, papaya endopeptidase IV, omega endopeptidase, chitinase, protease-inhibitors and proteins. Papaya fruits possess wound healing properties, papaya latex was applied to the burn wound using hydrogel as a vehicle system<sup>65</sup>.

***Allium cepa* Linn:** *Allium cepa* Linn. is a member of the Liliaceae, which consists of over 250 genera and 3700 species. *Allium cepa* Linn. is proved to show the anti-diabetic, anti-oxidant, anti-hypertensive, anti-thrombotic, hypoglycemic, antihyperlipidemic. The bulb of *Allium cepa* contains Kampferol,  $\beta$ -sitosterol, ferulic acid, myricic acid, prostaglandins. Bulb extract shown to have ecobolic effect in rats. Traditionally plant containing these constituents used as abortifaciant, the bulb extract of *Allium cepa* had showed ecobolic effect in mice and rats. *Allium cepa* treated group showed extensive growth of granulation started along its surface. The treated group of wound showed complete healing of wounds with almost normal architecture of the collagen and reticulin. Increase in tensile strength of treated group wound may be due to increase in collagen concentration, alcoholic extract of *Allium cepa* increase the collagen synthesis<sup>66</sup>.

***Tribulus terrestris* Linn:** *Tribulus terrestris* Linn. is a flowering plant in the family Zygophyllaceae, native to warm temperate and tropical regions of the southern Asia, through out Africa. *Tribulus terrestris* has long been a constituent in tonics in Indian ayurveda practice. Animals studies in rats, rabbits and primates have demonstrated that administration of *Tribulus terrestris* extract produce aphrodisiac activity by increasing the levels of testosterone. The active chemical in *Tribulus terrestris* is likely to be protodioscin. Apart from these it has diuretic, anthelmintic, cytotoxic, Antimicrobial and Anti-fungal activity. Decoction of entire plant is efficacious for anuria, burning micturation, UTI, Obstruction due to growth. The gel containing crude extracts of leaves of *Tribulus terrestris* promoted the breaking strength, wound

contraction and period of period of epithelialization. The wound healing activity of *Tribulus terrestris* aqueous leaves extract may at least be in part due to its potent antioxidant activity<sup>67</sup>.

***Gymnema sylvestre* R.Br:** *Gymnema sylvestre* R. Br. is a member of Asclepiadaceae. The leaf has been widely used in Ayurvedic traditional medicine leaves of the plant as anti-diabetes, astringent, bitter, acrid, thermogenic, anti-inflammatory, anodyne, digestive and liver tonic. Tannins and saponin are the chief chemical constituents present in *Gymnema sylvestre* and are known to possess wound healing property. In excision wound models, the percentage of wound area was found to be significantly increased in the animal grouped treated with the extract (16.73%)<sup>68</sup>.

***Arnebia densiflora* Ledeb:** The genus *Arnebia* are represented by 4 species in the flora of Turkey, one of which, *Arnebia densiflora* Ledeb. belongs to family Boraginaceae, is widespread in Sivas district and known as egnik by local people and used as red colouring for dyeing the carpets and the rugs. *Arnebia densiflora* roots soaked in butter are used in local wound healing care. The roots of this plant have been reported to contain alkanin derivatives, namely  $\beta,\beta$  dimethylacrylalkannin, teracrylalkannin, isovalerylalkannin,  $\alpha$ -methyl-n-butylalkannin. Rats treated with *Arnebia densiflora* showed rapid healing than the control group. Wound closure and collagen production were faster and healing occurred on the 14th day after wounding<sup>69</sup>.

***Adhatoda vasica* Linn:** *Adhatoda vasica* Linn. (Acanthaceae) known as chue Mue, grows as weed in almost all parts of the India. Leaves and stems of the plant have been reported to contain an alkaloid mimosine, leaves also contain mucilage and root contains tannins. *Adhatoda vasica* is used for its antihyperglycemic, anti-diarrhoeal, anti-convulsant and cytotoxic properties. The plant also contains turgorins, leaves and roots are used in treatment of piles and fistula. Paste of leaves is applied to hydrocele. The methanolic, chloroform and Diethyl ether extract ointment (10%w/w) of *Adhatoda vasica* has significant wound healing activity. In both extract ointment, the methanolic extract ointment (10%w/w) showed significant effect when compare to standard drug and other two extract in excision wound model<sup>70</sup>.

***Cordia dichotoma* Forst:** *Cordia dichotoma* Forst. belonging to family Boraginaceae is a medium sized tree with a short, grows in India, Sri Lanka and other warmer countries. The medicinal attributes of *Cordia dichotoma* have been known since long time. Its fruits are used as cooling, astringent, emollient, expectorant, anthelmintic

and purgative. Analgesic, anti-inflammatory and hepatoprotective activities have also been reported from the plant. *Cordia dichotoma* treated group showed extensive growth of granulation started along its surface. The treated group of wound showed complete healing of wounds with almost normal architecture of the collagen, reticulin. Increase in tensile strength of treated group wound may be due to increase in collagen concentration, alcoholic extract of *Cordia dichotoma* increase the collagen synthesis<sup>71</sup>.

***Lawsonia inermis* Linn:** The leaves of *Lawsonia inermis* Linn. (Lythraceae), commonly called as henna are used in the form of a decoction or ointment in the treatment of burns, skin inflammations, wounds and ulcers. The leaves also possess antifungal and antibacterial activities. Henna is reported to contain a naphthaquinone, lawsone, which is a natural dye. It was observed that the oral administration as well as topical application of ethanol extract of henna leaves and lawsone exhibited significant healing response in both the wound models. Further, it was found that the topical application of ethanol extract as well as isolated lawsone was more effective than the same given by the oral route. Thus, topical application of ethanol extract can be successfully formulated for the wound healing activity<sup>72</sup>.

***Alternanthera brasiliana* Kuntz:** *Alternanthera brasiliana* Kuntz belonging to the family Amaranthaceae, is a herbaceous plant commonly known in Brazil as Penicillin or Brazilian Joy Weed, is used against inflammation, cough and diarrhoea in Brazilian popular medicine. The extract of *Alternanthera brasiliana* exhibited anti-nociceptive effect in mice, anti-microbial effect and anti-herpes simplex virus activity. Wound healing activity of methanolic extract of leaves of *Alternanthera brasiliana* Kuntz was studied by excision and incision wound model (*in vivo*) in Sprague Dawley rats. In excision wound model, compared to the control group, per cent contraction of wound was significantly higher in *Alternanthera brasiliana* (5% w/w ointment) treated group. In incision wound model, tensile strength of the healing tissue after treatment with *Alternanthera brasiliana* was found to be significantly higher compared to the control group indicating better wound healing activity of the test plant<sup>73</sup>.

***Napoleona imperialis*:** *Napoleona imperialis* is of the family of plants called Lecythidaceae. It is a woody plant, several meters high, found mainly in tropical rain forest. The leaf is used locally as analgesic, tonic, anti-tussive, anti-asthmatic and wound dressing. The various ointments prepared with *Napoleona imperialis* exhibited a good wound healing effect, a standard antibiotic used in wound healing<sup>74</sup>.

## CONCLUSION

Pharmacological screened plants in this review are those with wound healing potentials. Plants are more potent healers because they promote the repair mechanism in the natural way. The healing process can be physically monitored by assessing the rate of contraction of the wound, period of epithelization, tensile strength, histopathology and weight of granuloma in different wound models. The healing tissue synthesizes more collagen to provide tensile strength. The information is recorded in plant's scientific name, common name of plant, family, part used for the wound healing activity, extract used, type of study and References. The demand of herbal drugs is increasing day by day in developed as well as developing countries because they are safer and well tolerated as compared to those allopathic drugs. Further investigation on the plants can increase the isolation of the newer molecules which will be helpful for the treatment of wound healing. These plants should be subjected to human studies to determine their effectiveness.

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